Treatment of Children with Autism Spectrum Disorders:

What we know and don't know

Jeremy Veenstra-Vander Weele,MD
Assistant Professor
Departments of Psychiatry, Pediatrics, and Pharmacology
Vanderbilt Kennedy Center for Research on Human Development
Vanderbilt Brain Institute

Zachary Warren, PhD
Assistant Professor
Departments of Pediatrics and Psychiatry
Vanderbilt Kennedy Center for Research on Human Development
Treatment and Research Institute for Autism Spectrum Disorders

Acknowledgements

Vanderbilt EPC Team:

Zachary Warren, Ph.D. – VKC LEND Faculty

Jeremy Veenstra-VanderWeele, M.D.
Wendy Stone, Ph.D.
Jennifer L. Bruzek, Ph.D.
Allison S. Nahmias, M.Ed.
Jennifer H. Foss-Feig, M.A.
Rebecca N. Jerome, M.L.I.S., M.P.H.
Shanthi Krishnaswami, M.B.B.S., M.P.H.
Nila A. Sathe, M.A., M.L.I.S.
Allison M. Glasser, B.A.
Tanya Surawicz, M.P.H.
Melissa L. McPheeters, Ph.D., M.P.H.

Vanderbilt Kennedy Center (VKC)– Elisabeth Dykens, Ph.D Director

VKC LEND – Mary Theresa "Terri" Urbano, Ph.D., M.P.H., R.N. - Director

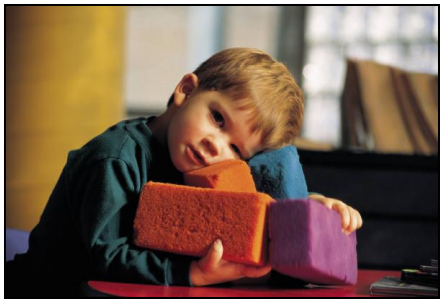
VKC UCEDD – Elisabeth Dykens, Ph.D., co-Director, Elise McMillan, J.D., co-Director

Financial Disclosure Dr. Veenstra-VanderWeele: American Academy of Child and Adolescent Psychiatry, Autism Speaks, AHRQ, NICHD, NIMH, Novartis, Roche Pharmaceuticals, Seaside Therapeutics

Financial Disclosure Dr. Warren: AHRQ, Autism Speaks, HRSA, MARI, MCHB, NICHD, NIMH, NSF, Simons Foundation

Outline

- Background and current context of ASD
- Presentation of systematic review
  - Medical Treatments
    - Including complementary & alternative
  - Behavioral Treatments
    - Early intensive intervention
    - Other behavioral treatments



- <u>What do we do for the children we serve?</u>

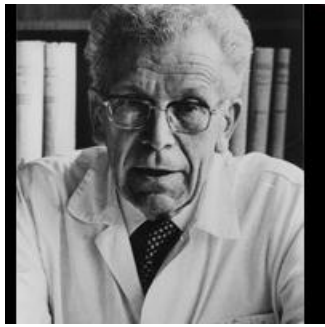
Defining:
Autism *Spectrum* Disorders

1943 – Leo Kanner – *Infantile autism*

1944 – Hans *Asperger*

1960s – Separation from schizophrenia

1970s – Biology / genetic underpinnings

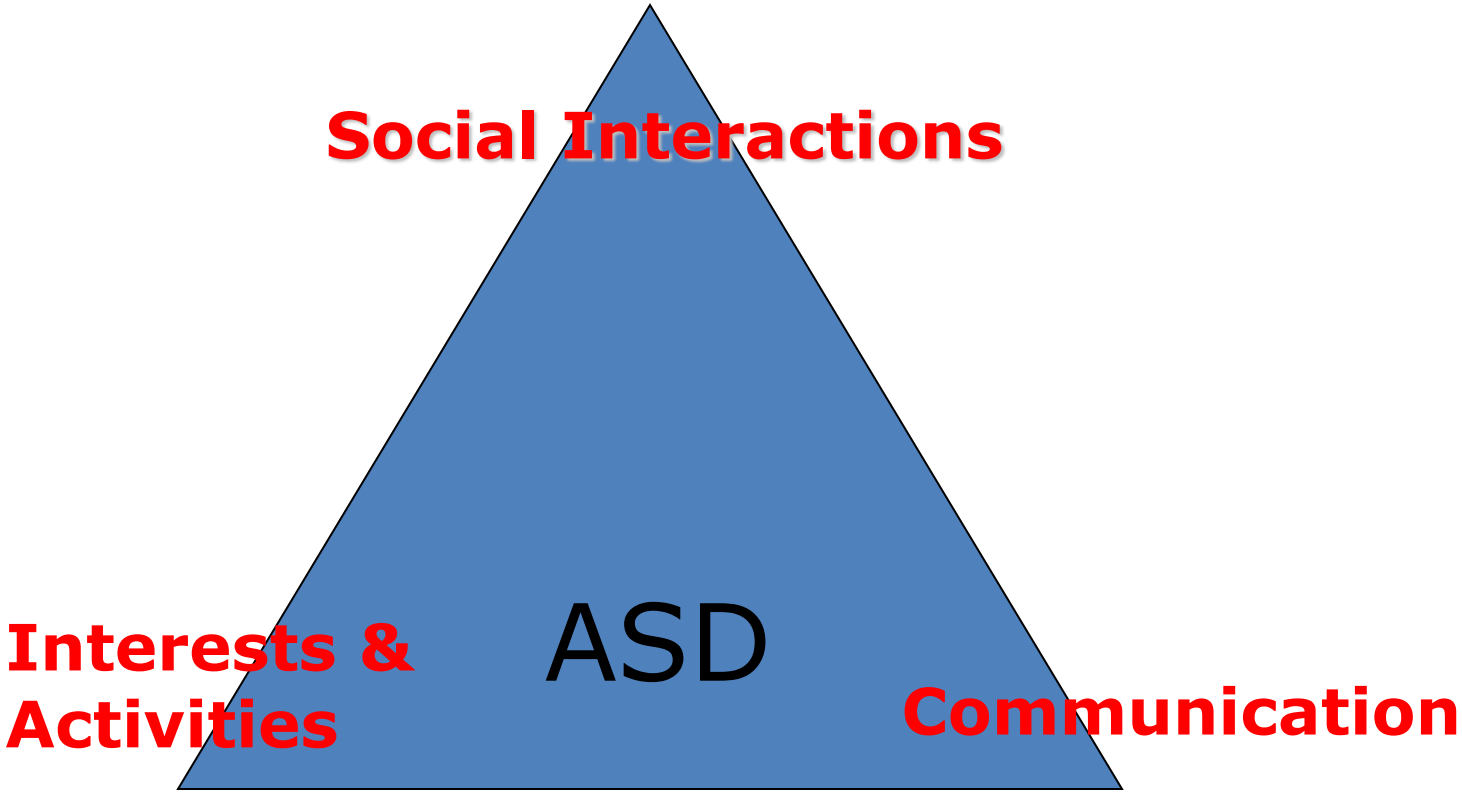


1980 – DSM-III – Pervasive Developmental Disorders

1987 – DSM-III-R - Autistic Disorder / PDD-NOS

1994 – DSM-IV – Asperger's Disorder

Core Neurodevelopmental Impairments

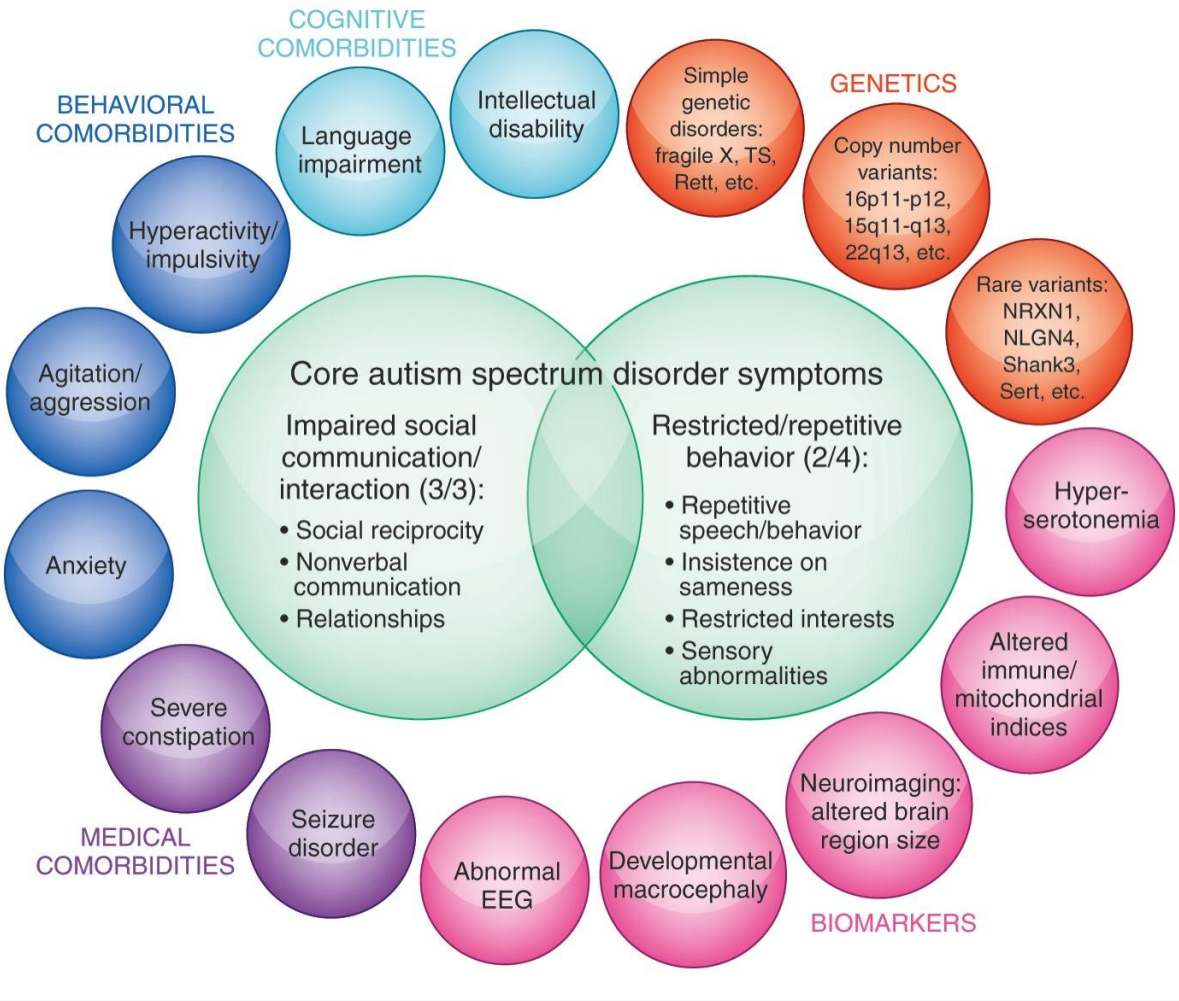


Major Diagnostic Features for DSM-IV Pervasive Developmental Disorders

Feature	Autistic Disorder	Asperger's Disorder	PDD-NOS
Social impairment	X	X	X
Lang/ Communication disorder	X		X[a]
Repetitive interests & activities	X	X	X[a]
Onset prior to 36 months	X		
Average intelligence		X	

