Summary of UAMS Developmental Pediatrics / Dennis Developmental Center Clinical Activities, with a Brief Review of Autism Standards of Practice

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UAMS Developmental/Behavioral Pediatrics

The sub-section of DBP is part of the larger section of Developmental Pediatrics / Rehabilitative Medicine within the Dept. of Peds.

The section is chaired by Eldon G. Schulz, M.D., Professor and Rockefeller Chair for Children with Special Healthcare Needs

Dennis Developmental Center

The James L. Dennis Developmental Center (DDC) is Arkansas' primary referral center for diagnostic evaluations of developmental disorders.

Jill Fussell, MD is the Medical Director of DDC

Other MD /APRN Staff

Eldon Schulz, MD **Tyra Reid, MD** **Maya Lopez, MD**

Jaime Flor, MD **Paulette Wy, MD**

Whitney Brooks, APRN **Lindsay Van Parys APRN**

Current DBP Fellows

Rachel Goode, MD **Angela Scott, MD** **Alberto Allegre, MD**

DDC Med Appointment Availability

The Administrative Director, Adam Gaban, has been assiduously addressing "the waitlist problem."

As a result, the dreaded "waitlist at DDC" went away in June 2015. DDC can now assign a medical appointment within 6 months of request (and working toward shortening that time), without putting families on a wait list.

DDC Med Appointment Availability

DDC receives between 300-400 referrals per month.

Because of the number of referrals and need to facilitate earlier diagnosis efforts, new patient appointments for medical diagnostic slots are generally restricted to children 12 years of age and younger.

DDC Med Appointment Availability

DDC now has a fully staffed care coordination office to answer referral questions and facilitate scheduling.

Call DDC 501-364-1830 and request transfer to that office for immediate assistance, or fax to the new intake number 501-978-6492

DDC Med Appointment Availability

Keep in mind that the initial appointment may not be a full team appointment,

because laws of physics.

Not every family referred for “a full team” actually needs or would benefit from that.

For those families that do need that service, a follow-up team evaluation is scheduled to occur in one or more visits less than six months from the initial visit, and the family is given recommendations for actions to take in the interim.

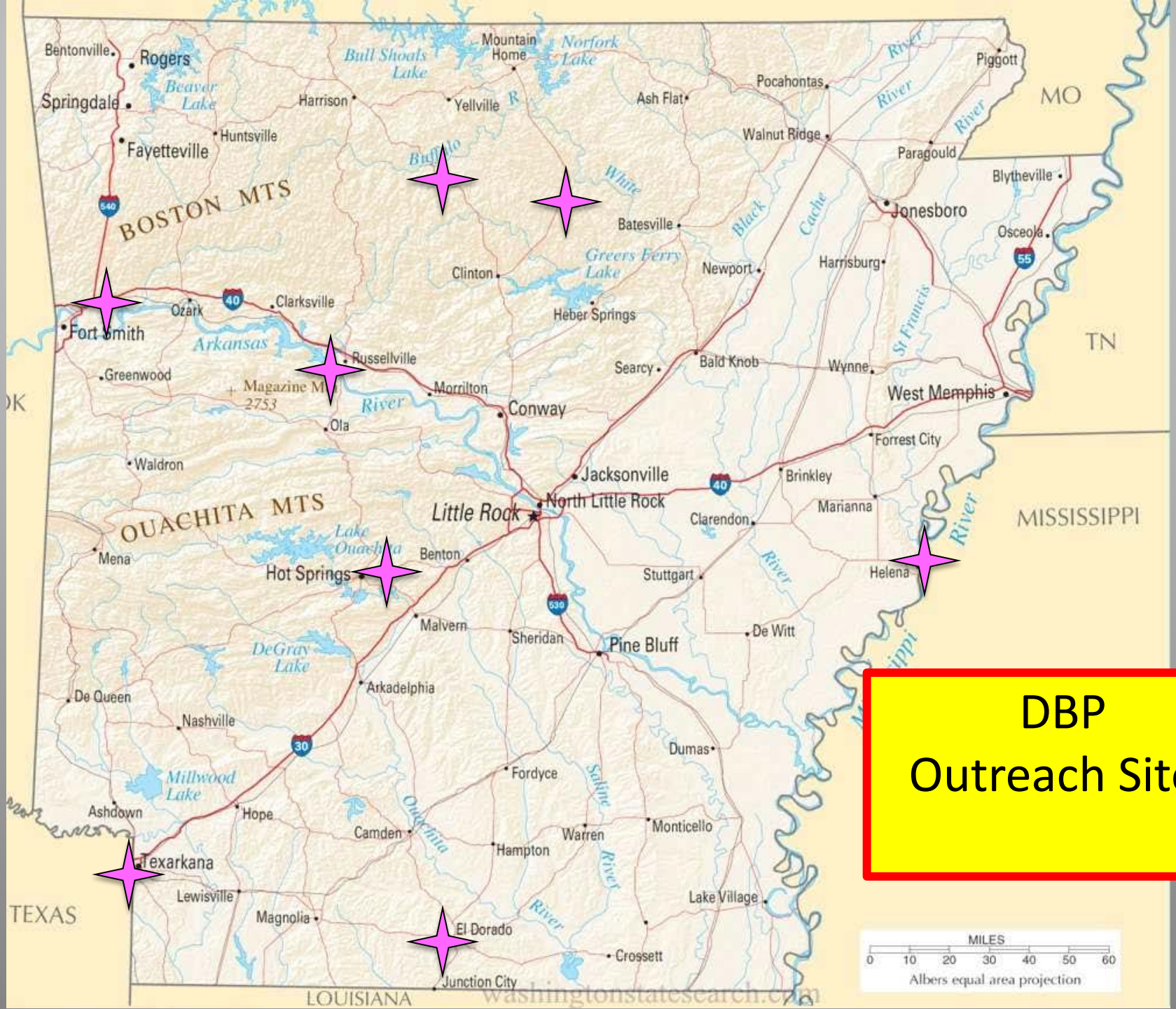
Things PCPs Could Do In The Interim

If the PCP has significant concerns about delays in any of the key areas — social communication, social interaction, or behavior — then referral should be made to the appropriate servicing agency (i.e., early intervention, early childhood, or the special education supervisor at the child's school district) while waiting for the specialty evaluation.

ASD Diagnostic Providers / Outreach

UAMS DBP also has a network of Outreach Clinics, which are conducted quarterly in 8 sites across the state.

These clinics (typically occurring within 50 miles of the patient's primary medical home), function both as regional triage clinics to conduct initial diagnostic interviews, and as consultative access for local providers


DBP
Outreach Sites
Bentonville
Rogers
Springdale
Fayetteville
Huntsville
Harrison
Yellville
Mountain Home
Bull Shoals Lake
Norfork Lake
Beaver Lake
Ash Flat
Pocahontas
Piggott
MO
Walnut Ridge
Paragould
Blytheville
Jonesboro
Osceola
Batesville
Clinton
Greers Ferry Lake
Newport
Harrisburg
Heber Springs
Ozark
Clarksville
Fort Smith
Arkansas
Russellville
Greenwood
Searcy
Bald Knob
Wynne
West Memphis
TN
Morrilton
Conway
Ola
Waldron
Forrest City
Jacksonville
Brinkley
Little Rock
North Little Rock
Marianna
Clarendon
MISSISSIPPI
Mena
Lake Ouachita
Benton
Hot Springs
Stuttgart
Helena
Malvern
Sheridan
Pine Bluff
De Witt
DeGray Lake
Arkadelphia
De Queen
Nashville
Dumas
Millwood Lake
Fordyce
Ashdown
Hope
Camden
Hampton
Warren
Monticello
Texarkana
Lewisville
Magnolia
El Dorado
Lake Village
Crossett
Junction City
TEXAS
LOUISIANA
BOSTON MTS
OUACHITA MTS
White River
Black River
Cache River
St Francis River
Saline River
Ouachita River
MILES
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ASD Diagnostic Providers / Outreach

- **Each clinic is staffed by UAMS DBP MD, RN, and SW**
  - **This clinic structure allows an increased number of children per clinic for initial investigation to direct next stage of assessment, if needed**
  - **There is also opportunity for teachers and therapists who work with these children to interface with the Outreach teams to provide additional diagnostic information, and problem solve together to target areas of concern**
- **Sometimes a medical diagnosis can be determined at these clinics, but if necessary the family is recommended to follow up at DDC or with other specialty providers in the state, depending on the provisional diagnostic impression**

