

The Evidence Base for Pharmacologic and Complementary-Alternative Medical Treatments in Autism Spectrum Disorders

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Autistic Spectrum Disorders (ASD): Guidelines for Effective Interventions

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Autism Spectrum Disorders (ASD)

- ◆ Neuro-developmental disorders including
 - Autistic prototype disorder (autism)
 - Pervasive developmental disorder not otherwise specified (PDD-NOS)
 - Asperger syndrome
- ◆ Common characteristics in 3 core areas
 - Impairments in social interaction
 - Impairments in verbal and non-verbal communication
 - Restricted and repetitive patterns of behavior
- ◆ Associated behavior and regulation problems

(DSM-IV-TR, American Psychiatric Association, 2000)

Objective: To Describe Preliminary Results of Systematic Review

- ◆ Explain the review methodology
- ◆ Describe review results to date
 - Broad picture
 - ◆ Pharmacologic treatments
 - ◆ Complementary and alternative medicine (CAM) treatments
 - Detailed impression, using two exemplar treatments (i.e., atypical antipsychotics and elimination diets)
 - ◆ Two target symptoms
 - ◆ Scientific quality
 - ◆ Outcomes

Objective: To Describe Preliminary Results of Systematic Review

- ◆ Set the stage for addressing research questions
 - How effective are interventions for individuals with ASD?
 - Which interventions for children with ASD are more effective than others in yielding specific outcomes?
 - What individual characteristics moderate response to interventions?
 - What research gaps exist?

Systematic Review Methodology

- ◆ What is a systematic review?
 - Structured review of scientific research with common elements (i.e., intervention, outcome, intervention setting, targeted population)
 - Explicit detailed search strategy to find as many published reports as possible
 - Reviews according to a written protocol
 - Pre-specified inclusion and exclusion criteria for determining which studies are reviewed

Systematic Review Methodology

- ◆ How do we handle the analysis of research studies?
 - Set methods to assess the quality of each study
 - Identify 2 individuals to independently extract the data
 - Interpret data from similar studies
 - Disseminate results in a clear, objective, and transparent manner

Systematic Review Methodology

- ◆ Why is research assessed against set criteria?
 - To reduce the risk of bias (in choosing which studies are considered)
 - To ensure that each study is objectively assessed and weighted appropriately

Data Collection

- ◆ Retrieval of intervention studies through comprehensive literature search
- ◆ Computerized database searches covering
 - PubMed/MEDLINE
 - Web of Science
 - Cochrane Database of Systematic Reviews
 - PsycINFO
- ◆ Hand searches
 - Reference lists of retrieved articles (trials and reviews)
 - Suggestions in response to reference list posting at <http://asdguidelines.org/>

What studies are included?

- ◆ Intervention must pertain to and include individuals with autism spectrum disorders (ASD)
- ◆ Intervention is Pharmacologic/Biomedical or Complementary/Alternative Medicine
- ◆ Individuals under study are 0-22 years of age

What studies are included?

- ◆ Experiment employs single-subject or group design of sufficient quality (no pre-experimental designs)
- ◆ Published in a peer-reviewed journal (thus, checking quality, ensuring comprehensiveness, and limiting bias of reported research)
- ◆ English language
- ◆ Dated between 1994 and May 2007

What studies are excluded?

- ◆ Sample size in group design is <10
- ◆ Non-human
- ◆ Editorial, commentary or letter
- ◆ Review
- ◆ Does not address an ASD topic
- ◆ Participants older than 22 years of age
- ◆ Non-treatment
- ◆ Non-biomedical intervention

Abstraction and Quality Rating of Included Studies

- ◆ Abstraction form developed, pilot-tested
- ◆ MS Access database created to hold abstraction data
- ◆ SPSS database created to document inter-rater reliability