a=At least one of these two features must be present

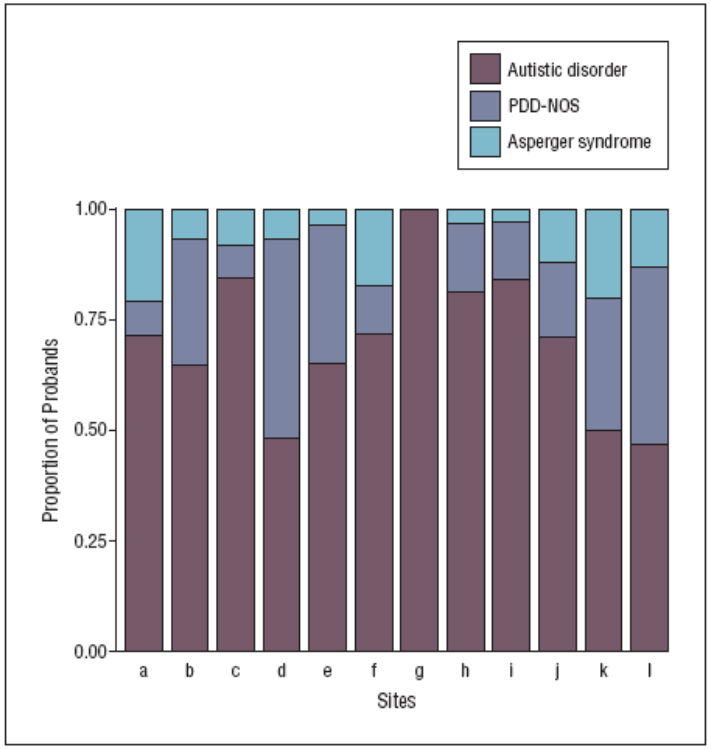
Autism Spectrum Disorders (ASD)

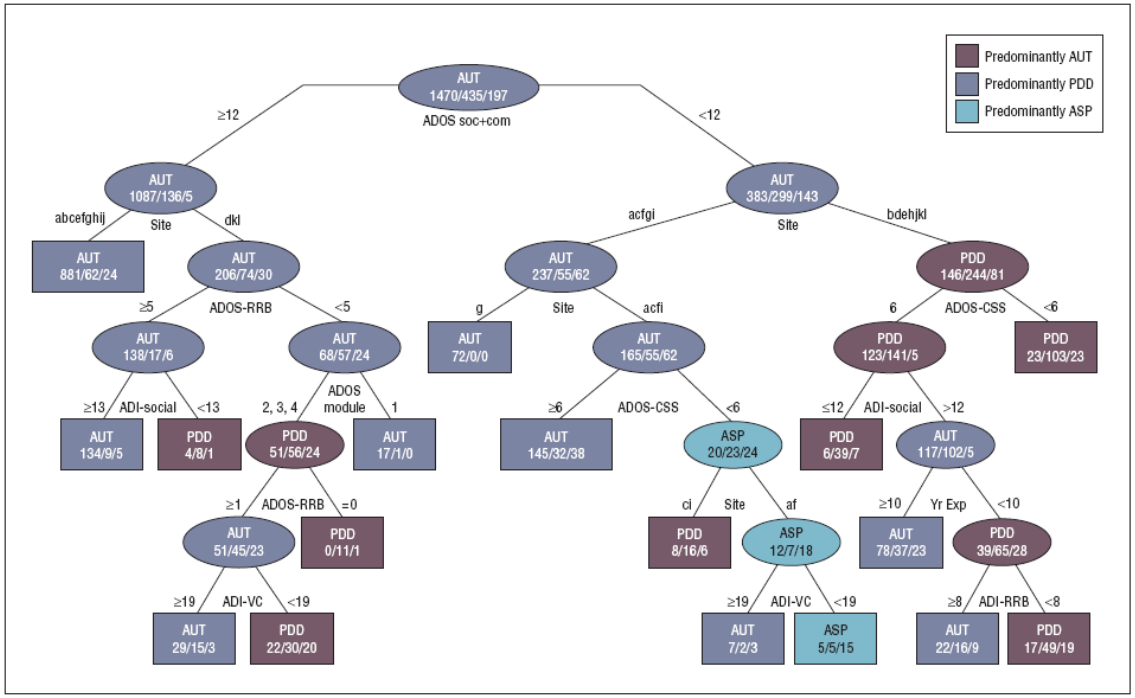


A Multisite Study of the Clinical Diagnosis of Different Autism Spectrum Disorders

Catherine Lord, PhD; Eva Petkova, PhD; Vanessa Hus, MSc; Weijin Gan, MS, MD; Feihan Lu, MA; Donna M. Martin, MD, PhD; Opal Ousley, PhD; Lisa Guy, PhD; Raphael Bernier, PhD; Jennifer Gerdts, MA; Molly Algermissen, PhD; Agnes Whitaker, MD; James S. Sutcliffe, PhD; Zachary Warren, PhD; Ami Klin, PhD; Celine Saulnier, PhD; Ellen Hanson, PhD; Rachel Hundley, PhD; Judith Piggot, MD, PhD; Eric Fombonne, MD; Mandy Steiman, PhD; Judith Miles, MD, PhD; Stephen M. Kanne, PhD; Robin P. Goin-Kochel, PhD; Sarika U. Peters, PhD; Edwin H. Cook, MD; Stephen Guter, MA; Jennifer Tjernagel, MS; Lee Anne Green-Snyder, PhD; Somer Bishop, PhD; Amy Esler, PhD; Katherine Gotham, PhD; Rhiannon Luyster, PhD; Fiona Miller, PhD; Jennifer Olson, PhD; Jennifer Richler, PhD; Susan Risi, PhD

Arch Gen Psychiatry.
Published online November 7, 2011.
doi:10.1001/archgenpsychiatry.2011.148





Testing the Construct Validity of Proposed Criteria for *DSM-5* Autism Spectrum Disorder

William P.L. Mandy, D.Clin.Psy., Tony Charman, Ph.D., David H. Skuse, M.D.

Journal of the American Academy of Child & Adolescent Psychiatry
VOLUME 51 NUMBER 1 JANUARY 2012

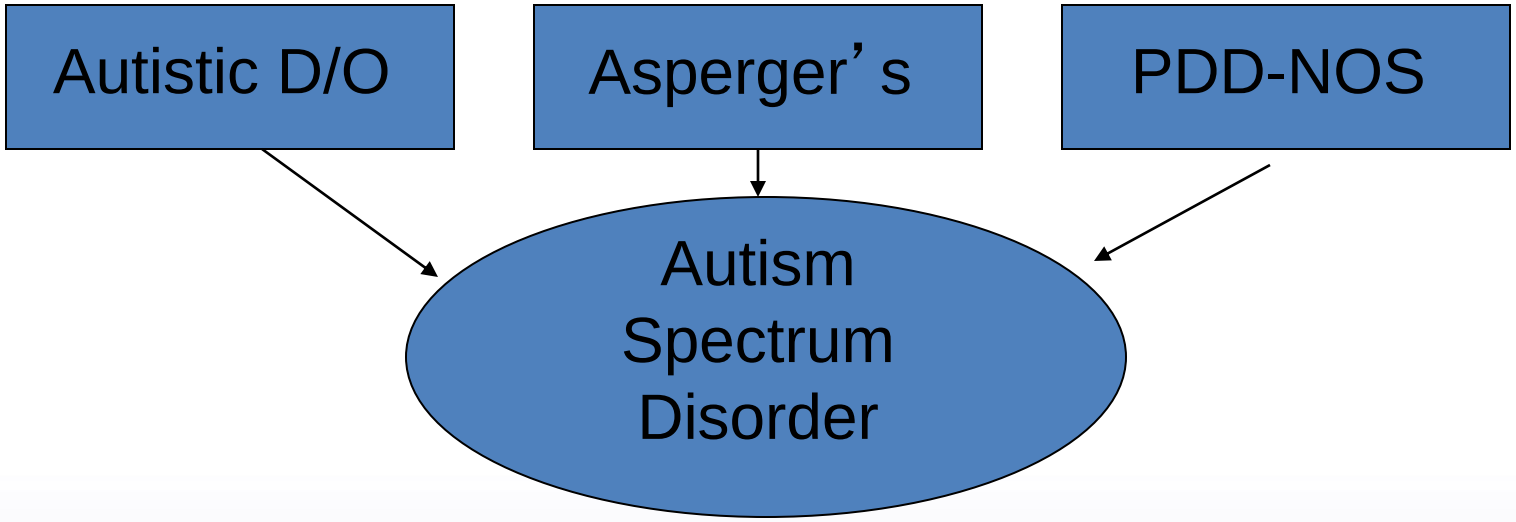
Validation of Proposed *DSM-5* Criteria for Autism Spectrum Disorder

Thomas W. Frazier, Ph.D., Eric A. Youngstrom, Ph.D., Leslie Speer, Ph.D., Rebecca Embacher, B.S., Paul Law, M.D., M.P.H., John Constantino, M.D., Robert L. Findling, M.D., Antonio Y. Hardan, M.D., Charis Eng, M.D., Ph.D.