Other ASD Diagnostic Providers

Other clinics within UAMS that provide some diagnostic evaluations to children and youth suspected to have ASD

- Schmieding Center in Northwest AR
- Child Psychiatry (the Child Diagnostic Unit, the Child Study Center, and Program for Young Adults)

Other ASD Diagnostic Providers

Diagnostic evaluations are also performed at

Arkansas Children's Hospital

- Growth and Development Clinic currently performs evaluations for young children aged birth to pre-K under the supervision of UAMS DBP clinicians
- ASD is in the differential diagnosis for several conditions that may be seen in Neurology Clinic, Genetics Clinic, and other neurodevelopmentally related clinics, where the medical diagnosis could be assigned

ASD Diagnostic Providers / CoBALT

Community Based Autism Liaison and Treatment Project (CoBALT)

- **CoBALT started in 2011 with the intent to improve referral efficiency to early intervention services, and to boost diagnostic capacity for early presenting developmental problems such as autism**
- **Since that time, a total of 10 mini-teams (Medical and SLP) have been trained to perform Tier 2 diagnostic assessments.**
  - **As of summer 2015, 5 of these teams are active.**
  - **Some initially trained teams have not been able to maintain diagnostic activities consistently for various reasons**

ASD Diagnostic Providers / CoBALT

June 2011

- El Dorado (Robin Ray MD)
- Jonesboro (Jane Sneed MD)
- Jonesboro (David Matthews MD)

October 2011

- Texarkana (Belinda Hutcheson MD)
- Clinton (Holly Hink, APN)

December 2011

- Lowell (Barry Allen MD)
- Fort Smith (Jon Hendrickson MD)

August 2013

- Forrest City (Curt Patton MD)
- Mena (Ron Beckel MD)
- Pine Bluff (Horace Green MD)

Team Physician or APN and location.
Each team also included a speech/language pathologist from the local area

ASD Diagnostic Providers / CoBALT

June 2015 Training Refresher Course

- **Fort Smith** - (Jon Hendrickson MD)
- **Jonesboro** - (Jane Sneed MD)
- **El Dorado** - (Robin Ray MD)
- **Forrest City** - (Curt Patton MD)
- **Clinton** - (Holly Hink APN)

Team Physician or APN and location.
Each team also included a speech/language pathologist from the local area

ASD Diagnostic Providers / CoBALT

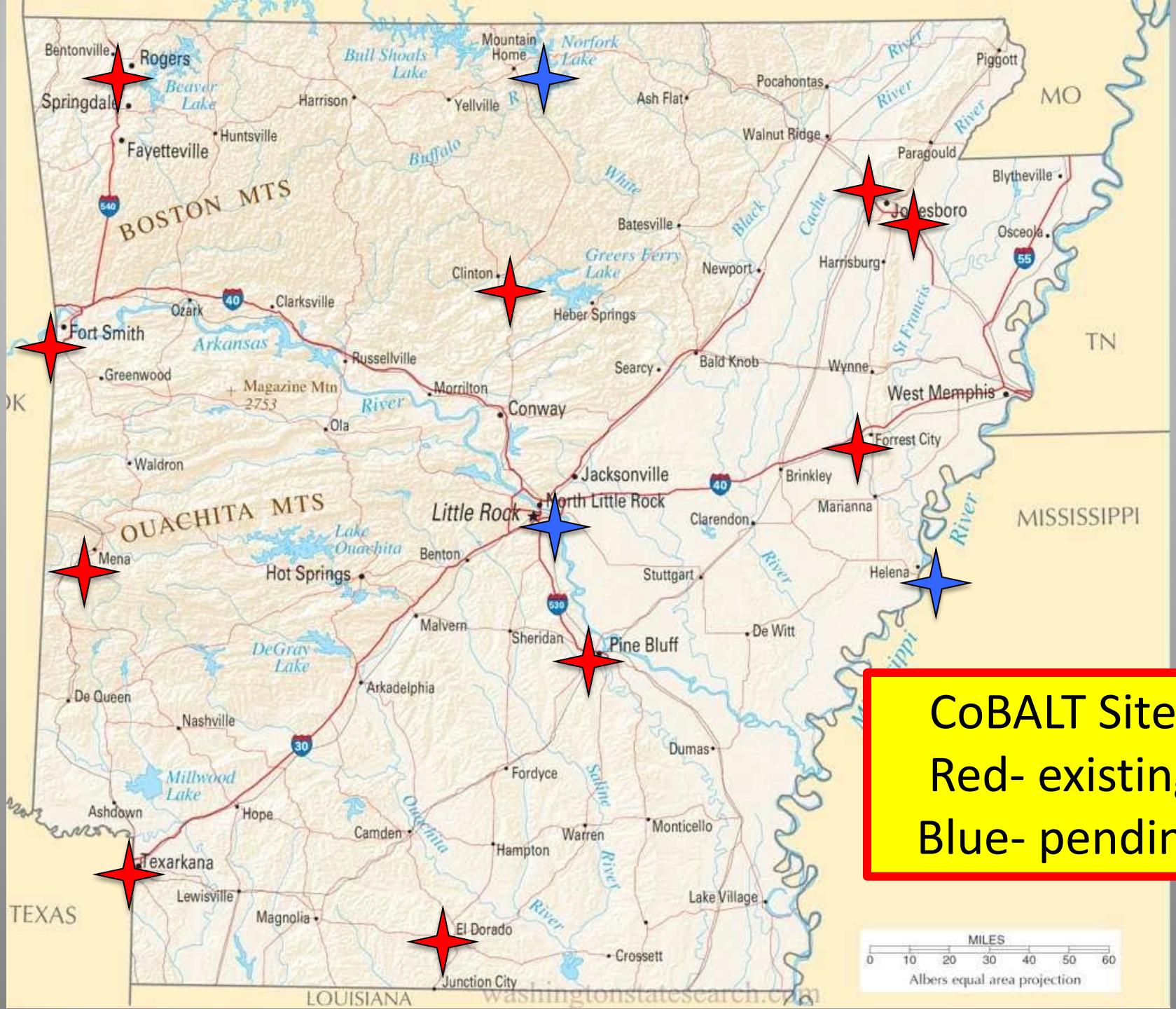
Upcoming training April 2016

- **Mt. Home (Rebecca Ramick, MD)**
- **Helena-West Helena (Jill Pillow, MD)**
- **Little Rock/ACH (Karen Young, MD)**

This session will also provide additional refresher training for new SLPs at sites that have been recently inactive due to lack of SLP

- **Mena**
- **Jonesboro**
- **Lowell**
- **Texarkana**

After the next round of training, we will be looking for additional funding to continue training activities



ASD Diagnostic Providers / CoBALT

CoBALT Tier 2 Assessment Instruments

- Diagnostic Interview
- Autism Detection in Early Childhood (ADEC; Young, 2007
  - Developed as a Level 2 clinician-administered ASD screening tool that can be used by general practitioners, maternal healthcare nurses, allied healthcare professionals, psychologists, therapists, special needs educators, takes 10-15 minutes (untimed)
  - Ability to screen children 12 months - 3 years
  - Assists in identifying specific behaviors that require intervention
  - Able to accurately discriminate autistic behaviors from learning disabilities and other developmental disorders
- M-CHAT – R/F (Revised, with Follow-up Questions)
- Ages & Stages Questionnaires (ASQ)

ASD Diagnostic Providers / CoBALT

Other 2016 CoBALT activities

- **Telemedicine activities will increase this year**
- **We will be increasing our use of teleconferences to occur on a regular schedule with all teams who have telemedicine capacity**
- **This will be in conjunction with other grant activities to solidify use of telemedicine capability**

ASD Diagnostic Providers / LEND

Leadership Education in Neurodevelopmental Disabilities (LEND)

Eldon Schulz, MD is Project Director.

LEND is a post-graduate training grant providing 300+ hours of additional work/training in the area of Autism and other Developmental Disabilities. UAMS is one of 39 grantees of the LEND program.

The project recruits, selects, and trains 26 long-term trainees and 8 intermediate trainees from 14 core disciplines each year.