Abstraction and Quality Rating: Coding categories

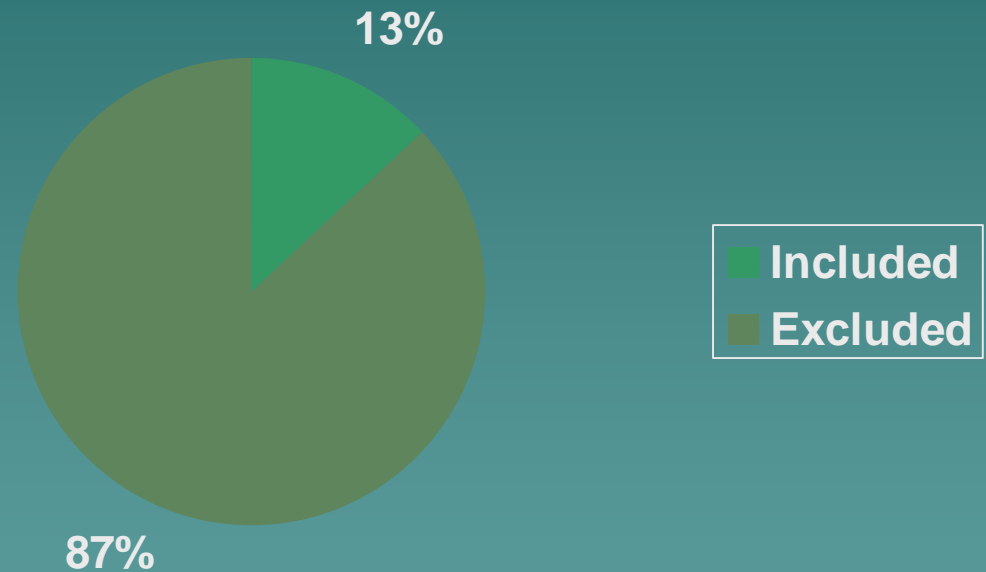
- Author and funding information
- Publication information
- Treatment intervention details
- Study design
- Participant characteristics (age, gender, comorbidity, family characteristics)
- Diagnostic model for ASD and standardized assessment
- Participant treatment information (compliance, randomization, eligibility)
- Identified outcomes (primary and secondary)
- Measurement strategies
- Availability of baseline scores