Journal of the American Academy of Child & Adolescent Psychiatry
VOLUME 51 NUMBER 1 JANUARY 2012

Towards DSM-V

Distinctions can be difficult both within the spectrum and across other disorders



DSM-V

- Deficits in social communication (all 3):
  - Deficits in nonverbal communication
  - Deficits in social and emotional reciprocity
  - Deficits in maintaining relationships
- Restricted, repetitive patterns of behavior, interest, and activities (2)
  - Stereotyped motor or verbal behavior
  - Unusual sensory behavior
  - Excessive adherence to routines and ritualized bhx
  - Restricted, fixated interests
- Symptoms present in early childhood (manifest when social demands exceed capabilities)

Neurodevelopmental Underpinnings

- Core and associated vulnerabilities likely have complex ***neurogenetic*** origins:

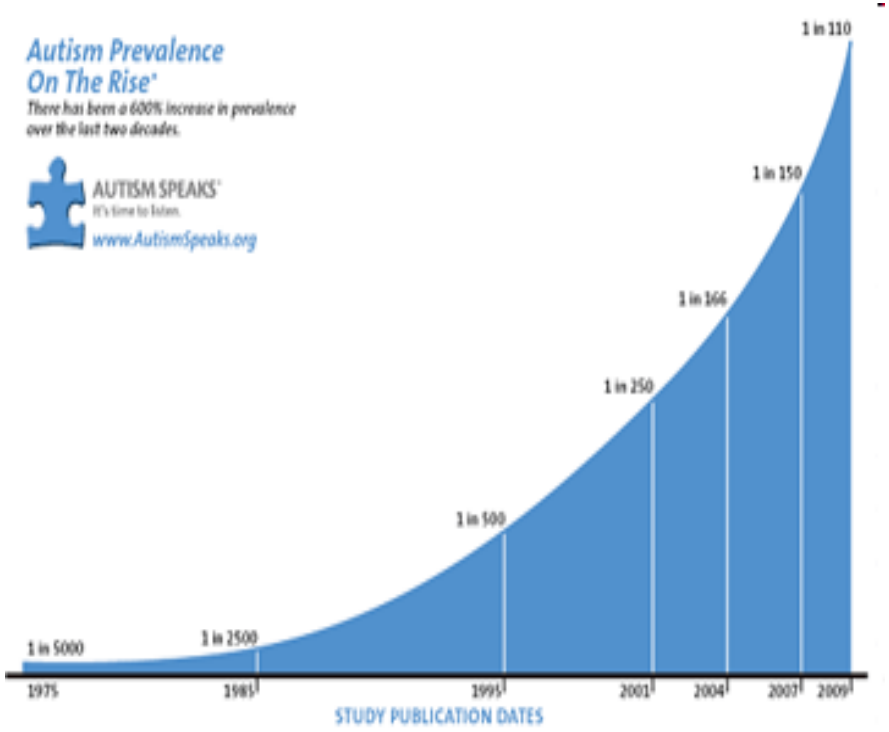
Evidence:

- Maleness (3:1 to 4:1)
- Familial loading/risk:
  - MZ twins: 58-96%
  - DZ twins: 0-31%
  - Sibs: 5-20%

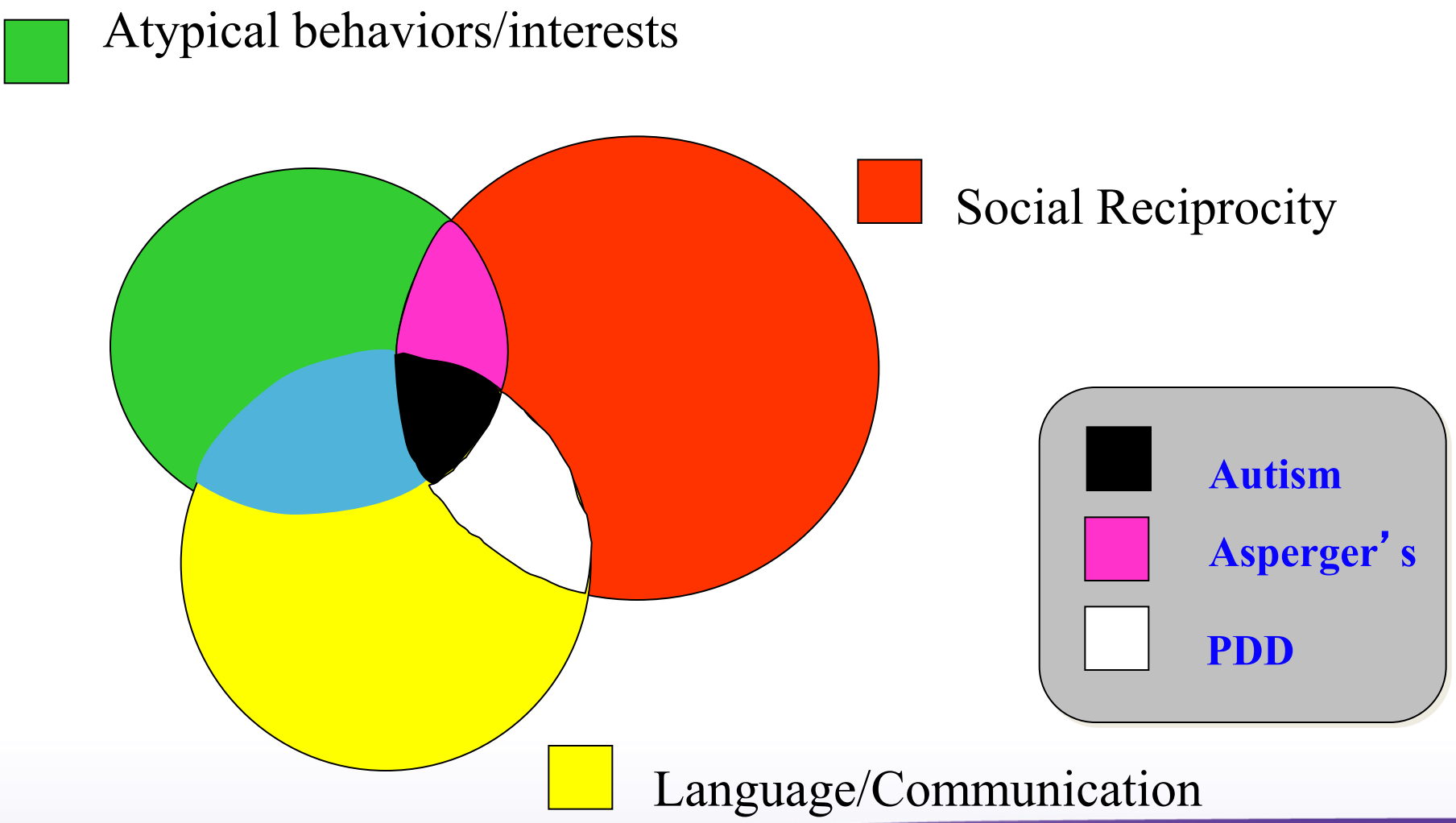
    (18.7% - Ozonoff et al., Pediatrics, 2011)
  - 1% - Population

Prevalence:
What once was rare…

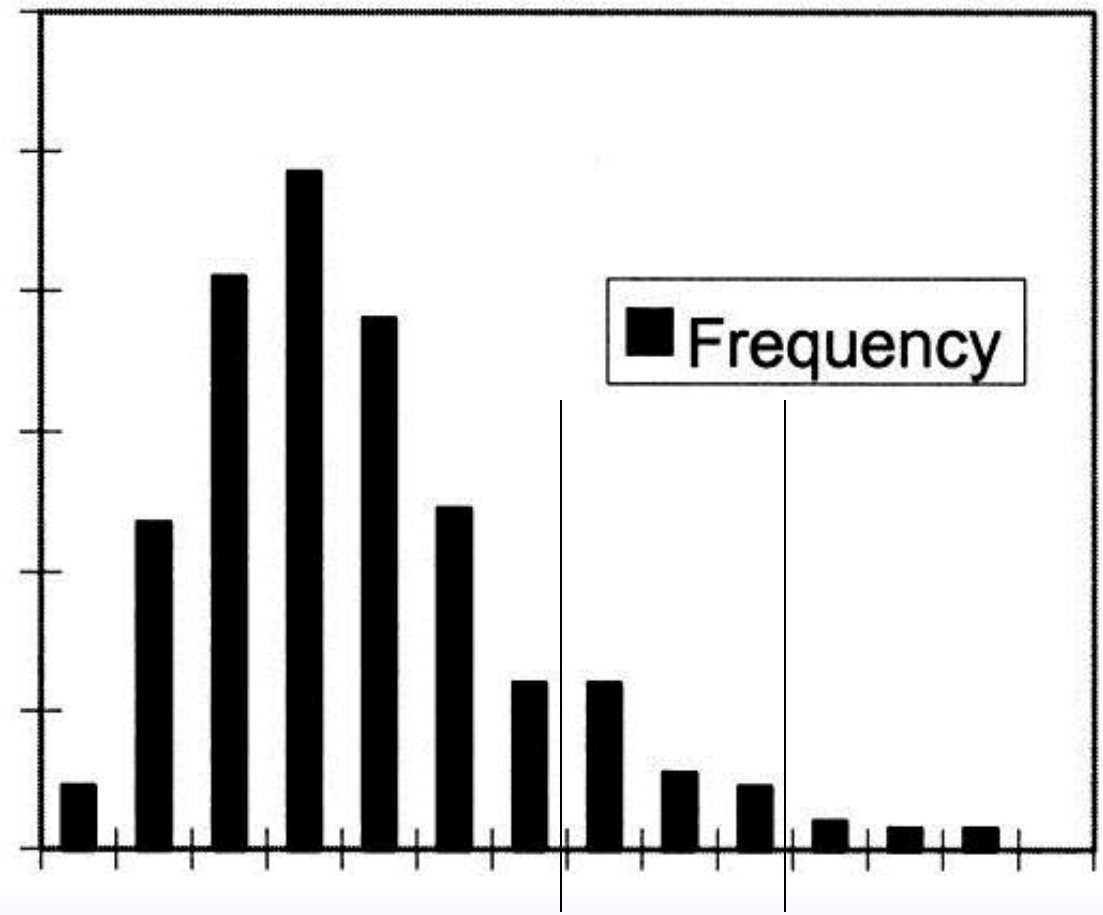
- Old estimate for autism:
  - ~ 1/2500 (1985)
- Recent estimates for autism:
  - ~ 1/500 (1995)
- Newest estimates for ASD:
  - 1/150 (CDC, 2007)
  - 1/110 (CDC, 2009)
  - *1/91 (NSCH, 2009)*
- What will it be in 2012?