ASD Diagnostic Providers / LEND

One of the five main goals of the program is to "improve the diagnosis and differential diagnosis of neurodevelopmental disabilities (ND) and autism spectrum disorders (ASD) in client populations," by increasing the skills of LEND trainees necessary to diagnose ND and ASD, and by increasing the knowledge and skills of LEND trainees in identifying ASD as co-morbid with other developmental or neurological disabilities.

Autism Treatment Network

From the Web site:

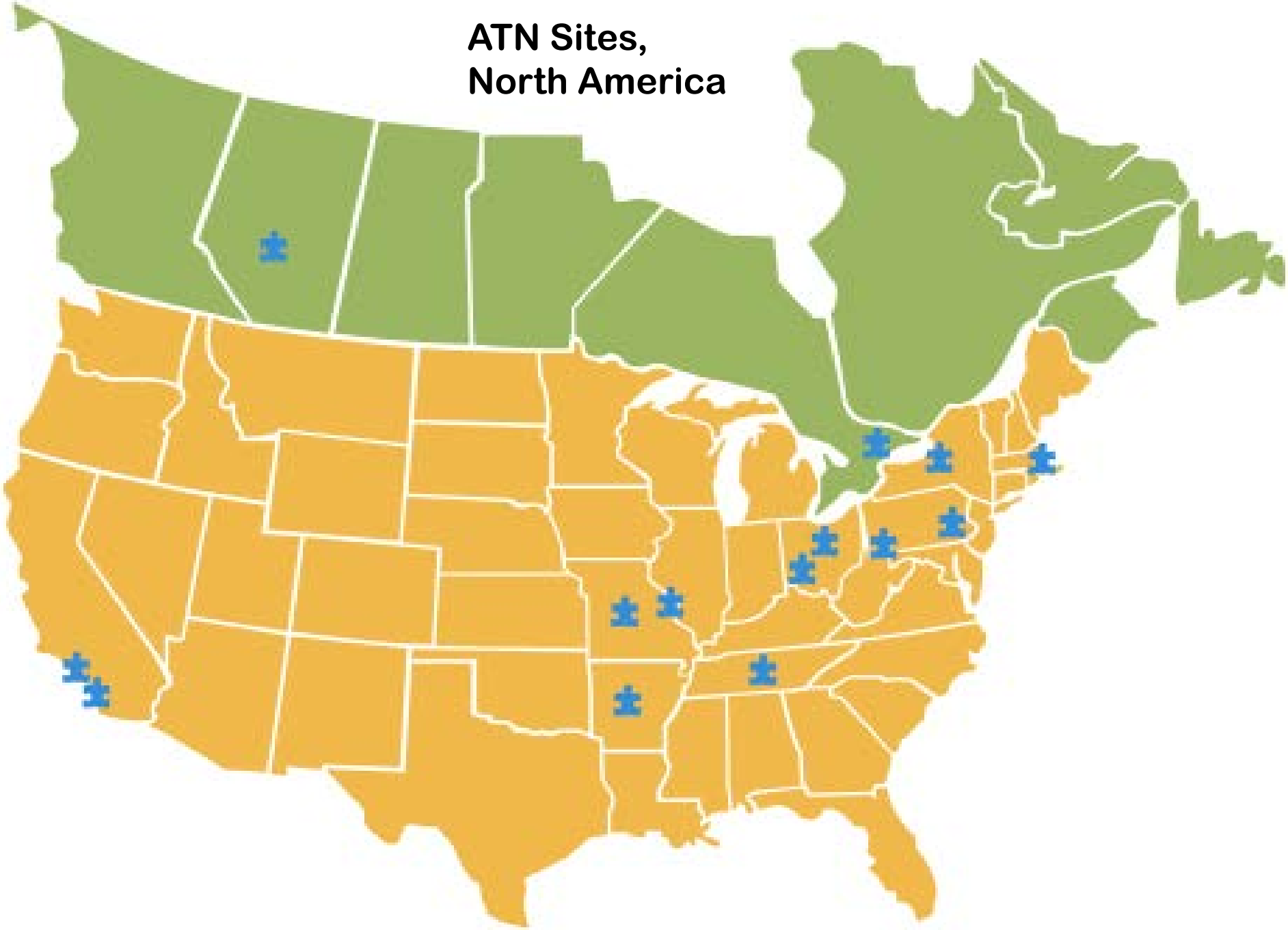
"The Autism Treatment Network (ATN) is a collaboration of Autism Speaks® and some of the finest children's hospitals and academic institutions in North America, specializing in multi-disciplinary medical care for children with autism. Together, they work to develop evidence-based protocols and standards of care for many of the most challenging medical conditions surrounding autism today. ATN best practices are shared with physicians and medical facilities nationwide to improve outcomes for all children with autism."

Autism Treatment Network

Currently the Autism Treatment Network (ATN) is a collaboration of 14 treatment and research centers dedicated to improving medical care for children and adolescents with Autism Spectrum Disorders (ASD).

ATN sites are selected through a competitive grant application process and are typically funded for up to three years.

ATN Sites, North America



Arkansas ATN

- Arkansas has been an ATN site since 2007
- Maya Lopez, MD (DBP) is Principal Investigator and Site Director.
- Co-Principal Investigators are Jill Fussell, MD (DBP) and Jill James, PhD

- Goals of Arkansas ATN since 2007 have included improving patient access, standardization of the diagnostic process, promoting family centeredness, increasing community outreach activities and fueling new research efforts.

Arkansas ATN / Activities

- Incorporated the AS-ATN Assessment Battery as standard of care at DDC
- Advocated for establishment of an ACH multispecialty clinic (Pediatric Gastroenterology and Nutrition, Pediatric Neurology, Genetics, and Sleep)
- Established a patient registry and a successful mechanism for recruitment in clinic to facilitate opportunities for autism research.
- lincreased community outreach and educational initiatives
- Developed Project SPAECS: Spotting Autism in Early Childcare Settings as part of Healthy Child Care Arkansas
- Ongoing partnership with AAROC

Arkansas ATN / Activities

- Created a Family Advisory Board (FAB), whose members work on a variety of ATN projects (Steve Dannaway and Regina Moore)
  - Autismo Arkansas, launched as an autism awareness campaign using social media and media contacts available through the Mexican consulate, and now providing family support for Latino families at DDC, among other outreach activities (Suzanne Mancera)

Arkansas ATN / Activities

- Created a Family Advisory Board (FAB), whose members work on a variety of ATN projects (Steve Dannaway and Regina Moore)
  - Project PAAK: Parent Advocates for Awesome Kids, working with parent advocates to conduct small group seminars for parents to demystify the developmental evaluation process and provide parent support (Angeletta Giles)

Arkansas ATN / Activities

- Created a Family Advisory Board (FAB), whose members work on a variety of ATN projects (Steve Dannaway and Regina Moore)

- Autism Connections Support Group, providing a personal and ongoing resource for parents who have questions about autism and who need help navigating the many aspects of care, offering regular meetings for education and support. Maintains an information kiosk at DDC (Steve and Teresa Dannaway, Erin Rice, et. al)
    - Typically meets at 10 am the first Wednesday every month at Panera Bread on University

Arkansas ATN / Activities

- Established the DDC Family Care Navigator Program (Teresa Dannaway and Angeletta Giles)
  - Mentors parents on the prevention and intervention of child development concerns.
  - Disseminates materials on community resources and supports for families
  - Collaborates and communicates with the clinical team working with a child
  - Provides one-on-one family support and follow up
- DDC clinicians refer to the Navigator Team via email to the team, or face to face on days when a Family Navigator is in clinic

Arkansas ATN / Activities

- Project SPAECS: Spotting Autism in Early Child Care Settings
- PIs: Maya Lopez, MD and Jayne Bellando, PhD
- This project has grown from a successful workshop for childcare providers on ASDs, covering diagnostic criteria, core behaviors and medical co-morbidities, debunking myths, how to talk to parents about their child's developmental concern, and classroom interventions to help children with communication, play, social and transition issues, to development of a web-based version of SPAECS (Web-SPAECS), accessible from the Healthy Child Care Arkansas (HCCAR) web site.

Arkansas ATN / Activities

- The SPAECS curriculum now includes newest information about autism, more videos to show behavioral symptoms of ASD (with neurotypical children as comparisons) and videos to show how to implement interventions.
- With Web-SPAECS, this training can have a wider reach among childcare providers as well as other professionals and parents.

- SPAECS
- Healthy Child Care Arkansas

Standards of Practice

The following resources are provided for information and reference, and may be relevant as the Task Force develops recommendations for future areas of focus.