Abstraction and Quality Rating: Dimensions of Scientific Quality and Weights

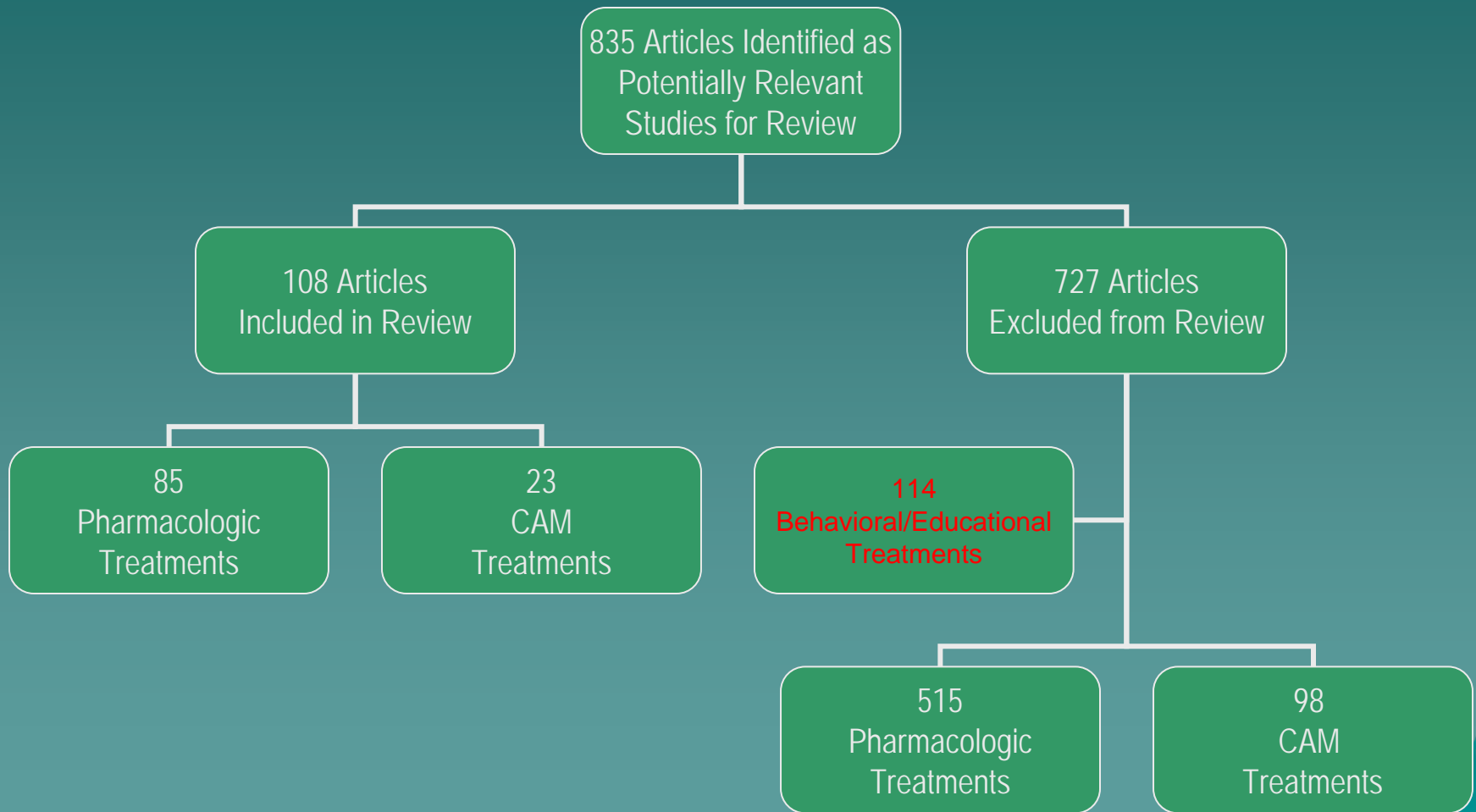
- ◆ Per National Autism Center
 - Design and Treatment Effects (.25)
 - Measurement of the Dependent Variable (Outcomes) (.25)
 - Measurement of the Independent Variable (Intervention) (.20)
 - Participant Ascertainment (.20)
 - Generalization of Treatment Effect (.10)
- ◆ Weights assigned to dimensions to reflect changes over time in research design criteria
- ◆ Also considered
 - Data-based conclusions by investigators
 - Funding source

Search Results

- ◆ Literature search revealed 835 documents related to pharmacologic or CAM treatments and ASD
- ◆ 108 studies met inclusion criteria
- ◆ 727 studies were excluded from further review