Why are numbers increasing:
The addition of regions of diagnosis?



Why are numbers increasing: *Broadening spectrum?*

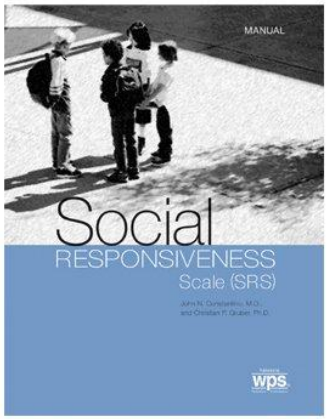


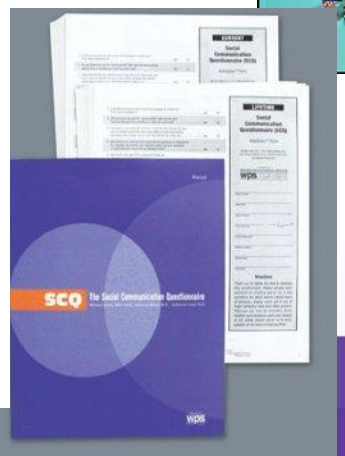
Constantino, JAACAP, 2003

Why are numbers increasing: *Better tools?*

- New diagnostic measures
  - Autism Diagnostic Interview (1989, 1994)
  - Autism Diagnostic Observation Schedule (1989, 2000)

- Screening tools/algorithms/instruments in wide use:
  - MCHAT / AAP guidelines
  - SCQ
  - SRS





Why are numbers increasing:
Lots of reasons?

- Diagnostic changes
  - Categories
  - Broadening
- Better tools and identification process
- Awareness
  - Mental health providers, **pediatricians**, **schools**
  - Media, **parents**

<u>Other factors:</u>

- Previous underestimates
- Methodology for obtaining epidemiological data
- What else???

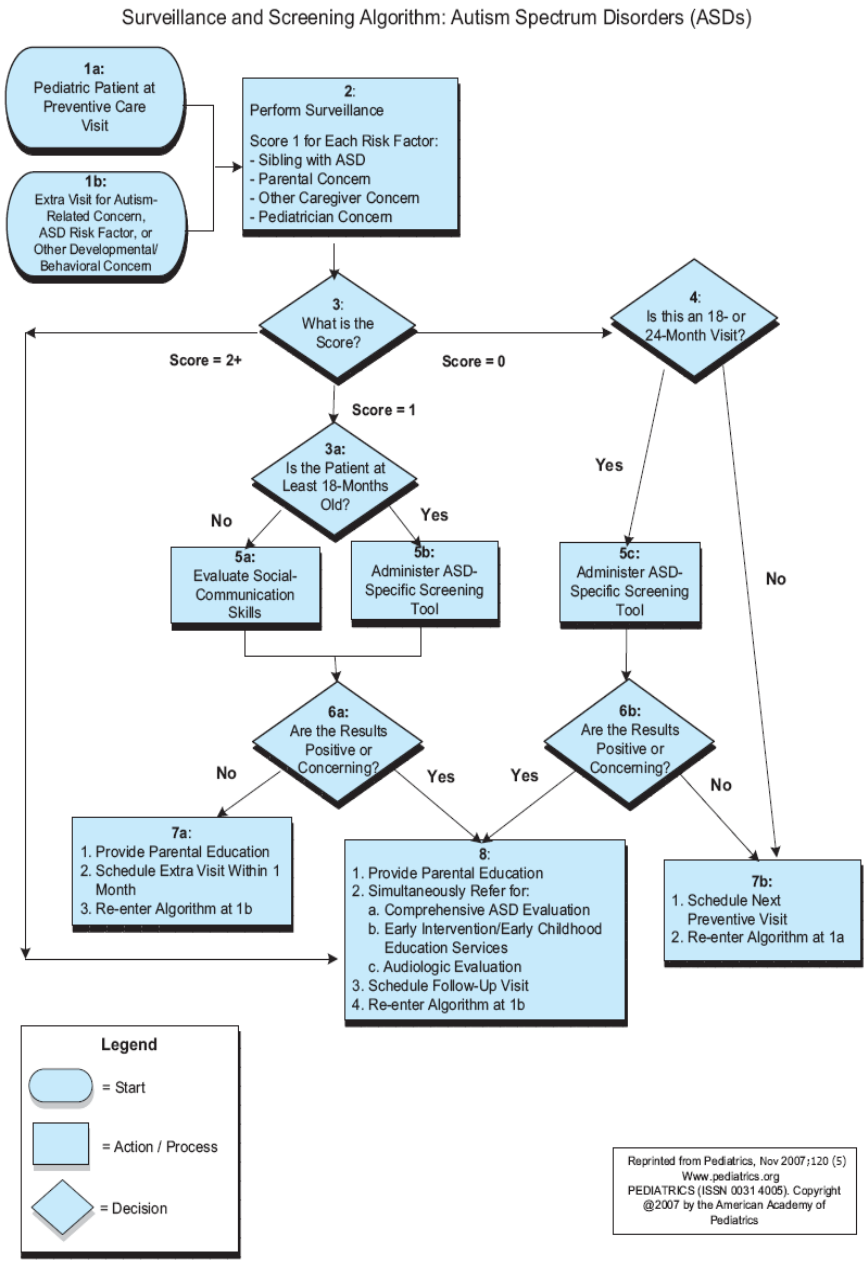


FIGURE 1
Surveillance and screening algorithm: ASDs. (Reproduced with permission from Pediatrics)

The American Academy of Pediatrics recommends autism-specific screenings at the 18- and 24-month visits

Reprinted from Pediatrics, 2006; 117:404-419.

“Critical” Items:

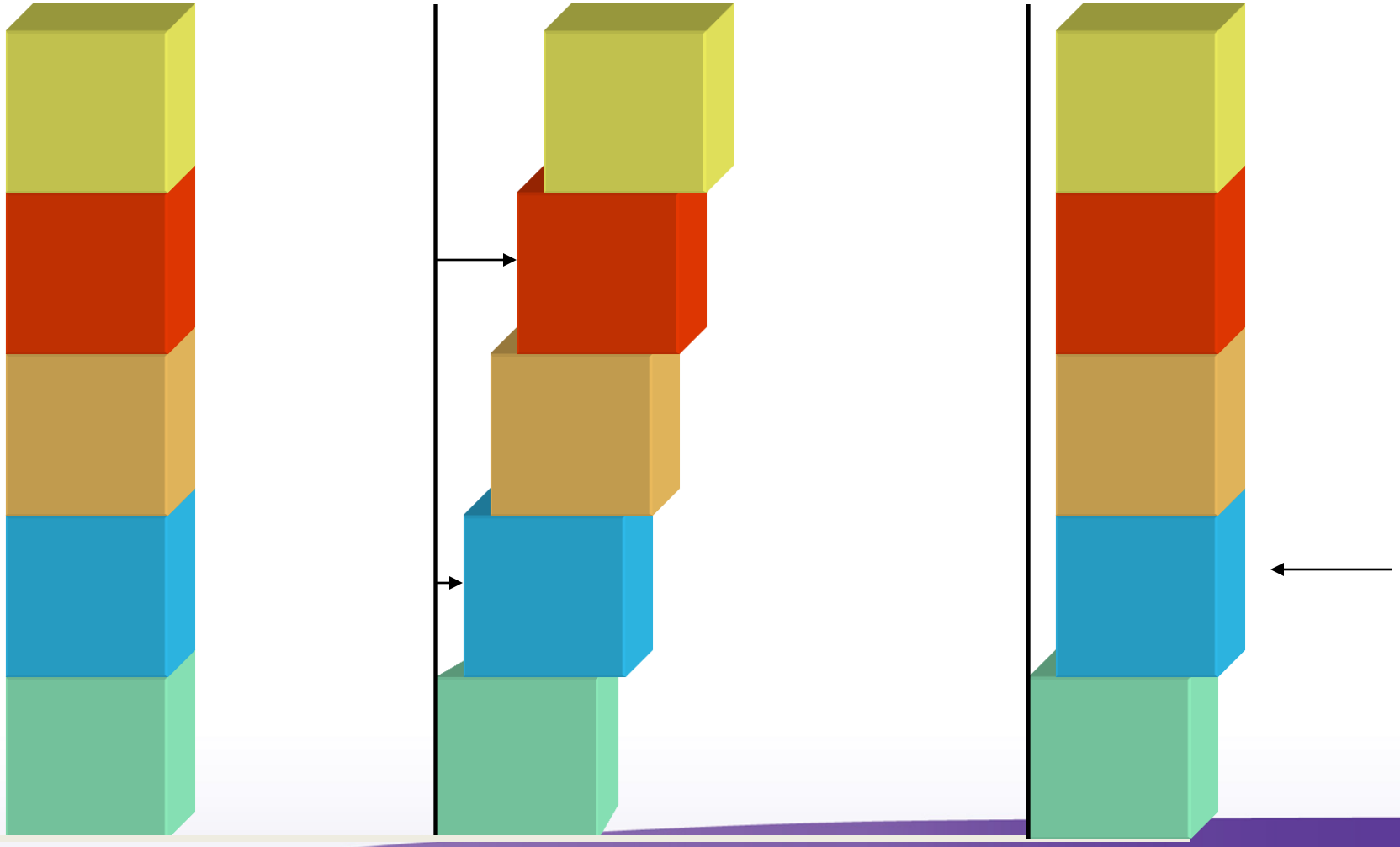
2,7,9,13,14,15

M-CHAT

Please fill out the following about how your child usually is. Please try to answer every question. If the behavior is rare (e.g., you've seen it once or twice), please answer as if the child does not do it.