Standards of Practice

Sources of information (see web sites for details)

- American Academy of Pediatrics (AAP)
- American College of Medical Genetics and Genomics (ACMG)
- Autism Speaks®
- Centers for Disease Control and Prevention
- Cochrane Reviews©
- National Autism Center, National Standards Project, Phase 2
- UpToDate®

Standards of Practice

Diagnosis and Workup

Information synthesized from listed sources where there was consensus of recommendations.

See sources for details of recommendations

First Tier Evaluation

- At a minimum, the diagnostic evaluation should include documentation of whether the child's symptoms meet DSM-5 and/or ICD-10 criteria for ASD
- The diagnostic evaluation also should include use of a diagnostic instrument with at least moderate sensitivity and high specificity for ASD
  - recommended by the American Academy of Child and Adolescent Psychiatry, the American Academy of Neurology, and the American Academy of Pediatrics:
    - Measures relying on parent report – The Autism Behavior Checklist (ABC), Gilliam Autism Rating Scale, 2nd edition (GARS-2), and the Autism Diagnostic Interview-Revised (ADI-R)
    - Measures using direct observation – The Childhood Autism Rating Scale (CARS) and the Autism Diagnostic Observation Schedule-Generic (ADOS-2)

First Tier Evaluation

- Should include a comprehensive assessment, preferably by a team that has expertise in the diagnosis and management of ASD
- Includes search for conditions that are known to play etiologic role in ASDs
- May also determine whether coexisting medical conditions are present

First Tier Evaluation

Best practice guidelines identify the following six components of a comprehensive diagnostic evaluation for autism:

1. Parent or caregiver interview
   - Standardized parent interviews regarding current concerns and behavioral history
   - A complete history (incl. 3-generation family pedigree, psychosocial)
2. Review of relevant medical, psychological, and/or school records
3. Cognitive/developmental assessment
4. Direct play observation
5. Measurement of adaptive functioning
6. Comprehensive medical examination
   - Physical examination (incl. growth and HC, birthmarks, etc., dysmorphology)
   - Neurologic examination (incl. vision, hearing)

First Tier Evaluation

If ASD is confirmed (i.e., meets DSM-5 and/or ICD-10 criteria), then

- Genetic diagnostic testing should be offered to all patients
  - May identify a reason for child's developmental disability
  - Help family understand recurrence risk
  - If a specific disorder is identified, can alert family to potential health conditions in affected child or other family members.

First Tier Evaluation

Identification of a genetic diagnosis may provide additional information about prognosis, expected outcome, and recurrence risk.

However, few studies have evaluated the effect of genetic testing on such outcomes and it is unclear whether or not genetic testing affects health outcomes.

First Tier Evaluation

- DNA testing for fragile X (to be performed routinely for male patients only)
- DNA testing for fragile X in females if indicators present (e.g., family history and phenotype).
- Chromosomal Microarray (CMA)

Second Tier Evaluation

- If specific syndromic diagnosis is suspected, proceed with targeted testing
- If appropriate clinical indicators present, perform metabolic and/ or mitochondrial testing
- Alternatively, consider a referral to a metabolic specialist

Second Tier Evaluation

Other Genetic Testing

- MECP2 gene mutation and sequence analysis for girls with microcephaly or deceleration of head growth and other features of Rett syndrome, or who present with stereotypical hand-wringing movements and developmental regression (AAP)
  - ACMG recommends MECP2 sequencing for all females with ASDs
- MECP2 gene mutations are extremely rare in males but consider in boys with clinical features of Rett syndrome or severe developmental regression, consult with genetic specialist.

Second Tier Evaluation

- PTEN testing only if the head circumference is >2.5 SD above the mean
- Karyotype indicated for patients where a balanced translocation is suspected (microarray will not detect these lesions)
  - If there is a history of more than 2 miscarriages
  - If a specific chromosomal syndrome such as Down syndrome is suspected clinically
- Additional genetic testing (beyond CMA, fragile X, and possibly karyotype) is indicated only for individuals with dysmorphic features, microcephaly, macrocephaly, cognitive impairment, suspicious medical or family history, or in cases where prenatal genetic counseling is desired

Second Tier Evaluation

Metabolic Testing

- **Disorders of amino acid, carbohydrate, purine, peptide, and mitochondrial metabolism account for less than 5 % of cases of ASD.**
- **Although metabolic testing is not necessary in routine evaluation of all children with ASD, it may be indicated if there are symptoms or signs of a metabolic disorder.**

Second Tier Evaluation

Clinical symptoms that prompt metabolic or mitochondrial testing

- Lethargy (esp. associated with mild illnesses)
- Hypotonia/dystonia
- Poor growth, microcephaly
- Seizures (especially early onset)
- Developmental regression (esp. associated with illness or fever)
- Dysmorphic or coarse features
- Ataxia or other movement disorder
- Cyclic vomiting
- Gastrointestinal dysfunction, gastroparesis
- Specific food intolerance (e.g., protein)
- Unusual odors
- Lactic acidosis
- Acid/base or electrolyte disturbances
- Anemia with an elevated mean corpuscular volume

Second Tier Evaluation

Other Medical Workup

- Serum lead and ferritin levels.
  - Children with pica should be monitored as long as pica persists
  - Serum ferritin may also be indicated to monitor iron stores
- There is no evidence that hair analysis, micronutrient levels, intestinal permeability studies, stool analyses, tests for yeast metabolites, urinary peptides, or mercury levels are helpful

Second Tier Evaluation

Other Medical Workup

- **Electroencephalogram (EEG)**
  - **Screening EEGs on all children with ASDs are not currently recommended**
  - **EEG rec for children with hx of seizures, acute developmental regression, unexplained behavioral change, or suspicion of subclinical seizures**
- **Magnetic resonance imaging (MRI)**
  - **Isolated, stable macrocephaly is not, in itself, an indication**
  - **Consider in children with acute regression, microcephaly, midline facial defects, neurocutaneous lesions, or abnormalities on neurologic examination**

Standards of Practice

Interventions

Information synthesized from listed sources where there was consensus of recommendations, except where noted.

See sources for details of recommendations

Goals of Treatment

- Early diagnosis and early intensive treatment have the potential to affect outcome, particularly with respect to behavior, functional skills, and communication
- Treatment of ASD focuses on behavioral and educational interventions that target the core symptoms.
  - Treatment programs should be monitored to ensure appropriate response to therapy; the program should be modified as the child's needs change
  - Pharmacologic interventions may be used as an adjunct to address medical or psychiatric comorbidities.

Goals of Treatment

- The goals of treatment are to maximize functioning, move the child toward independence, and improve the quality of life.
- Specific goals are to improve core symptoms and adaptive skills, decrease negative behaviors, and promote academic functioning and cognition.
- Practical and ethical factors have made it challenging to evaluate intervention programs in randomized controlled trials.
- Systematic reviews of behavioral and educational interventions for children with ASD suggest that earlier and more intensive therapies are associated with better outcomes.
- However, the evidence is insufficient to endorse any particular therapy.

UpToDate

Attributes Of Successful Programs

- A high staff-to-student ratio of 1:1 or 1:2
- Individualized programming for each child
- Teachers with special expertise in working with children with autism
- A minimum of 25 hours per week of services
- Ongoing program evaluation and adjustment
- A curriculum emphasizing attention, imitation, communication, play, and social interaction
- A highly supportive teaching environment
- Predictability and structure
- Functional analysis of behavior problems
- Transition planning
- Family involvement
- Close monitoring and modification as a child's needs change

UpToDate

The Strength of Evidence Classification System

- The National Standards Project, Phase 2 (NSP2) reviewed studies published between 2007 and February of 2012.
- The combined results of NSP1 and NSP2 include data from more than 1,000 studies. This is the largest review of its kind for individuals with ASD.

- NSP2 developed various classification systems to grade ASD interventions.

