



# Making an Autism Spectrum Disorder Diagnosis

Endorsed by the American Academy of Pediatrics and the Society of Developmental and Behavioral Pediatrics

Developed in partnership with  
Health Resources and Services Administration  
Maternal and Child Health Bureau





# Making an Autism Spectrum Disorder Diagnosis



## Abstract

Billy is a 3½-year-old boy whose mother brings him to see you because of concerns about behavior problems at home and in school. After listening to the mother's concerns, observing Billy in your office, and reviewing his history, you refer Billy for a comprehensive evaluation for autism spectrum disorder (ASD). You follow up with Billy's mother and with specialists involved in his evaluation to ensure the process is completed and to learn the results.

## Case Goal

The diagnosis of autism spectrum disorder (ASD) is made on the basis of detailed information obtained from the child's caregivers, careful observation and assessment of the child, and the use of standardized tools designed to aid in the diagnosis of ASD. *After completion of this module, learners will be able to:*

1. Be familiar with the basic principles regarding the diagnosis and epidemiology of ASD.
2. Understand the diagnostic approach to evaluating a child with suspected ASD.

## Three Steps to Prepare - In 15 Minutes or Less!

- 1 Read through the Facilitator's Guide and make copies of the case and learner worksheet for distribution.
- 2 Identify the key topics you wish to address. Consider:
  - Knowledge level of learners
  - Available time
  - Your familiarity with the subject
- 3 Select and prepare the optional teaching tools you wish to use. *Each case provides a variety of **optional materials** to enhance the learning environment, support facilitator style, focus on different themes, or accommodate different time limitations. These materials are optional for facilitators to use at their discretion.*
  - Handouts: select any you wish to use and make copies for distribution
  - PowerPoint: decide if you wish to use and confirm necessary technical equipment
  - Video: review embedded video and video library, decide if you wish to use, confirm necessary technical equipment, and conduct test run

The following case was developed by the authors. It does not necessarily reflect the views or policies of the Department of Health and Human Services (HHS) or the Centers for Disease Control and Prevention (CDC).

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# Making an Autism Spectrum Disorder Diagnosis

## Key Learning Objectives of This Case

1. *Be familiar with the basic principles regarding the diagnosis and epidemiology of ASD.*
  - a. Describe the two primary areas of impairment in ASD and the severity rating system. (Prompt 3.3 and Handout IV: DSM-5 Diagnostic Criteria for ASD)
  - b. Know the currently reported estimate of the prevalence of ASD in the U.S. (Prompt 4.1)
  - c. Describe the current evidence for the genetic etiology of ASD. (Prompts 4.2 and 4.3)
2. *Understand the diagnostic approach to evaluating a child with a suspected ASD.*
  - a. Identify the important elements of a comprehensive history. (Prompts 1.1 and 1.2)
  - b. Recognize the important features to assess when observing a child's behavior.
  - c. List the aspects of the physical exam that are of particular importance when evaluating for ASD. (Prompt 1.4)
  - d. Describe the components of a comprehensive diagnostic evaluation for ASD. (Prompt 3.1 and Handout I: Components of a Comprehensive Evaluation for ASD)

## Only Have 30 Minutes to Teach? :30

Focus your discussion on principles of diagnosis and the diagnostic approach. Use:

- Handout I: Components of a Comprehensive Evaluation for ASD and Handout IV: DSM-5 Diagnostic Criteria for ASD
- Potential Prompts: 1.1, 1.4, 3.1, and 3.3

## Materials Provided

- Case Worksheet for Learners
- The Case Study: Part I, II, III, IV, V
- Optional Teaching Tools
  - PowerPoint with Embedded Videos
  - Handouts
    - Handout I: Components of a Comprehensive Evaluation for ASD
    - Handout II: Differential Diagnosis of Autism Spectrum Disorder
    - Handout III: AAP screening guidelines
    - Handout IV: DSM-5 ASD Checklist
    - Handout V: Fragile X Syndrome Fact Sheet
  - Video Library
- References

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# Making an Autism Spectrum Disorder Diagnosis

## Getting Started

This case is designed to be an interactive discussion of a scenario residents may encounter in their practice. Participation and discussion are essential to a complete learning experience. This Facilitator's Guide provides potential prompts, suggestions for directing the discussion, and ideas for incorporating the optional teaching tools. It is not designed as a lecture.