1.	Does your child enjoy being swung, bounced on your knee, etc.?	Yes No
2.	Does your child take an interest in other children?	Yes No
3.	Does your child like climbing on things, such as up stairs?	Yes No
4.	Does your child enjoy playing peek-a-boo/hide-and-seek?	Yes No
5.	Does your child ever pretend, for example, to talk on the phone or take care of a doll or pretend other things?	Yes No
6.	Does your child ever use his/her index finger to point, to ask for something?	Yes No
7.	Does your child ever use his/her index finger to point, to indicate interest in something?	Yes No
8.	Can your child play properly with small toys (e.g. cars or blocks) without just mouthing, fiddling, or dropping them?	Yes No
9.	Does your child ever bring objects over to you (parent) to show you something?	Yes No
10.	Does your child look you in the eye for more than a second or two?	Yes No
11.	Does your child ever seem oversensitive to noise? (e.g., plugging ears)	Yes No
12.	Does your child smile in response to your face or your smile?	Yes No
13.	Does your child imitate you? (e.g., you make a face-will your child imitate it?)	Yes No
14.	Does your child respond to his/her name when you call?	Yes No
15.	If you point at a toy across the room, does your child look at it?	Yes No
16.	Does your child walk?	Yes No
17.	Does your child look at things you are looking at?	Yes No
18.	Does your child make unusual finger movements near his/her face?	Yes No
19.	Does your child try to attract your attention to his/her own activity?	Yes No
20.	Have you ever wondered if your child is deaf?	Yes No
21.	Does your child understand what people say?	Yes No
22.	Does your child sometimes stare at nothing or wander with no purpose?	Yes No
23.	Does your child look at your face to check your reaction when faced with something unfamiliar?	Yes No

Developmental Impact of Intervention:
Prevention of Cascading Effects?



The Importance of *Effective* Early Diagnosis and Treatment: A public health perspective

- Earlier diagnosis = More intervention opportunities

- More opportunities = Optimal intervention benefit
  - Core features: social communication / atypical behaviors
  - Cognitive and adaptive functioning
  - Fully integrated classroom placements
  - *Potentially* promoting optimal adaptive independence
  - *Potentially* reducing considerable lifetime cost and service system demands associated with ASD and related care

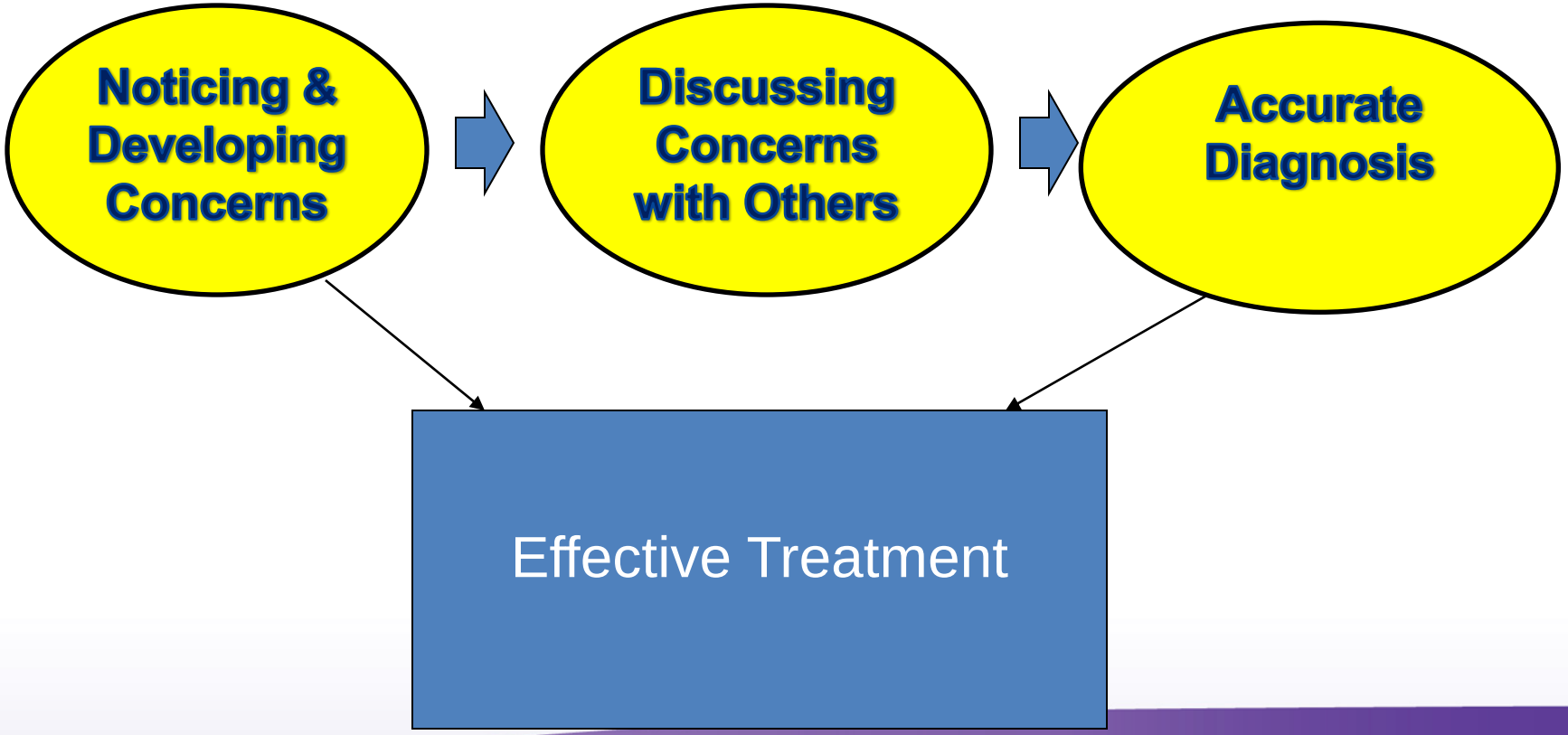
Costs of ASD

- Recent estimates of annual incremental costs
  (see Amendah et al., 2011)
  - $2,100 – $11,200 medical expenditures
  - $13,000 educational costs
  - $40,000-$60,000 intensive behavioral tx
  - $60,000-$128,000 residential costs for adults w/ASD
  - *Productivity loss, overall lifetime costs, quantification of impact of early intervention programs*

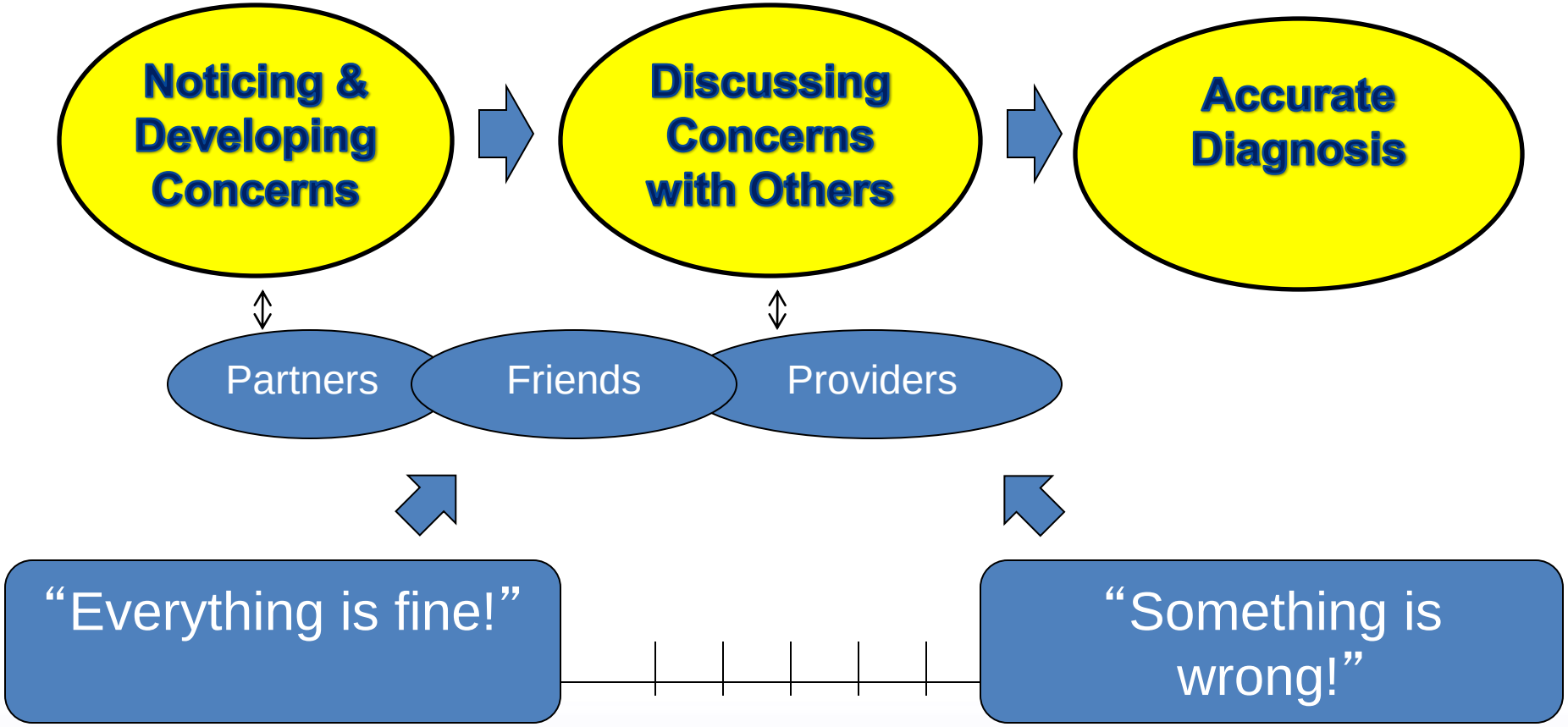
- Most quoted total lifetime costs = $3.2 million (Ganz, 2007)

- Mean medical expenditures for Medicaid enrolled children 6 times greater for children with ASD: $10,709 to $1,816 (Peacock, 2012)