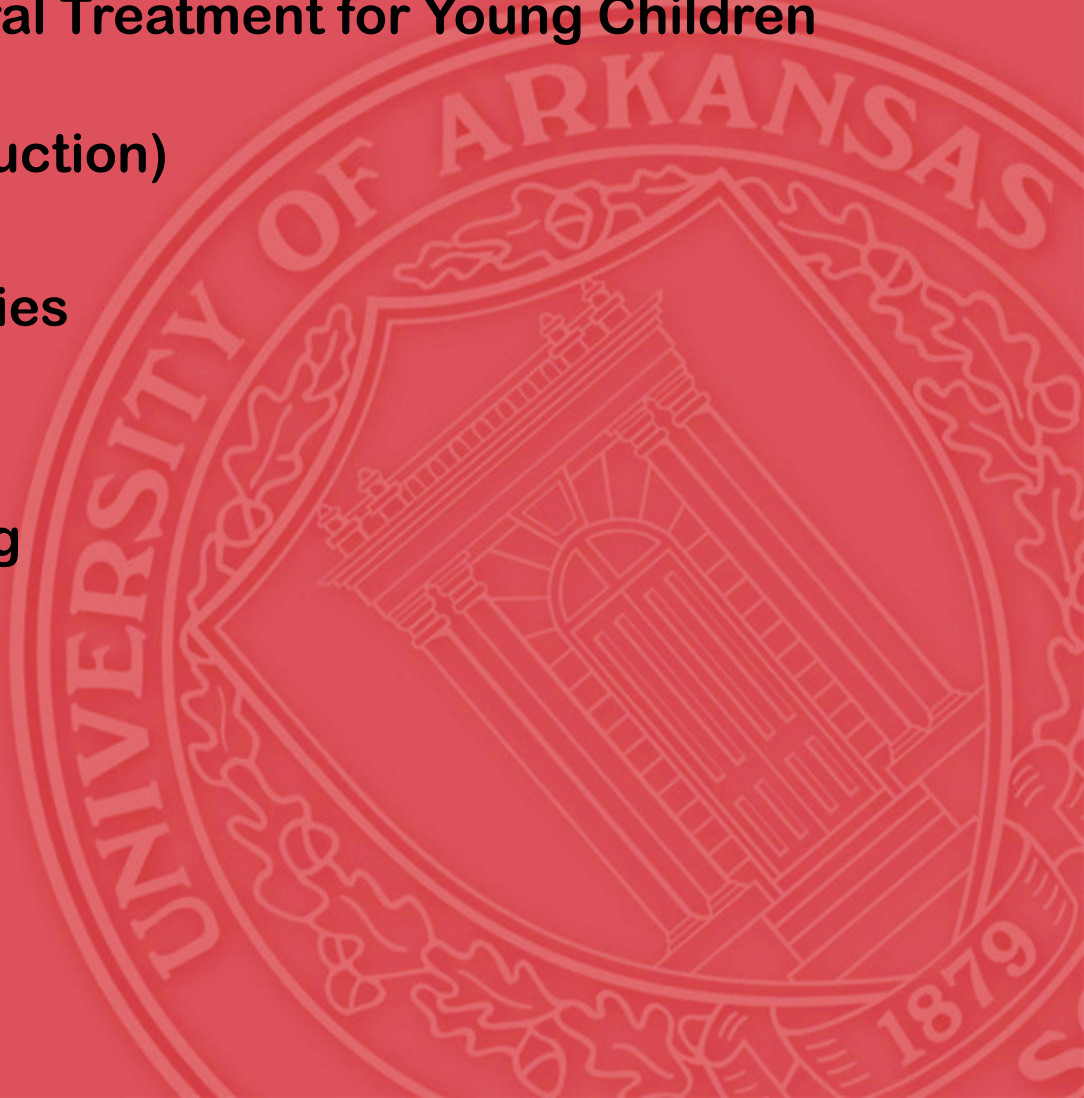
The Strength of Evidence Classification System

The Strength of Evidence system includes three levels

- **Established → Sufficient evidence is available to confidently determine that an intervention produces favorable outcomes for individuals on the autism spectrum. That is, these interventions are established as effective.**
- **Emerging → Although one or more studies suggest that an intervention produces favorable outcomes for individuals with ASD, additional high quality studies must consistently show this outcome before we can draw firm conclusions about intervention effectiveness.**
- **Unestablished. → There is little or no evidence to allow us to draw firm conclusions about intervention effectiveness with individuals with ASD. Additional research may show the intervention to be effective, ineffective, or harmful.**

Interventions at the Established Level of Evidence

- Behavioral Interventions
- Cognitive Behavioral Intervention Package
- Comprehensive Behavioral Treatment for Young Children
  - Aka ABA, EIBI
- Language Training (Production)
- Modeling
- Natural Teaching Strategies
- Parent Training
- Peer Training Package
- Pivotal Response Training
- Schedules
- Scripting
- Self-management
- Social Skills Package
- Story-based Intervention
  - e.g., Social Stories

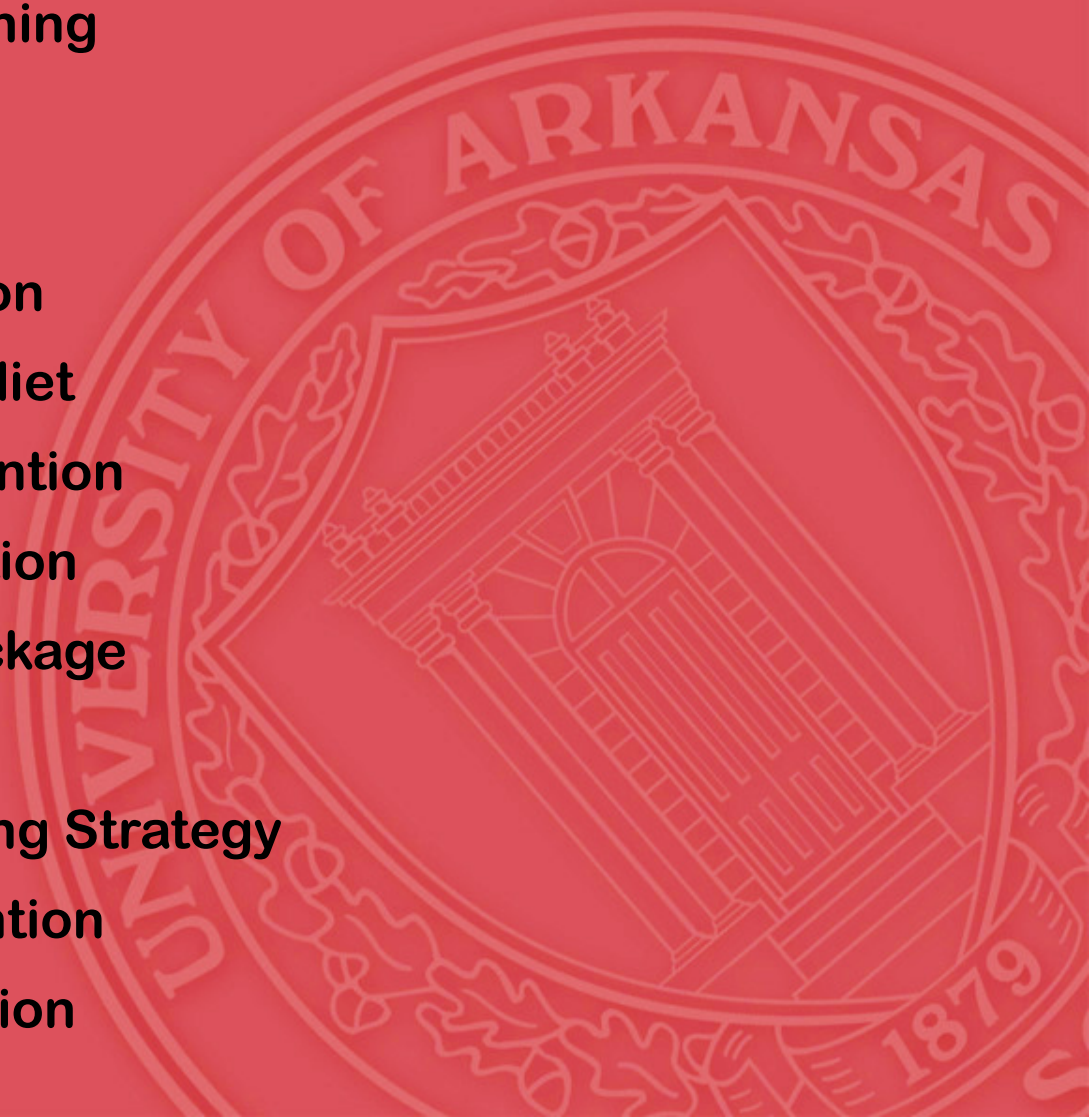


Interventions at the Emerging Level of Evidence

- Augmentative and Alternative Communication Devices
- Developmental Relationship-based Treatment
- Exercise
- Exposure Package
- Functional Communication Training
- Imitation-based Intervention
- Initiation Training
- Language Training (Production & Understanding)
- Massage Therapy
- Multi-component Package
- Music Therapy
- Picture Exchange Communication System (PECS)
- Reductive Package
- Sign Instruction
- Social Communication Intervention
- Structured Teaching/TEACCH
- Technology-based Intervention
- Theory of Mind Training