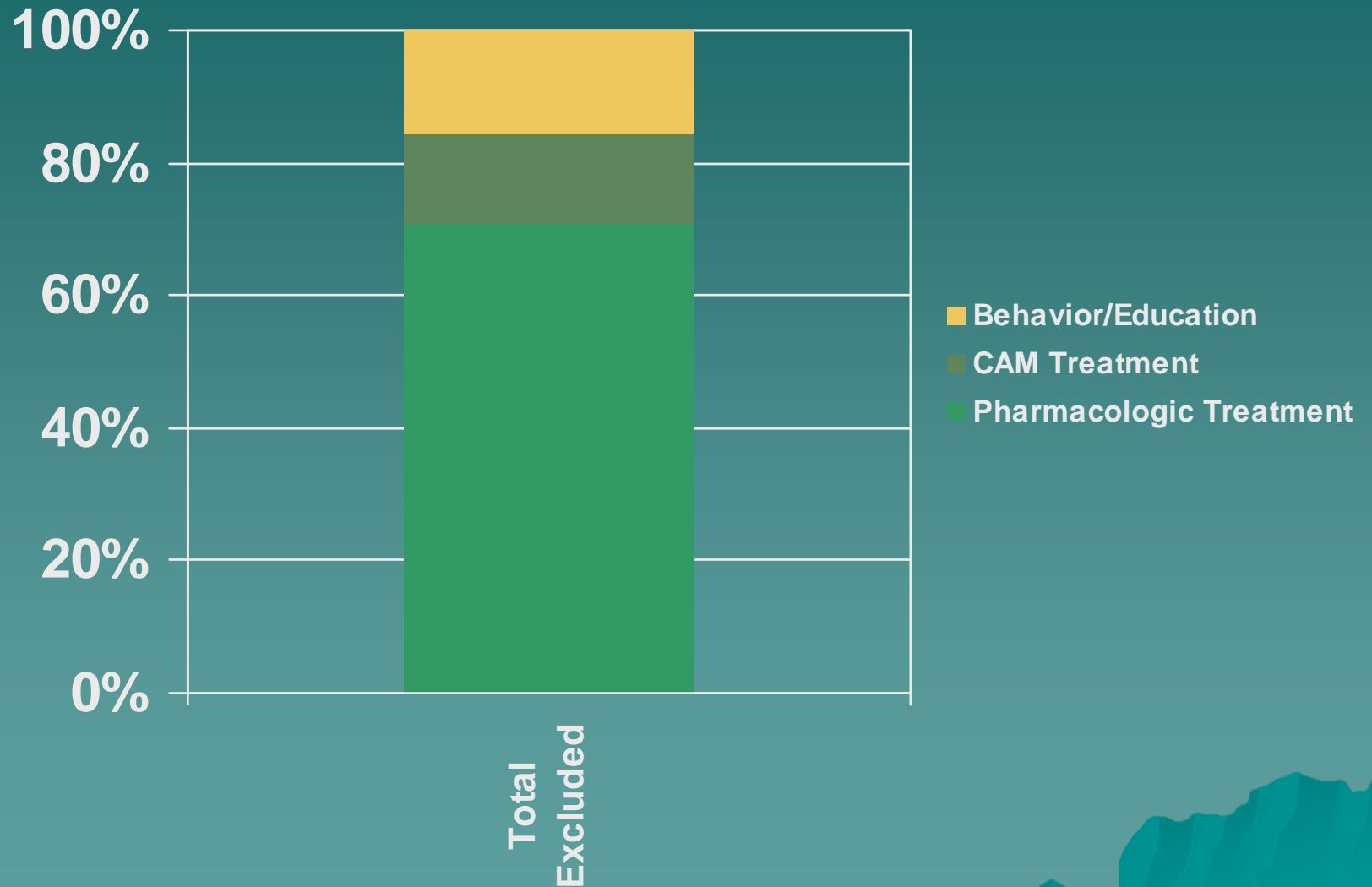


Articles Identified in Original Search



Excluded Articles

Total=727



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Excluded Articles that Address Pharmacologic Treatments

515 Pharmacologic Treatment

271 Did not address a treatment intervention

66 Were Comment, Editorial, Or Letter

51 Sample size <10*

24 Did not address an ASD Topic

15 Only had older adult subjects

13 Did not have article in English language

6 Did not have human subjects

64 Were review articles

5 Were duplication studies

*Note made of reports with small samples; 4 appear to be rigorous single-case designs that will be examined separately