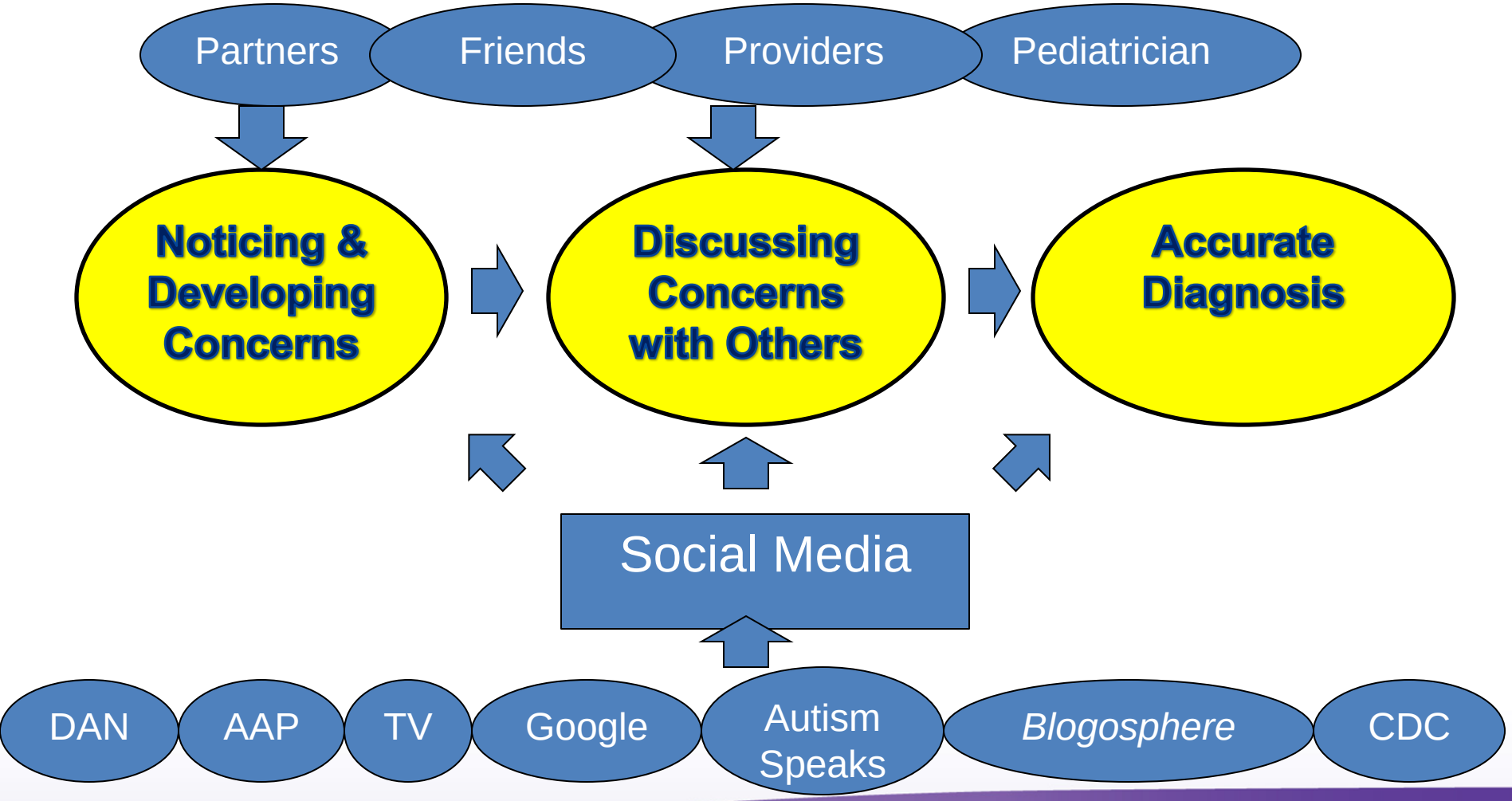
From Concern to Effective Treatment



Complex and Stressful Process for Families



Science in Context



Why Are We Doing This?
Our fundamental assumption…

Accurate early identification of a specific common neurodevelopmental disorder in childhood ***should*** help us connect to ***specific intervention*** and treatment options that optimize functioning for children and families


Google
Web
Images
Groups
News
Advanced Search
Preferences
Google Search
I'm Feeling
Search:
the web
Advertising Programmes
Business

Treatments and Therapies

78,300,000 results (0.08 seconds)

- Auditory Integration
- Sensory Integration
- ABA
- Discrete Trial Training
- Lovaas/UCLA Intervention
- Early Start Denver Model
- Holding Therapy
- Dolphin Assisted Therapy
- Facilitated Communication
- Augmentative Communication
- Vision Therapy
- Vitamins
- Hyperbaric Oxygen
- Psychopharmacological treatments
- Floortime
- Music Therapy
- Social Skills Training
- Incidental Teaching
- TEACCH
- PECS
- Pivotal Response Therapy
- Son-Rise
- RDI
- Chelation
- Diets
- Drugs
- Supplements

Historical Perspective

- Not far removed from an "*untreatable*" era

- Rutter (1970):
  - <2% functioning "normally"
  - 60% requiring institutional placement/support

- Lovaas (1987): UCLA Young Autism Project
  - Intensive ABA = 9 / 19 (47%) "recovered" or "normal fx"
  - A breakthrough with major methodological concerns

Two decades of research findings:

- Over short periods of time findings related to:
  - language acquisition
  - nonverbal communication
  - reduction in challenging behaviors
  - social skills
- Over longer periods of time:
  - cognitive ability / IQ
  - educational success
- Suggestions of medications and complementary agents:
  - primarily associated symptoms
  - claims of broad effects

Highlighting Categories of Intervention

- A striking number of children with ASD are treated with medical interventions
  - Some 3/4 of adolescents or adults with ASD receiving psychotropic medication in past year (Esbensen, 2009)
  - Multiple psychotropic medication use common
  - Majority (30-70%) of individuals within ASD clinics report complementary and alternative *medical interventions* (see Levy & Hyman, 2011)
- For many children behavioral interventions form the core of treatment
  - Early intensive behavioral and developmental interventions

Systematic Review of Treatments for Children with Autism Spectrum Disorders

What do we want to know?

- **<u>Which treatments work for specific children?</u>**

- Autism treatments vary widely:
  - *Scope, Focus, Intensity, Duration, Methodology*
  - Packages and combinations

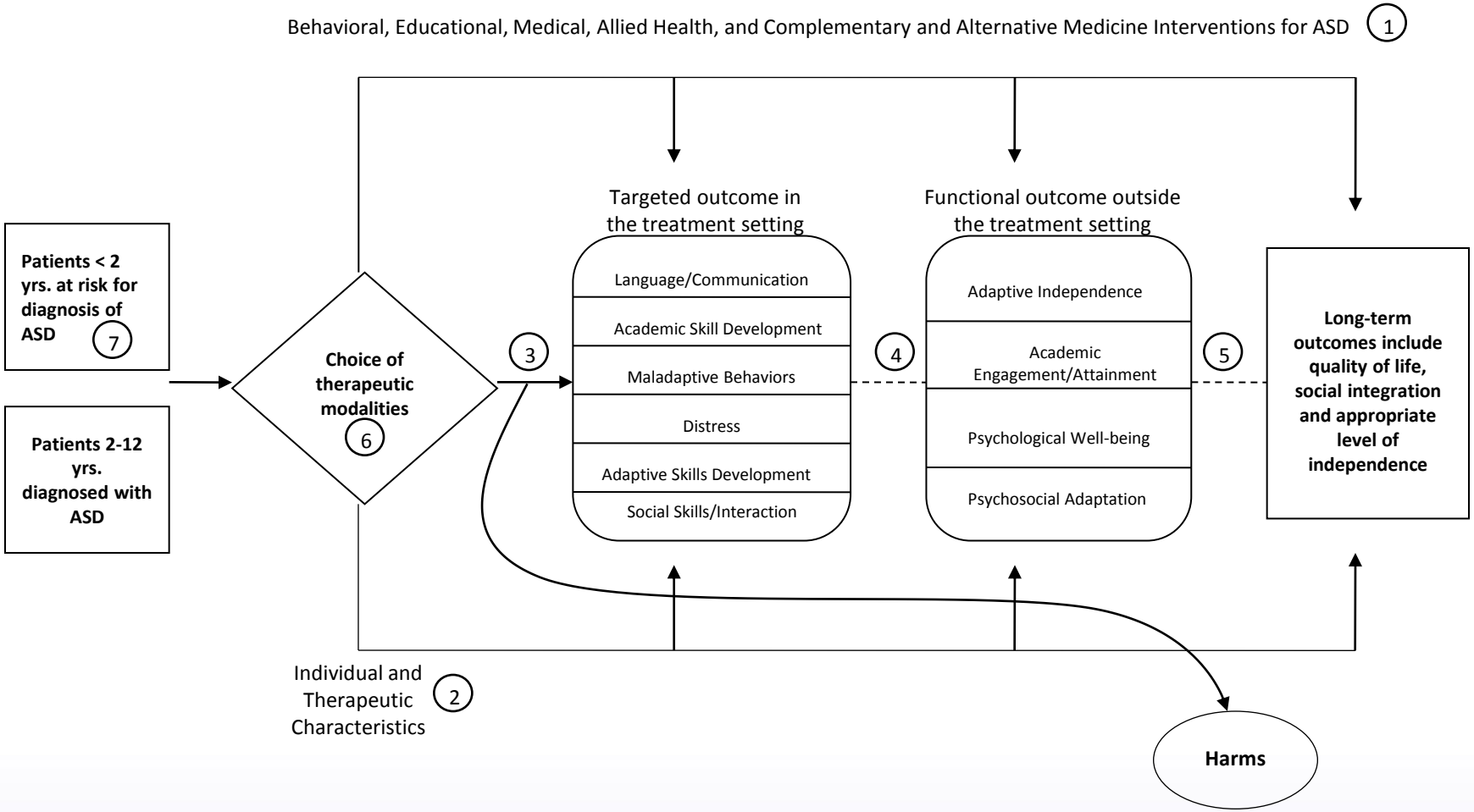
- Children with ASD vary widely
  - Core features
  - Associated characteristics - IQ / challenging behavior
  - Additional behavioral characteristics and medical vulnerabilities
  - Families, communities, systems of care

- *Different causes – different disorders*
  - Single gene causes of ASD
  - Copy number variants

AHRQ Systematic Reviews

- Topic proposed to AHRQ
  - *Centers for Medicare and Medicaid Services*
  - *Autism Speaks*
- Refined developed through discussions with key informants, TEP, public comment, review
- Employed comprehensive search strategy
- Extracted data and assessed study quality

Analytic Framework



Key Questions

- **KQ1. Clinical outcome:** What are the the short- and long-term effects of available behavioral, medical, allied health, or CAM treatment approaches?
    - **Core features**
    - **Associated symptoms**
- **KQ2. Modifiers:** What are the modifiers of outcome for different treatments or approaches?
- **KQ3. Early Response to Treatment:** Are there any identifiable changes early in the treatment phase that predict treatment outcomes?
- **KQ4. Functional Outcomes:** What is the evidence that effects measured at the end of the treatment phase predict long-term functional outcomes?