Interventions at Unestablished Level of Evidence

- Animal-assisted Therapy
- Auditory Integration Training
- Concept Mapping
- DIR/Floor Time
- Facilitated Communication
- Gluten-free/Casein-free diet
- Movement-based Intervention
- SENSE Theatre Intervention
- Sensory Intervention Package
- Shock Therapy
- Social Behavioral Learning Strategy
- Social Cognition Intervention
- Social Thinking Intervention



Interventions for Adults (22+ Years)

- The only intervention identified as Established is Behavioral Interventions.
  - The Behavioral Intervention category consists of applied behavior analytic interventions to increase adaptive behaviors and decrease challenging behaviors.
- The only intervention identified as Emerging is the Vocational Training Package
- The following interventions fall into the Unestablished level of evidence for Adults:
  - Cognitive Behavioral Intervention Package
  - Modeling
  - Music Therapy
  - Sensory Integration Package

Technical Expert Panel, HRSA Autism Intervention Research – Behavioral (AIR-B) Network

Pediatrics, November 2012, VOLUME 130 / ISSUE Supplement 2

Nonmedical Interventions for Children With ASD: Recommended Guidelines and Further Research Needs

Information edited from TABLE 2 Summary of Evidence

Findings	Strength of Evidence
Comprehensive programs targeting multiple core deficits	
Behavioral programs based on Lovaas/ applied behavioral analysis (ABA)	
There was not enough evidence to suggest the superiority of 1 behavioral curriculum over others.	Moderate
Higher intensity (hours per week) and higher duration (in months or years) led to better outcomes. Twenty hours per week was the minimum intensity of most comprehensive programs.	Moderate
Developmental	
Scottish Autism Center comprehensive program. Improvements in socialization, daily living skills, and motor and adaptive behavior were reported.	Low

Technical Expert Panel, HRSA Autism Intervention Research – Behavioral (AIR-B) Network

Information edited from TABLE 2 Summary of Evidence

Findings	Strength of Evidence
Comprehensive programs targeting multiple core deficits	
Integrative: Behavioral + Developmental	
Early Start Denver Model has reported significant gains in cognitive ability and other core deficits in preschool-aged children.	Moderate
Other programs such as STAR, the Walden Toddler Program, and ABA combined with TEACCH showed improvements in core deficits in 1 uncontrolled observational study each.	Low
Environmental support	
2 poor-quality nonrandomized controlled trials of TEACCH to nonspecific educational programs. Both small studies were conducted in Italy by the same researchers.	Low

Technical Expert Panel, HRSA Autism Intervention Research – Behavioral (AIR-B) Network

Information edited from TABLE 2 Summary of Evidence

Findings	Strength of Evidence
Social skills programs for higher-functioning children and adolescents	
There was moderate, consistent evidence that social skills programs as a whole are effective for both children and adolescents. Effect sizes tend to be significant and fairly large. However, analyses could not determine which approaches are best for which children. Effective interventions took place in both individual and group settings.	Moderate
Interventions for children with no or limited language	
Picture Exchange Communication System (PECS)	
Results in communication/social skills were consistently positive in the short term but inconsistent in the long term. The outcome effect sizes varied across studies.	Moderate

Technical Expert Panel, HRSA Autism Intervention Research – Behavioral (AIR-B) Network

Information edited from TABLE 2 Summary of Evidence

Findings	Strength of Evidence
Interventions for children with no or limited language	
Augmentative and alternative communication devices	
There are no controlled trials or observational studies on the efficacy or effectiveness of Augmentative and Alternative Communication (AAC) interventions; only single-subject studies have been reported.	Insufficient
Auditory integration training	
A previous systematic review reported no significant improvements in sound sensitivity in 3 controlled trials. None of these trials reported significant improvement in core deficits. In a trial published after the review, there was no improvement in sound sensitivity, but did report improvements in language, intelligence, and social skills.	Moderate: for ineffectiveness

Behavioral And Educational Interventions

- **Interventional models for treatment may include**
  - **Intensive behavioral interventions (based upon the principles of Applied Behavior Analysis)**
  - **Structured Teaching (including the Treatment and Education of Autistic and related Communication-handicapped CHildren [TEACCH] model)**
  - **Developmental/relationship-based models (such as Developmental Individual Difference [DIR or Floortime])**
  - **Models that integrate various approaches.**
  - **The evidence is insufficient to recommend one of these models over another.**
  - **However, there is moderate evidence that greater intensity (in hours per week) and greater duration (in months) of treatment lead to better outcomes**

UpToDate

Types of Applied Behavior Analysis (ABA)

ABA encourages positive behaviors and discourages negative behaviors in order to improve a variety of skills. The child's progress is tracked and measured.

There are different types of ABA. Examples include:

- Discrete Trial Training (DTT)
  - DTT is a style of teaching that uses a series of trials to teach each step of a desired behavior or response. Lessons are broken down into their simplest parts and positive reinforcement is used to reward correct answers and behaviors. Incorrect answers are ignored.
- Verbal Behavior Intervention (VBI)
  - VBI is a type of ABA that focuses on teaching verbal skills.

UpToDate

Types of Applied Behavior Analysis (ABA)

- Pivotal Response Training (PRT)
  - PRT aims to increase a child's motivation to learn, monitor his own behavior, and initiate communication with others. Positive changes in these behaviors should have widespread effects on other behaviors.
- Early Intensive Behavioral Intervention (EIBI)
  - This is a type of ABA for very young children with an ASD, usually younger than five, and often younger than three.

UpToDate

Early Intensive Behavioral Intervention (EIBI)

- Cochrane review 2012 of early intensive behavioral intervention (EIBI) for increasing functional behaviors and skills in young children with ASD reported there is some evidence that EIBI is an effective behavioral treatment for some children with ASD.
- However, current state of evidence is limited because of reliance on data from non-randomized studies (CCTs) due to the lack of RCTs.
- Additional studies using RCT research designs are needed to make stronger conclusions about effects of EIBI for children with ASD.

UpToDate

Behavioral And Educational Interventions

- Parent-mediated interventions may help families interact with their child, promote development, and increase parental satisfaction, empowerment, and mental health.
- However, which parental interventions maximize outcomes is unknown.
- In addition to providing direct interventions, general parental involvement in the treatment program is essential and should include parent training and collaboration.

UpToDate

Behavioral And Educational Interventions

- Children with ASD benefit most from language interventions that span settings and are incorporated into their daily routines.
- There is insufficient evidence to support a specific methodology (e.g., traditional speech and language interventions, behaviorally based strategies, augmentative communication strategies, visual support), and a variety of methods may be used.

UpToDate

Types of Interventions

- Traditional occupational therapy is often used to address deficits in adaptive functioning and fine motor skills.
  - There is little research regarding traditional occupational therapy for children with ASD.
- Sensory integration therapy for children with ASD is controversial.
  - The evidence regarding its benefits is inconsistent.
  - It may be warranted for specific indications (e.g., to calm the child, reinforce desired behaviors, or help with transitions) within a comprehensive behavioral and educational program.
  - Continued use of sensory integration should be based upon the treatment response in the individual child.

UpToDate

Social Skills Interventions

- Interventions that address social skills deficits that have evidence of benefit from well-controlled studies include interventions that address joint attention, modeling, peer training, and story-based interventions.
- There is less evidence to support social and pragmatic groups, although these are used in clinical practice with success.
- Cochrane review in 2012 noted that for social skills groups for people aged 6 to 21 years with ASD, there is some evidence that such groups can improve social competence for some children and adolescents with ASD.
- More research is needed to draw more robust conclusions, especially with respect to improvements in quality of life.

UpToDate

Complementary And Alternative (CAM) Therapies

Evaluation of biologic-based complementary and alternative (CAM) interventions for autism spectrum disorder (ASD) is ongoing.