Excluded Articles that Address CAM Treatment

98 CAM Treatment

54 Did not address a treatment intervention

14 Were Editorial, Comment or Letter

7 Did not address an ASD topic

1 Only had older adult subjects

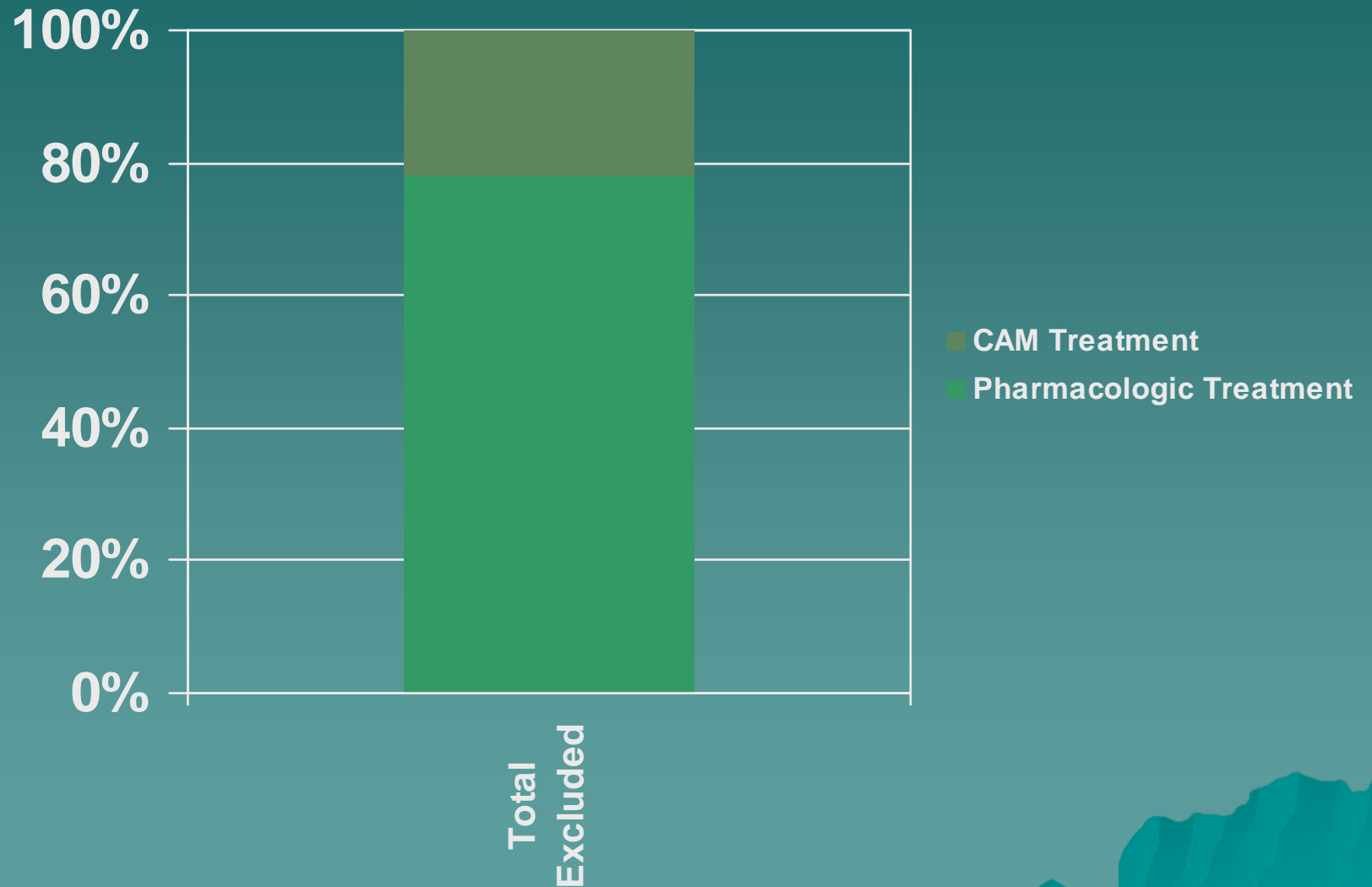
2 Did not have article in English Language

2 Did not have human subjects

18 Were Review Articles

Included Articles

Total= 108



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Included Pharmacologic Treatment