Key Questions

- **KQ5. Generalization:** What is the evidence that specific intervention effects measured in the treatment context generalize to other contexts?
- **KQ6. What Drives Treatment:** What evidence supports specific components of treatment as driving outcomes, either within a single treatment or across treatments?
- ***KQ7. Earliest Intervention:*** *What evidence supports the use of a specific treatment approach in children under the age of two who are at high risk of developing autism based upon behavioral, medical, or genetic risk factors?*

Methods

- MEDLINE®, ERIC and PsycInfo®, reference lists
- Included studies
  - January 2000 – May 2010
    - *DSM-IV-TR, ADOS, ADI*
  - $n \geq 30$ medical / $n \geq 10$ behavioral
- Dual review of abstracts
- Extracted clinical data to standardized forms
- Two reviewers assessed quality for each study
  - Studies rated as good, fair, or poor
- Overall strength of evidence assessed using *EPC Methods Guide for Effectiveness and Comparative Effectiveness Reviews*
  - Strength of evidence presented as insufficient, low, moderate, or high

Quality Assessment

- Study design
  - Group design / Appropriate comparison
  - Random assignment / Appropriateness
- Diagnostic approach
  - Standardized within study approach
  - ADOS / ADI / CBE
- Participant ascertainment
  - Developmental / cognitive / language / severity
  - Inclusion / exclusion
- Intervention characteristics
  - Was the intervention fully described?
  - Was treatment fidelity or adherence measured?
- Outcomes measurement
  - Reliable / valid measures
  - Blind coding
- Statistical analysis
  - Appropriateness of analysis

Strength of Evidence

- Assessment of literature done by considering both the observed effectiveness of interventions and confidence in the stability of those effects in the face of future research.
- Assessment based on consideration of four domains:
  - Risk of bias
  - Consistency in direction of the effect – *requires > 1 study*
  - Directness in measuring intended outcomes
  - Precision of effect

Strength of Evidence

- *High:* High confidence that the evidence reflects the true effect. Further research is unlikely to change estimates.
- *Moderate:* Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
- *Low:* Low confidence that the evidence reflects the true effect. Further research is likely to change confidence in the estimate of effect and is also likely to change the estimate.
- *Insufficient:* Evidence is either unavailable or does not permit a conclusion.

Strength of Evidence

- SOE approach **minimum** requirements:
  - 3 fair studies required to assign a low strength of evidence
  - 1 good study required for moderate strength of evidence
  - 2 good studies for high strength of evidence
- Downgraded the rating when the cumulative evidence was not sufficient to justify the higher rating
  - Happened only once

Important Point:
Lack of *current* evidence **does not** equal lack of effect or *potential* effect of treatment

Literature Review Results

- Abstracts reviewed: 4,120
- Full text studies reviewed: 714
- Full text studies retained: 159
  - 78 - *Behavioral*
    - early intervention, social skills interventions, CBT, play/interaction-based approaches
  - 15 - *Educational*
    - broad-based approaches in educational setting, computer-based approaches, TEACCH
  - 42 - *Medical studies*:
    - antipsychotics, SRIs, stimulants, secretin, diets, supplements, hyperbaric oxygen, chelation, other medical
  - 17 - *Allied health studies*:
    - speech/language, sensory and auditory integration, recreational and other approaches
  - 7 - *CAM studies*
    - massage and acupuncture

Medical Treatment

Overview of Medical and Related Treatment

- 42 unique studies addressing medical interventions
  - 27 RCT(s)
  - 9 Prospective Case Series
  - 6 Retrospective Case Series
- Quality: 9 good, 18 fair, 15 poor
- Categorized as antipsychotics; serotonin reuptake inhibitors; stimulants and other medications for hyperactivity; *secretin; and dietary and other interventions*

Outcomes of Medical Treatment: Antipsychotics

Key Findings

- 9 studies: 3 good, 4 fair, 2 poor quality

Risperidone - (4 RCTs / 1 good, 3 fair)

- 1 RUPP, 1 manufacturer sponsored RCT:
  - Decrease targeted syptoms: ABC – Irritability / Hyperactivity
  - Secondary outcome: improvements in repetitive behavior
    - ABC-Stereotypy and CY-BOCS
- RCT drug discontinuation: relapse – 2/16 compared to 10/16

- SOE Moderate: Improvements in challenging behavior and repetitive behavior

- SOE High: Adverse effects, prolactin elevations, including weight gain (2.7kg), sedation/somnolence (53 of 89) and extrapyramidal effects

Outcomes of Medical Treatment: Antipsychotics

Aripiprazole (2 RCTs / good quality)

- 8 week trials sponsored by manufacturer
- Improvements in target of challenging behavior: ABC-I
- Secondary improvements: ABC-H & repetitive behavior
- Adverse effects, including weight gain (1.3-2.0kg), sedation/sedation (66 of 210) and extrapyramidal side effects (44 of 210).

- SOE High: Reducing challenging behavior and repetitive behavior
- SOE High: Adverse events, common side effects include weight gain, sedation, and extra-pyramidal effects

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Cyproheptadine + haloperidol (1 RCT / fair quality)

- Behavioral improvement reported but without indicating specific domains in one study
- SOE Insufficient

Outcomes of Medical Treatment: Serotonin Reuptake Inhibitors

Key Findings

- 5 studies: 1 good, 2 fair, 2 poor quality

Fluoxetine - 1 RCT Fair quality / 1 retrospective case series

- Greater change in repetitive behavior (CY-BOCS) with fluoxetine compared with placebo when second arm collapsed
- Reduction in dosages due to agitation / no group differences

Citalopram / escitalopram – 1 RCT good quality & 1 prospective case series

- No significant difference between the groups on repetitive behavior
- Significant but clinically small reduction in challenging behavior in the treatment group compared with placebo
- Activation – increased energy disinhibition, decreased sleep

- SOE insufficient

Stimulants and Other Medications to Treat Hyperactivity

Key Findings

- 4 studies: 1 RCT good quality, 3 retrospective case series

Methylphenidate: RUPP Autism Network double-blind crossover

- Improvements ABC-H / CGI
- Adverse events, including increases withdrawal/lethargy, irritability, appetite and sleep changes.

- SOE Insufficient

Secretin

Secretin: 7 RCTs (2 good, 5 fair), 1 case series

- No studies showed significantly greater improvements in the secretin group
- No difference for porcine or synthetic secretin

- SOE High: *Lack of effectiveness*
  - language, cognition, behavior, communication, autism symptom severity, and socialization.

Dietary and Additional Interventions

Key Findings

- 16 studies: 2 good, 7 fair, 7 poor / SOE Insufficient

Oral dietary supplements:

- Iron (1 prospective case series)
- Magnesium-vitamin B6 (1 prospective case series)
- Melatonin (1 retrospective case series)
- Ketogenic diet (1 prospective case series)
- Fish oil / Evening primrose oil (1 prospective case series)
- L-Carnosine (1 RCT fair)
- N,N dimethylglcine (1 RCT fair)
- Digestive enzyme supplement (1 RCT fair)

Other medical:

- Amantidine (1 RCT fair)
- Piracetam or perntoxifylline to respiridone (2 RCTs fair)
- Hyperbaric therapy (1 RCT good)
- Oral human immunoglobulin (1 RCT good)
- Dimercaptosuccinic acid (DMSA) (1 RCT poor)
- Rivastigmine tartrate (1 Prospective case series)
- Donezepil hydrocholride (1 RCT fair)

Behavioral Treatment

Early Intensive Behavioral and Developmental Interventions (EIBDI)

- Comprehensive (see Rogers and Vismara, 2008)
  - Focus on several areas of functioning vs. skill specific intervention
- Draw from principles of Applied Behavior Analysis (ABA)
  - Method and setting
- *ABA umbrella term for learning principles/techniques*
    - *Teach new behaviors, reduce challenging behaviors*
    - *Systematic reinforcement*
- *ABA is a term existing for decades prior to specific adoption within autism intervention literature*

EIBDI Literature

34 studies addressing EIBDI:

- 1 good
- 12 fair
- 21 poor quality

Early intensive behavioral and developmental interventions

- <u>UCLA/Lovaas model & variants:</u>
  - Intensive intervention (18-36 hr) utilizing operant conditioning, emphasis on structure and discrete trial toward generalization of skills
  - Variants of Early Intensive Behavioral Intervention (EIBI)
  - *Is this a category?*
- <u>Comprehensive approaches for children under 2:</u>
  - ABA principles within a developmental and relational framework
  - Early Start Denver Model (ESDM) / Early social communication training :
  - Range: Intensive intervention (15-20 hours) to lower levels
- <u>Parent-training:</u>
  - Pivotal Response Training, Social Pragmatic Intervention, More than Words, etc.

Key Findings-UCLA/Lovaas and Variants

Design:

- 1 RCT / fair quality
- 3 nRCT / fair quality
- 3 prospective cohort / fair quality
- *Poor:* 2 prospective cohort, 2 retrospective cohort, 6 prospective case series, 6 retrospective case series

Treatment:

- 4/7 utilizing manualized approach in some form
- Intensity: 18 – 36/40 hours
- Duration = .75 – 4 years
- Comparisons to community, parent, training, low intensity

Sample

- Assignment often upon availability, parent decisions
- Preschoolers (i.e., typically > 3 years; range - 29-63 months)
- Basal IQ = 54 – 76

NO STUDIES MADE THE SAME COMPARISONS IN TERMS OF INTERVENTIONS AND POPULATIONS

UCLA/Lovaas: The RCT of fair quality

Smith (2000): An attempt to replicate Lovaas' original work
N=28; IQ = 51 (35-75); Age= 36 months (18-42); absence of med problems

Intervention: 25 hrs/week individual treatment (1st yr; <2nd yr)

Comparator: parent training over 3-9 months

Results:

- Mean IQ increase 15 pts, no change in control
- 4/15 unsupported educational placements
- Largest gains in PDD-NOS relative to Autistic Disorder
- No group differences in adaptive or challenging behavior

Key Findings-UCLA/Lovaas and Variants
Our Fair Studies

Study	Year	N	EIBI hrs	Basal IQ	IQ Shift	Educational Placement	Adaptive
Zachor	2007	39	35	76	2	NR	NR
Reed	2007	48	NR	56	13	NR	13
Smith*+	2000	28	25	51	16	4/15	-2
Hayward*	2009	44	36	54	17	NR	6
Cohen*	2006	42	35-40	62	25	6/21	20
Eikeseth*	2002	25	18	63	25	0/13	12
Howard	2005	61	35-40	59	30	NR	11