Case study icons:



Call-out: step-by-step teaching instructions



Note: tips and clarification



Slide: optional slide, if using PowerPoint



Filmstrip: optional slide contains an embedded video



Paper: potential place to distribute an optional handout



Digital clock: tips if you only have '30 Minutes to Teach'

**Making an Autism Spectrum Disorder Diagnosis**

**Case Study Part 1**

Billy is a 3 1/2-year-old boy you are seeing for the first time in your resident practice. He was born full term following a normal pregnancy and delivery. His newborn screen and neonatal hearing test were normal. At 18 months, he underwent bilateral myringotomy tube placement following repeated bouts of otitis media. His mother also had concerns that he was not speaking any words, and his doctor said, "It's well and good." A follow-up appointment was scheduled for when he turned 2. At his 2-year well-child check, because of the history of global developmental delay, he was referred to early intervention (EI) services.

Three months ago, Billy began attending a specialized preschool in the local school district; there, he receives speech, physical, and occupational therapies. This is the first preschool Billy has attended. He was asked to leave his previous schools because of behavioral problems. Billy's mother reports that his current preschool teacher recommended that she take him to the pediatrician given concerns about his behavior. Since he began preschool, his teachers have reported that he is extremely hyperactive, does not follow directions, and single ignores the children in the class.

Billy's mother reports that he has been in good health recently. She tells you that all of his milestones were delayed, particularly his language. She denies any history of developmental regression. She adds that Billy has made some nice progress since he began receiving EI services. He will now use single words like "juice" and "cookie" to make requests. At home, Billy is a "handful," but he will usually calm down when she turns on his favorite cartoon. She describes him as a sweet and loving boy, but she also shares that he will have prolonged tantrums when denied what he wants and that tantrums will often occur when they are attempting to leave their house. During these tantrums, he will frequently bang his head and bite his hand, which frightens her. For some time now she has been concerned that Billy does not like to play with his siblings because during family get-togethers, but she thought this was because he was an only child and didn't like to share. She had been eagerly awaiting his first day of preschool so that he could spend more time around other children.

When asked about family history, Billy's mother reports that her sister's 7-year-old son is in special education, but she is not sure what kind of evaluation has been done as her sister "does not like to talk about these kinds of things." She mentions that it has been hard for the family, and she finds Billy's preschool reports to be embarrassing and discouraging. She is frustrated and wants the best for Billy.

**Autism Case Training**  
A Developmental-Behavioral Pediatrics Curriculum

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## Why is This Case Important?

It is important for parents to understand that there is no specific lab test or procedure to diagnose ASD. Rather, the diagnosis is made on the basis of detailed information obtained from the child's caregivers, careful observation of the child, and the use of standardized tools specifically designed to help diagnose ASD. The diagnosis may be made by a clinician who has expertise in the diagnosis of ASD or by a team of specialists that may include developmental-behavioral pediatricians, child neurologists, child psychiatrists, psychologists, speech-language pathologists, occupational or physical therapists, educators, and social workers.

Introduce the session goal and format of the case study

## Cultural Competence

It is important for clinicians to understand how different childrearing practices and cultural norms may influence key decisions that parents make regarding their child, including obtaining evaluations and treatment, future planning, and acceptance of the child's diagnosis. Clinicians can approach parents openly and honestly by asking them about their unique style of parenting and how the information or recommendations provided are received.

See the curriculum introduction for additional information on cultural competence and potential discussion questions.



# Making an Autism Spectrum Disorder Diagnosis

## Case Study Part I

Billy is a 3 ½ -year-old boy you are seeing for the first time in your resident practice. He was born full term following a normal pregnancy and delivery. His newborn screen and neonatal hearing test were normal. At 18 months, he underwent bilateral myringotomy tube placement following repeated bouts of otitis media. His mother also had concerns that he was not speaking any words, and his doctor said, “Let’s wait and see.” A follow-up appointment was scheduled for when he turned 2. At his 2-year well-child check, because of the history of global developmental delay, he was referred to early intervention (EI) services.

Three months ago, Billy began attending a specialized preschool in the local school district; there, he receives speech, physical, and occupational therapies. This is the third preschool Billy has attended. He was asked to leave his previous schools because of behavioral problems. Billy’s mother reports that his current preschool teacher recommended that she take him to the pediatrician given concerns about his behavior. Since he began preschool, his teachers have reported that he is extremely hyperactive, does not follow directions, and largely ignores the children in the class.