85 Pharmacologic Treatment

28 Atypical antipsychotic

18 Hormone/Neuro-peptide

10 Anti-depressant/anti-anxiety

9 ADHD treatment

7 Anti-opioid

4 Anti-convulsant

9 Other

Other

3 Immune-focused (IVIG, anti-viral)

2 Cognition enhancement (anti-Alzheimer)

2 GI-focused (antibiotic, anti-fungal)

2 Anti-histamine

0 Anti-hypertensive

0 Analgesic

Included CAM Treatment

23 CAM Treatments (22 + 1)

22 Biologically Based Practices

7 Vitamin

6 Whole Diet

5 Protein & Amino Acid

1 Chelation

1 Fatty Acid

1 Hyperbaric Oxygen

1 Mineral

Included CAM Treatment

23 CAM Treatments (22 + 1)

1 Mind-Body Medicine

1 Neurofeedback

0 Manipulative or Body-Based Practi

0 Energy Therapies

Pharmacologic Treatment: # of Articles Addressing Core Symptoms

	Impaired Social Interaction	Impaired Communication	Restricted or Repetitive Behavior
Atypical anti-psychotic	12	14	14
Hormone/Neuro-peptide	12	14	11
Anti-depressant/anti-anxiety	7	7	8
ADHD treatment	5	5	6
Anti-opioid	3	3	3
Anti-convulsant/ Mood stabilizer	4	4	4
Other	6	6	6

Pharmacologic Treatment: # of Articles Addressing Problem Behaviors

	General Functional Impairment	Hyperactivity/ Inattention/ Impulsivity	Irritability	Aggression	Self-Injury
Atypical anti-psychotic	20	9	8	1	2
Hormone/ Neuro-peptide	8	6	6	0	0
Anti-depressant/ anti-anxiety	1	4	5	0	0
ADHD treatment	6	9	4	2	0
Anti-opioid	6	5	2	0	0
Anti-convulsant/ Mood stabilizer	3	4	2	2	0
Other	4	6	8	1	0

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Pharmacologic Treatment: # of Articles Addressing Dysregulation

	Depression- Anxiety	GI Problems	Sleep Problems	Eating Problems	Sensory Problems
Atypical anti-psychotic	3	0	2	0	0
Hormone/ Neuro-peptide	1	8	3	0	0
Anti-depressant/ anti-anxiety	2	0	1	0	0
ADHD treatment	0	0	0	0	0
Anti-opioid	3	0	0	0	0
Anti-convulsant/ Mood stabilizer	2	0	0	0	0
Other	2	1	1	0	0

CAM Practices: # of Articles Addressing Core Symptoms

	Impaired Social Interaction	Impaired Communication	Restricted or Repetitive Behavior
Vitamins	4	4	3
Minerals	0	0	0
Fatty Acids	1	1	1
Proteins & Amino Acids	4	3	3
Probiotics	0	0	0
Whole Diets	3	3	3
Hyperbaric O2	1	1	0
Chelation	1	1	0

CAM Practices: # of Articles Addressing Problem Behavior

	General Functional Impairment	Hyperactivity/ Inattention/ Impulsivity	Irritability	Aggression	Self-Injury
Vitamins	5	2	0	0	0
Minerals	1	0	1	0	0
Fatty Acids	0	1	1	0	0
Proteins & Amino Acids	2	1	1	0	0
Probiotics	0	0	0	0	0
Whole Diets	2	0	0	0	1
Hyperbaric O2	1	0	0	0	0
Chelation	1	0	0	0	0

CAM Practices: # of Articles Addressing Dysregulation

	Depression/ Anxiety	GI Problems	Sleep Problems	Eating Problems	Sensory Problems
Vitamins	0	1	1	0	0
Minerals	0	0	1	0	0
Fatty Acids	0	0	0	0	0
Proteins & Amino Acids	0	0	0	0	0
Probiotics	0	0	0	0	0
Whole Diets	2	0	0	0	0
Hyperbaric O2	0	0	0	0	0
Chelation	0	0	0	0	0

A Closer Look at...

Atypical Antipsychotics

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A stylized silhouette of a mountain range in a darker shade of teal, located in the bottom right corner of the slide.

Specific Questions

- ◆ What is the scientific quality of articles describing the effect of antipsychotics on
 - Impaired Social Interaction?
 - Hyperactivity?
- ◆ What is the direction and consistency of the findings in these articles?