- **Few CAM therapies have been proven effective / ineffective or safe in controlled trials.**
- **The scientific evidence for most interventions is insufficient to make recommendations for or against use.**
  - **In such cases, the clinician and family must weigh the potential benefits and risks, including competition with validated treatment for time, effort, and financial resources.**

UpToDate

Complementary And Alternative (CAM) Therapies

- CAM therapies, as defined by the National Center for Complementary and Alternative Medicine (NCCAM), are "a group of diverse medical and healthcare systems, practices, and products that are not generally considered to be part of conventional medicine."
- Ask families of children with ASD specifically about the use of CAM therapies.
- It is important for clinicians who care for children with ASD to become knowledgeable about CAM therapies and to provide balanced information and advice about the potential benefits and risks.

UpToDate

Examples of complementary and alternative medicine therapies used for autism spectrum disorders

Mind-body medicine
Acupuncture*
Auditory integration training*
Biofeedback and neurofeedback*
Electroencephalography¶
Hypnosis*
Interactive metronome*
Music therapyΔ
Neuromodulation*
Yoga*

* There is little evidence of efficacy or safety; clinicians and families must weigh the unknown benefit against the potential risks (including competition with validated therapies for time, effort, and financial resources).
¶ There is little evidence that these treatments are effective but they have the potential to be harmful.
Δ There is some evidence of efficacy and little evidence of harm.
◇ There little evidence that these treatments are effective, but they have the potential for serious adverse events.
§ There is good evidence that these therapies are not effective.
¥ Therapeutic horseback riding is associated with a risk of injury similar to that in other "limited contact" recreational activities (eg, baseball, skating); appropriate supervision is necessary.

Examples of complementary and alternative medicine therapies used for autism spectrum disorders

Biologically based practices
Antibiotics, antifungals¶
Live cell and stem cell therapy◇
Chelation◇
Diet (may include probiotics, yeast-free, gluten-free/casein-free, specific carbohydrate diet, vitamin, mineral, and other dietary supplements, etc)¶
Digestive enzymes*
Gamma-aminobutyric acid (GABA)*
Homeopathy¶
Hyperbaric oxygen therapy (HBOT)◇
Intravenous immune globulin (IVIG)◇
Secretin§
Sulforaphane*
Supplements: carnitine, coenzyme Q, dimethylglycine, folinic acid, lysine, melatonin, omega-3 fatty acids, trimethylglycine, tuarine, vitamin B6-magnesium, vitamin B12*

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Examples of complementary and alternative medicine therapies used for autism spectrum disorders

Manipulation
Chiropractic¶
Craniosacral manipulation¶
Massage/touch therapy/craniosacral therapy*
Qigong*
Body-based practices, energy medicine
Prayer*
Hippotherapy (therapeutic horseback riding)*¥
Transcranial magnetic stimulation◇
Miscellaneous
Facilitated communication§

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Music Therapy ☺

- Based upon hypothesis that musical improvisation processes (perhaps a kind of nonverbal or preverbal language) may help to develop communicative skills, social interaction capacity.
- Cochrane review in 2014 found evidence that music therapy may help children with ASD improve skills in primary outcome areas including social interaction, verbal communication, initiating behavior, and social-emotional reciprocity; may also enhance non-verbal communication skills within therapy context. In secondary outcome areas, may contribute to increasing social adaptation skills and to promoting quality of parent-child relationships.
- Findings should be interpreted with caution but suggest some benefit. Additional studies with larger sample sizes are needed to confirm this result.
- Application of music therapy requires specialized academic and clinical training.

UpToDate

Melatonin ☺

- A hormone produced by the pineal gland that regulates sleep.
  - Potential benefits for sleep regulation have been suggested by a few scientific studies.
    - Results suggest melatonin may be effective in short-term in helping children with ASD to fall asleep and sleep longer when provided 30 minutes before bedtime.
    - There are no standard dosing guidelines for administration
    - No information on long-term use or side effects
    - Side effects may include difficulty waking, daytime sleepiness, and enuresis
  - [We] suggest melatonin for patients with ASD who have difficulty falling asleep and staying asleep despite appropriate sleep hygiene and behavioral or environmental interventions

UpToDate

‘Theory of Mind’ Interventions 😐

- A 2014 Cochrane review of evidence on the use of interventions for people with ASD, based on the psychological model ‘Theory of Mind’ found some evidence that ToM, or a precursor skill, can be taught to people with ASD, but little evidence of maintenance of that skill, generalization to other settings, or developmental effects on related skills.
- Evidence has been graded of 'very low' or 'low' quality
- Further longitudinal designs and larger samples are needed to help elucidate both the efficacy of ToM-linked interventions and the explanatory value of the ToM model itself.

UpToDate

Hippotherapy (Horseback Riding) 😐

- Based upon hypothesis that therapeutic horseback riding stimulates multiple domains of functioning (e.g., cognitive, social, gross motor).
- Although there is some evidence to support benefits, additional studies are necessary before it can be recommended.
- Therapeutic horseback riding is associated with a risk of injury similar to that in other "limited contact" recreational activities (e.g., baseball, skating). It is important to emphasize the need for appropriate supervision in families who choose to participate.

UpToDate

Omega-3 Fatty Acids 😐

- EPA and DHA are essential fatty acids with documented cardiovascular benefits.
- Some studies suggest that plasma omega-3 concentrations in children with ASD are decreased, but no clinical correlation has been established.
  - It is not clear whether omega-3 supplementation is beneficial for children with ASD.
  - The American Heart Association suggests two servings of fish per week for the cardiovascular benefit.
  - A systematic review and meta-analysis concluded that there is insufficient evidence to endorse the use of omega-3 fatty acids for improvement of ASD symptoms

UpToDate

B6-Magnesium 😐

- Long history of use of vitamin B6 (pyridoxine) and magnesium for treatment of mental health disorders (magnesium added to reduce side effects of B6).
- However, there has been little research specifically evaluating this intervention for ASD.
  - A 2005 systematic review of three small and methodologically flawed randomized controlled studies (total of 33 patients) of vitamin B6 and magnesium therapy for children with ASD found the data inconclusive.
  - Megadoses of vitamin B6 (>100 mg/day) may result in neuropathy.

UpToDate

Probiotics 😐

- The use of probiotics as a treatment for autism is based upon the hypothesis that there is an imbalance in intestinal microbes in individuals with ASD.
- Evidence from high-quality studies supporting the efficacy of probiotics in children with ASD is lacking.
- There are no current studies demonstrating harm.
- Probiotics are regulated by the US Food and Drug Administration (FDA) for impurities and quality.

UpToDate

Dimethylglycine (DMG) 😐

- Derivative of amino acid glycine, thought to reduce lactic acid build-up during stress, enhance oxygen use during times of hypoxia, and reduce seizure activity.
- Use is based upon hypothesis that metabolic abnormalities contribute to development of autism.
- There is insufficient information about efficacy and safety of DMG to make recommendations about its use in children with ASD.
  - Small randomized controlled trials in children with ASD have demonstrated no benefit.
  - Adverse effects have not been documented.

UpToDate

Sulforaphane 😐

- An antioxidant derived from broccoli sprout extracts.
- It increases activity of genes that protect aerobic cells against oxidative stress, inflammation, and DNA damage; hypothesized to reverse abnormalities associated with ASD including neuroinflammation; oxidative stress; and decreased glutathione synthesis, mitochondrial function, and oxidative phosphorylation.
- Preliminary study results are promising, but pending additional study, [we] do not suggest sulforaphane supplementation for children with ASD; this study was too small to adequately assess adverse effects.

UpToDate

Oxidative Therapies 😐

- Vitamin C and other oxidative therapies (e.g., methylcobalamin and folinic acid) have some evidence of potential benefit for children with ASD but not sufficiently strong to make a recommendation for or against use.
- Zinc and digestive enzymes have not been evaluated in controlled trials.

UpToDate

Antifungal Agents 😐

- The use of antifungal agents (e.g., nystatin, fluconazole) as a treatment for autism is based upon hypothesis that there is yeast overgrowth secondary to an imbalance in microbes in individuals with ASD.
- There is insufficient information about the efficacy and safety of the antifungal agents to make recommendations about their use in children with ASD.
  - No controlled trials have evaluated these therapies in children with ASD.
  - Adverse effects of antifungal agents may include hepatotoxicity, anemia, diarrhea, and exfoliative dermatitis.