Billy’s mother reports that he has been in good health recently. She tells you that all of his milestones were delayed, particularly his language. She denies any history of developmental regression. She adds that Billy has made some nice progress since he began receiving EI services. He will now use single words like “juice” and “cookie” to make requests. At home, Billy is a “handful,” but he will usually calm down when she turns on his favorite cartoon. She describes him as a sweet and loving boy, but she also shares that he will have prolonged tantrums when denied what he wants and that tantrums will often occur when they are attempting to leave their house. During these tantrums, he will frequently bang his head and bite his hand, which frightens her. For some time now she has been concerned that Billy does not like to play with his similar-aged cousins during family get-togethers, but she thought this was because he was an only child and didn’t like to share. She had been eagerly awaiting his first day of preschool so that he could spend more time around other children.

When asked about family history, Billy’s mother reports that her sister’s 7-year-old son is in special education, but she is not sure what kind of evaluation has been done as her sister “does not like to talk about these kinds of things.” She mentions that it has been hard for the family, and she finds Billy’s preschool reports to be embarrassing and discouraging. She is frustrated and wants the best for Billy.

Distribute Case Study Part I

Slide 3

# Making an Autism Spectrum Disorder Diagnosis

## Case Study Part I: Discussion Question

After reading the case, ask participants, “What stands out to you about this case?”

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## Case Study Part I: Potential Prompts

- 1.1 What important information have you learned from this introduction? :30
- 1.2 What else do you want to know?
- 1.3 What is your differential diagnosis at this point?
- 1.4 What kinds of things should you look for on observation and physical exam? :30
- 1.5 What type of screening should have occurred at Billy’s 18-month exam?

Follow up with student responses to encourage more discussion:

- What in the case supports that?
- Why do you think that?
- What makes you say that?

## Supporting Information for Potential Prompts

- 1.1 *What important information have you learned from this introduction?* :30
  - History of attainment of milestones
    - History of global developmental delay (delay in multiple developmental domains), particularly language delay
    - No history of regression
  - History of behavior problems
    - Hyperactive
    - Does not follow directions
    - Has extreme tantrums that often include self-injurious behaviors
    - Has difficulty with transitions
  - Possible social-communicative concerns
    - Does not play with other children at school
  - Possible medical causes/contributors to current functioning
    - Normal newborn screen; passed newborn hearing screen
    - History of recurrent otitis media
  - Relevant family history
    - Male cousin in special education
  - Response to intervention
  - Has made improvements since starting early intervention

I. Components of a Comprehensive Evaluation for ASD

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## 1.2 *What else do you want to know?*

:30

- Has he had his hearing tested after the newborn screen?
- How does he let you know what he wants/needs?
- Does he make eye contact?
- Does he have joint attention?
  - Joint attention is shared enjoyment between two people observing an object or event. The child points to an object and looks alternatively between the object and the other person to direct their attention to the object of interest.
- Will he take an object to his parents to show them because he thinks it is interesting or will he only take them something if he needs help? (Does he have “show-and-tell” behavior?)

## 1.3 *What is your differential diagnosis at this point?*

- Autism spectrum disorder
- Hearing problem
- Speech/language delay
- Cognitive impairment/global developmental delay

II. Differential Diagnosis of Autism Spectrum Disorder



## 1.4 *What kinds of things should you look for on observation and physical exam?*

:30

- How does he interact with the examiner? How does he interact with his mother?
- Does he make eye contact with you?
- How does he communicate? Does he use single words, phrases, or sentences? Does he point at objects in the room? Does he use gestures?
- Make note of growth parameters, including head circumference.
- Are there any dysmorphic features?
- Are there any motor stereotypies, such as hand flapping, toe walking, or other unusual repetitive behaviors?

Consider polling the class to learn opinions on differential diagnosis

## 1.5 *What type of screening should have occurred at Billy's 18-month exam?*

- Developmental screening
- ASD-specific screening
- Assessment of family support mechanisms

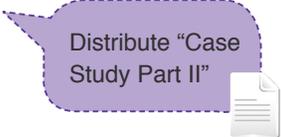
# Making an Autism Spectrum Disorder Diagnosis

## Case Study Part I: Discussion Question

Before moving to Part II, ask participants, “What would you do next?”