Key Findings-UCLA/Lovaas and Variants:

- Young preschool children receiving high intensity interventions over extended durations (18-36) hours a week for extended durations (1-3) years by well-trained therapists
- Improvements in areas of cognitive, language, adaptive functioning
- Extremely variable range of outcomes within and across these domains
- Subgroups of children appear to display differentiated response to this intervention, but the subgroups with moderated/positive response are not well characterized

- *Low SOE: language, cognitive, educational, adaptive outcomes, ASD symptom severity*

Comprehensive approaches for children under 2:

Design:

- 1 RCT / good quality – Early Start Denver Model
- 1 nRCT / fair quality - Hanen More Than Words
- 2 prospective case series

Early Start Denver Model: An RCT of good quality

Dawson (2010):

- Manualized intervention for young children
- N=48
- IQ = 60 (35-75)
- Age= 23 months at entry

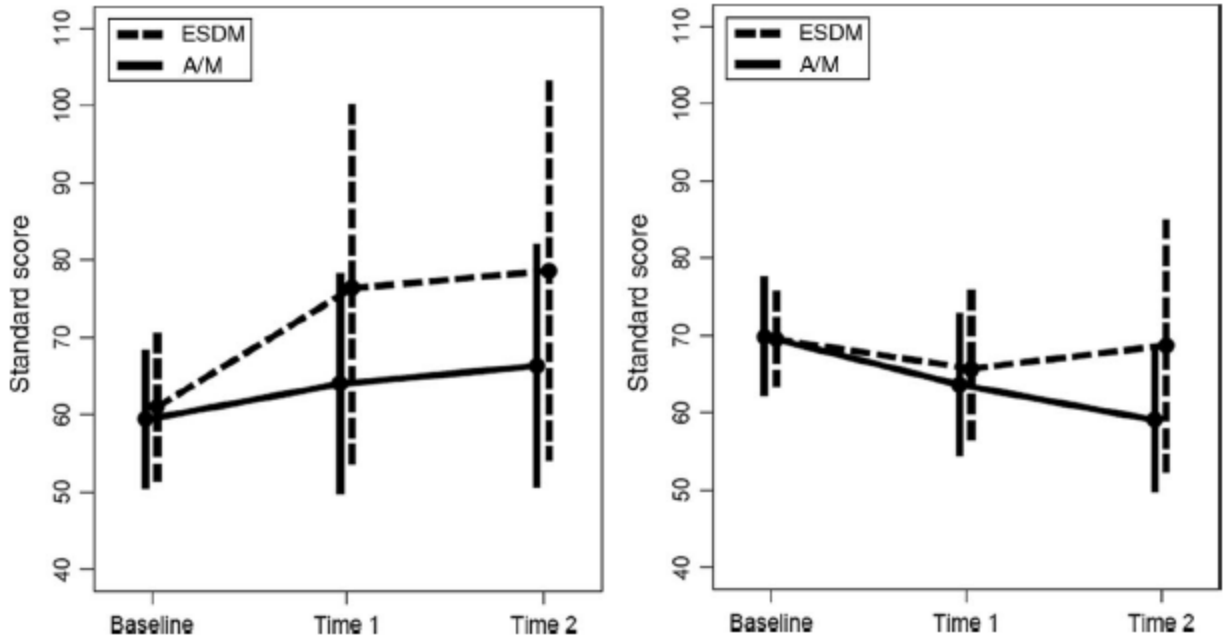
Intervention: 20 hrs/week, 5/parent, + community

Comparator: Community care (18 hrs: 9 individual + 9 group)

Early Start Denver Model: Outcomes

Results:

- Mean IQ increase 17.6 pts, to 7.0 for control
- Trend toward less decline in adaptive behavior (-.8 vs -11.2)
- ADOS severity scores or challenging behavior scores not different
- Shifts in diagnosis within category? (PDD <- AD)



Comment: Cohort continues to be followed; receive treatment

Parent Training

- 7 studies:
  - 3 fair RCTs, 4 (1 nRCT, 3 case series) poor quality

- Drew, 2002(fair) – parent-intervention vs. community
  - 1 year parents reported more word use
  - No differences nonverbal IQ, symptom severity, observed words/communication
  - Children in treatment lost IQ points
- Aldred, 2004 (fair) - parent-intervention vs.treatment as usual
  - Improvements in ADOS scores, expressive vocabulary
  - Young lower functioning children most improvement
  - Lacked standardized measures and baseline assessment data
- Green, 2010 (fair) parent-intervention vs. treatment as usual
  - Parent but not teacher rated improvements in language
  - Positive rating shifts via observation

Key Findings: Parent Training

- Some indication of short-term improvements in language, social, and adaptive skills for children whose parents receive training in these areas but studies vary in interventions and outcomes studied.
- Data do not yet demonstrate long-term functional improvements across domains for any specific form of training.

- *Insufficient SOE*

Summary: Early Intensive Intervention for ASD

- Individual studies document positive outcomes from a variety of approaches in cognitive performance, language, adaptive behavior when delivered intensively over substantial intervals of time
- Subset of individuals demonstrating *tremendous* response/plasticity
- Variability / heterogeneity *tremendous*
  - Change related to core, associated features
    - Response (i.e., moderated vs. rapid)
    - Limited understanding of subgroups
  - Approaches utilized / outcomes assessed
- Highly specified individualized treatments not yet identifiable
  - Predictions of early response -> Movement to other models
  - *The value of moderated response?*

Other categories: Insufficient SOE

Social Skills/Play-based Interventions:

- Positive results / selected samples
- Varied measures, approaches, generalization

Cognitive Behavioral Therapy:

- Initial positive results related to anxiety / selected samples
- Lack sufficient replication and study

Educational Interventions:

- Broad-based interventions, specialize nursery, computer assisted learning, TEACCH

Allied Health:

- Sensory/Auditory Integration, Music Therapy
- Language interventions - PECS / RPMT

CAM:

- Massage and acupuncture
- Small effects with unvalidated tools

Where does this leave us now?

Conclusions

- *Some* medications may benefit *some* behaviors of children with ASD:
  - Risperidone and Aripiprizole – problem and repetitive behavior
  - Strong evidence for adverse effects
  - Limited evidence for impact on core ASD features / impairments
  - Need further research on many medical interventions:
    - SRIs, methylphenidate, omega 3 fatty acids, melatonin
  - Some medical interventions clearly not efficacious - secretin
  - Even though in wide use, poorly studied

Conclusions

- Evidence for early intensive behavioral and developmental intervention:
  - Evidence for improvements: cognitive, language, adaptive behavior for *some* children
  - Subgroups of rapid gain may drive effects
    - Robust gains / continued impairment
    - Moderated response / quality of life improvement
  - Impact on core features -> functional meaningful distal outcomes
  - No studies directly compare models – vary widely in approach
  - Need replication/extension of models given current evidence
  - Small samples, poor comparisons, heterogeneity within/across studies interventions/outcomes, effectiveness/feasibility

Unanswered Questions

- **Moderators:** Few studies appropriated designed or powered
  - One study of RPMT / PECS – Object exploration / joint attention
  - IQ / language, age, social responsiveness, imitation subtypes
- **Early change predicting outcome:**
  - Little information
  - Change in IQ?
- **Functional change/Generalization:**
  - Limited investigation
  - Some outcomes are likely to represent generalization by report
- **Key Drivers**
  - No specific studies identified

Methodology *is* limiting our understanding of intervention impact / potential

How do you critically evaluate?

> 40% failed to use a comparison group

> 100 distinct outcomes in literature base

Few comparisons of typical/common approaches/combinations

Poorly described interventions

Poorly indexed populations – despite baseline heterogeneity

Gaps in populations studied:

- Late preschool intensive intervention; elementary/school medications, social skills, broad educational
- Clinics / University administered interventions
- Medical complexities

Limited health services research regarding feasibility/accessibility

Methodology *is* limiting our understanding of intervention impact / potential

Lack of *current* evidence **<u>does not</u>** equal lack of effect or *potential* effect of treatment

Some current and available ASD interventions do make a tremendous impact for *some children*

How do we best serve children in our backyards?

Thank You

- Agency for Healthcare Research and Quality (AHRQ)
  - Karen Siegel – Task Order Officer
- Centers for Medicare and Medicaid Services
- Autism Speaks
  - Geraldine Dawson – Chief Science Officer
- Vanderbilt EPC
  - Melissa McPheeters, Nila Sathe, Allison Glasser
- Vanderbilt Kennedy Center (VKC)
  - Elisabeth Dykens
  - Jan Rosemergy & Craig Boerner
- Treatment and Research Institute for Autism Spectrum Disorders (TRIAD)

Thank You

Parents and families in our community

- Expert panel
- Those who help us understand this disorder and our science better

Technical Expert Panel

- Robin Dea
- Bryan King
- Susan Levy
- Cathy Lord
- Doris Lotz
- Gary Mesibov
- Tristram Smith
- Paul Yoder

Other approaches

- Practice statements / Reviews:
  - National Autism Center /National Standards Project (2010):
    - *Established Treatments*
  - Reichow and Wolery, 2009 - EIBI review and meta-analysis
  - Evaluative Method for Evaluating and Determining Evidence-Based Practices in Autism (Reichow, Volkmar, Cicchetti, 2007)
  - Rogers and Vismara, 2008 - Comprehensive treatments
    - *APA Division 12 – Well-established, probable/possible efficacious*
  - National Research Council, 2001
    - *Little evidence to support one treatment over another*
    - *Effective treatments share many features in common*
    - *Focus on these commonalities to address core deficit areas*

How do we choose and value treatments?

Individualized intervention:

- What works for which children and why?
- What is the meaningful social and functional impact?
    - Range of outcomes to be expected ?
    - How do we value therapeutic changes?

A changing landscape:

- Improved understanding of disorder
- Improved study and improved interventions
- Methodologically rigorous and meaningful investigation

How do we choose and value treatments?

- Appropriate interventions must be actually delivered vs. practices of a research article or theoretically grouping

- Tremendous opportunities for service systems to dramatically improve our fundamental understanding of the disorder and intervention
  - Public/private insurers – legislative mandates regulation
  - Systems of educational care

- This is not a distant problem for many service systems