UpToDate

Gluten-free casein-free (GFCF) Diet 😐

- Hypothesis is that increased permeability allows gluten and casein peptides to leak from gut, causing excessive opioid activity and resulting in behaviors observed in ASD.
  - Not confirmed that children with ASD have increased rates of celiac disease or excessive opioid-like compounds in their urine.
  - Insufficient information about efficacy and safety of GFCF diet to make recommendations about use
    - Pending further study, the UK 2013 NICE clinical guideline on ASD suggests that potential risks of GFCF diet outweigh benefits.
    - A 2014 systematic review of studies (1970 to 2013) evaluating the GFCF diet in children with ASD concluded that evidence is limited and weak.
  - Although GFCF diet does not appear to have beneficial effects at the population level, benefits for individuals in certain subgroups (e.g., those with significant GI disease) cannot be excluded.
  - Potential risks (e.g., lower intake of calcium, vitamin D, and amino acids; decreased bone density)

UpToDate

Hyperbaric Oxygen 😐

- Based upon hypothesis that increasing atmospheric pressure enhances oxygen delivery to brain to reduce swelling and promote brain recovery.
- [We] do not suggest the use of HBOT as a treatment for ASD.
- There is insufficient information about efficacy.
  - Available trials have reported clinical benefits, but studies are not well designed, and no information reported about whether meaningful improvement was sustained over time.

UpToDate

Transcranial magnetic stimulation (TMS) 😐

- An energy-based therapy that is proposed to work through electromagnetic induction, which modifies neuroexcitability, proposed in ASD based upon hypothesis of disturbance of cortical modularity.
- [We] do not suggest TMS for children with ASD.
- Additional study is necessary before TMS can be recommended.
  - Controlled and uncontrolled studies have demonstrated potential benefit in patients with depression, bipolar illness, schizophrenia, epilepsy, and Tourette syndrome.
- Unrelated to the use of commercially obtained magnets, which are applied topically.

UpToDate

Nonbiologic-based interventions that have some evidence of potential benefit 😐

- **Nonbiologic-based intervention therapies that have some evidence of potential benefit for children with ASD, but not sufficiently strong to make a recommendation for or against use**
  - **Yoga**
  - **Qigong massage**
  - **Acupuncture**
  - **Neurofeedback**

UpToDate

Auditory Integration Training (AIT) *☹

- Based upon hypothesis that repeated exposure to altered sound via headphones functionally modifies central auditory processing, impacting language and behavior.
- The AAP considers AIT to be investigational therapy.
- The Technical Expert Panel (experts in psychology, dev. pediatrics, child psychiatry, and education, and parents of children with autism) recommends against it.
  - A systematic review of six RCTs of AIT in children with ASD found inconsistent results: 3 studies = no benefit, 3 = some improvements on a checklist with uncertain clinical relevance.
  - Another systematic review found that AIT was ineffective in 4 out of 5 trials.
- Cochrane review in 2011 found there is no evidence to support the use of auditory integration therapy at this time.

UpToDate

Intravenous Immunoglobulin (IVIG) *☹

- The use of intravenous immunoglobulin (IVIG) and other immune therapies for children with ASD is based upon hypothesis that fetal brain development is related to the prenatal immune response.
  - However, the data underlying this hypothesis are limited.
- [We] do not suggest IVIG for the treatment of ASD in the absence of other indications for IVIG (e.g., documented immune deficiency)
  - An open trial of IVIG in 10 children with autism suggested subjective improvement. However, subsequent case series failed to replicate this finding.
  - Potential adverse effects of IVIG and other immune therapies include transmission of bloodborne pathogens.

UpToDate

Facilitated Communication ☹

- Technique in which a facilitator physically guides the hand of a nonverbal child in using an output device (e.g., keyboard, mouse, etc.) for communication.
- [We] do not recommend facilitated communication as a means of communicating with children with ASD.
- Reviews of published studies found no evidence to support its use for individuals with communication impairment. Controlled studies revealed that the facilitator, rather than the child, was providing information.
- Facilitated communication must be distinguished from augmentative communication, a method of nonverbal communication in which manual sign, picture exchange, switches, or voice output devices are used without the aid of a facilitator.

UpToDate

Secretin ☹

- A gastrointestinal hormone that inhibits intestinal motility and release of gastric acid and stimulates secretion of pancreatic fluid and bicarbonate.
- Use as a potential therapy for children with ASD is based upon hypothesis that autism is related to GI abnormalities.
- Cochrane review in 2012 stated there is no evidence that single or multiple dose intravenous secretin is effective and as such currently it should not be recommended or administered as a treatment for ASD.

UpToDate

Chelation Therapy ☹

- Process of administering a substance (such as EDTA or DMSA or DMPS) to remove heavy metals from the body.
- Given prior reports of serious adverse events, such as hypocalcaemia, renal impairment and reported death, the risks of using chelation for ASD currently outweigh proven benefits.
- Cochrane review 2015 included data from only one study, which had methodological limitations. As such, no clinical trial evidence was found to suggest that pharmaceutical chelation is an effective intervention for ASD.
- Before further trials are conducted, evidence that supports a causal link between heavy metals and autism and methods that ensure the safety of participants are needed.

UpToDate

Nonbiologic-based interventions that have not been evaluated in controlled trials

- Craniosacral therapy
- Chiropractic care
- Therapeutic touch
- Healing touch
- Reiki

Effective Treatment	Symptoms Addressed	Most Frequently Occurring Side Effects
Risperidone	Core symptoms (generally), maladaptive behavior, hyperactivity, irritability	Weight gain and sedation
	It is the only medication approved by the FDA for the treatment of children and young adults with ASD. *Note: Has marginal evidence of improving sleep disturbance*	
Methylphenidate	Inattention and hyperactivity (but response rate may be lower in children with ASD)	Significant agitation
	Note: (1) Methylphenidate is known to be ineffective with restricted/repetitive behavior and irritability; (2) Methylphenidate has marginal evidence of improving behavioral symptoms and maladaptive behavior.	
Medication with Marginal Evidence	**Symptoms Possibly Addressed**	**Most Frequently Occurring Side Effects**
NRI anti-depressants	Core symptoms, hyperactivity	Dry mouth, insomnia, nausea, headaches, stomach upset
SSRI anti-depressants (especially fluoxetine and escitalopram)	Restricted, repetitive nonfunctional behavior	Nausea, diarrhea, headaches, agitation
Antihistamines	Core symptoms	Drowsiness, dizziness, headache, loss of appetite, stomach upset, vision changes, irritability, dry mouth and dry nose
Atypical antipsychotics (beyond risperidone)	Core symptoms, behavioral symptoms and maladaptive behavior, hyperactivity	These side effects are medication specific.
Automatic cognition enhancers	Core symptoms, social interactions	None
Certain proteins/amino acids	Social interactions	None
Naltrexone	Behavioral symptoms and maladaptive behavior	Anxiety, appetite loss, chills, constipation, delayed ejaculation, diarrhea, dizziness, drowsiness, feeling down, headache, increased energy, increased thirst, irritability, joint and muscle pain, low energy, nausea, nervousness, sleeplessness, stomach pain/cramps, vomiting
	Note: Naltrexone is known to be ineffective in the treatment of communication, social interaction, or restricted, repetitive, nonfunctional patterns of behavior.	
Psychostimulants such as methylphenidate	Behavioral symptoms and maladaptive behavior	Significant agitation
Secretin	Hyperactivity	Difficulty breathing, shortness of breath, dizziness or lightheadedness, rash or itching, slow or irregular heart rate or palpitations, stomach upset, headache, diarrhea, sweating
	Note: Secretin is known to be ineffective in the treatment of core symptoms, stereotypic behavior, and GI disturbance.	
Anti-epileptics (particularly levetiacetam and topiramate)	Hyperactivity	Dizziness, drowsiness, and mental slowing; other side effects like weight gain, metabolic acidosis, nephrolithiasis, angle closure glaucoma, skin rash, hepatotoxicity, colitis, movement and behavioral disorders

From the
National Autism Center
Parent Manual

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Autism Speaks

- https://www.autismspeaks.org
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"Autism Speaks has grown into the world's leading autism science and advocacy organization, dedicated to funding research into the causes, prevention, treatments and a cure for autism; increasing awareness of autism spectrum disorders; and advocating for the needs of individuals with autism and their families."

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