Generic and Brand Names

- ◆ Atypical anti-psychotics
 - Risperidone (Risperdal)
 - Olanzapine (Symbax)
 - Ziprasidone (Geodon)
 - Aripiprazole (Abilify)
 - Quetiapine (Seroquel)

Atypical Antipsychotics: Impaired Social Interaction

Scientific Quality Composite Score	# of Articles	Demonstrated significant improvement
5 (<i>Rigorous</i>)	0	
4 (<i>Solid</i>)	2 (n's=19, 49)	0 of 2
3 (<i>Adequate</i>)	4 (n's=11, 27, 38, 63)	2 of 4
2 (<i>Weak</i>)	5 (n's= 11, 13, 18, 18, 22)	4 of 5
1 (<i>Poor</i>)	0	
0 (<i>Unsatisfactory</i>)	0	

Atypical Antipsychotics: Hyperactivity/Inattention/Impulsivity

Scientific Quality Composite Score	# of Articles	Demonstrated significant improvement
5 (<i>Rigorous</i>)	0	
4 (<i>Solid</i>)	2 (n's=19, 49)	2 of 2
3 (<i>Adequate</i>)	4 (n's= 24, 27, 38, 63)	3 of 4
2 (<i>Weak</i>)	2 (n's=19, 22)	2 of 2
1 (<i>Poor</i>)	1 (n=10)	1 of 1
0 (<i>Unsatisfactory</i>)	0	

Answers to Specific Questions

- ◆ Scientific quality of articles describing effect of antipsychotics on
 - Impaired Social Interaction
 - ◆ 11 articles ranging from 'solid' to 'weak' in quality
 - Hyperactivity
 - ◆ 9 articles ranging from 'solid' to 'poor' in quality
- ◆ Direction and consistency of findings in these articles
 - Impaired Social Interaction
 - ◆ 'Strong' evidence suggesting atypical antipsychotics have no significant effect on impaired social interaction
 - Hyperactivity
 - ◆ 'Strong' evidence suggesting atypical antipsychotics can decrease hyperactivity symptoms

A Closer Look at...

Whole Diets (Elimination Diets)

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Specific Questions

- ◆ What is the scientific quality of articles describing the effect of whole diets on
 - Impaired Social Interaction?
 - Hyperactivity?
- ◆ What is the direction and consistency of the findings in these articles?

Generic and Specific Names

- ◆ Whole diets
 - Gluten-free, casein-free
 - Ketogenic
 - Specific carbohydrate
 - Low salicylate

Whole Diets: Impaired Social Interaction

Scientific Quality Composite Score	# of Articles	Demonstrated significant improvement
5 (<i>Rigorous</i>)	0	
4 (<i>Solid</i>)	0	
3 (<i>Adequate</i>)	1 (n=8)	0 of 1
2 (<i>Weak</i>)	1 (n=10)	0 of 1
1 (<i>Poor</i>)	1 (n=36)	0 of 1
0 (<i>Unsatisfactory</i>)	0	

Whole Diets: Hyperactivity/Inattention/Impulsivity

Scientific Quality Composite Score	# of Articles	Demonstrated significant improvement
5 (<i>Rigorous</i>)	0	
4 (<i>Solid</i>)	0	
3 (<i>Adequate</i>)	0	
2 (<i>Weak</i>)	0	
1 (<i>Poor</i>)	0	
0 (<i>Unsatisfactory</i>)	0	

Answers to Specific Questions

- ◆ Scientific quality of articles describing effect of whole diets on
 - Impaired Social Interaction
 - ◆ 3 articles ranging from 'adequate' to 'poor' in quality
 - Hyperactivity
 - ◆ 0 articles
- ◆ Direction and consistency of findings in these articles
 - Impaired Social Interaction
 - ◆ 'Modest' evidence suggesting whole diets have no significant effect on impaired social interaction
 - Hyperactivity
 - ◆ No studies available

Impressions and Next Steps

- ◆ Scientific literature in this arena is complex and evolving
 - At least 15 groups of pharmacologic interventions
 - At least 8 groups of CAM interventions
 - At least 16 outcome variables
- ◆ Treatment study results in this arena are challenging to aggregate
- ◆ Next steps
 - Maintain active communication and exchange with Behavioral/Educational Methodology team
 - Complete article abstraction and rating
 - Formulate best strategy for written communication of information

Thank you

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