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Distribute “Case Study Part II”

### Case Study Part II

At first, Billy clings to his mother, but as you continue to speak with her, he climbs down from her lap and runs around the room touching everything in sight. When you give him a few toys to play with, he briefly inspects them, smells them, and then throws them down. Billy spots a ball in your bag of toys. He points at it and says “ball” without looking at you or his mother. When you toss him the ball, he laughs and makes brief eye contact with you, but then proceeds to kick and chase the ball around the room, ignoring your efforts to engage him in play. You call his name several times and he doesn’t answer. When his mother begins to undress him for the exam, he begins to scream and jump up and down while flapping his hands. She says he tends to have difficulty transitioning from one activity to another. On physical examination, Billy is at the 75th percentile for weight and height, and his head circumference is at the 98th percentile. His ears are prominent, and he has a wide nasal bridge. He has mildly hyperextensible joints. The remainder of his exam is within normal limits.



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## Case Study Part II: Discussion Question

Has your opinion changed with this new information?



Slide 7

## Case Study Part II: Potential Prompts

- 2.1 What do you think about Billy’s behavior in your office?
- 2.2 What next steps should be taken?
- 2.3 What will you tell Billy’s mother?
- 2.4 What are the strengths of this child and family?

# Making an Autism Spectrum Disorder Diagnosis

## Supporting Information for Potential Prompts

### 2.1 *What do you think about Billy's behavior in your office?*

- Does the fact that Billy clings to his mother exclude a diagnosis of ASD?
  - It is sometimes thought that children with ASD do not show any emotions or have attachments with caregivers. While this may sometimes be true, many children with ASD do have relationships with others. However, there are qualitative impairments in these social interactions.
- Note the level of activity
- Note that he smelled several objects.
  - This behavior might suggest sensory preoccupation or sensitivities.
- Billy pointed to a ball. Does the fact that he pointed mean that he does not have ASD?
  - Billy did point to the ball as he named it. However, there was no joint attention involved with the point. He did not look at his mother to see her response as he referenced the ball.
- Billy makes brief eye contact with you. Does this make a diagnosis of ASD more or less likely?
  - Children with ASD may not have a complete lack of a particular skill.
  - Making brief eye contact only once during the entire office visit would be considered marked impairment.
- What do you think about Billy's behavior when his mother took off his clothes?

### 2.2 *What next steps should be taken?*

In this case, there were both parental and physician concerns. This goes directly to “Step 8” of the algorithm:

- Provide parental education
- Simultaneously refer for:
  - Comprehensive ASD evaluation
  - Early intervention/early childhood education services, if not already enrolled
  - Audiologic evaluation
- Schedule a follow-up visit

What “red flags” indicate immediate need for further assessment? (Practice Parameter from the American Academy of Neurology)

- No babbling or pointing or other gesture by 12 months
- No single words by 16 months
- No two-word spontaneous (not echolalic) phrases by 24 months
- Loss of language or social skills at any age

*Note: Billy is older. However, it might be helpful to ask about these when taking a history.*

III. AAP Screening  
Guidelines



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## 2.3 *What will you tell Billy's mother?*

- When you are discussing your concerns with a family, it is often helpful to give specific examples of your concerns (e.g., poor eye contact, lack of joint attention). It is also important to emphasize good skills that the child is exhibiting (e.g., Billy seems to be very attached to you. I'm glad to hear that he has been making progress since he started therapy.)
- Explain the importance of further evaluation and arriving at a diagnosis. It is also important to acknowledge the parents' worries. Many parents do not want their child to be "labeled" and may be hesitant to have a diagnosis given. Explain that having a specific diagnosis helps ensure that their child will receive appropriate therapies and interventions.
- It is important to refer the child for early intervention services as soon as ASD or other developmental disability is suspected. Educate the family on the importance and benefits of starting therapy as early as possible without creating undue panic or alarm.
- Find out what the family knows about ASD. It is usually helpful to explain that ASD is a spectrum and that no two children will have exactly the same characteristics. Each child will have his or her own individual strengths and weaknesses and a child may need more support in some areas than others.
- Give the family literature on ASD and direct them to resources available in the area.
- Answer any questions the family may have and be available if they have questions in the future.
- Emphasize that children with ASD do continue to have warm relationships. It is important for families to have a balance of reality and optimism.

See the "Communicating Abnormal Results from a Screening Tool" module for more detailed information.

## 2.4 *What are the strengths of this child and family?*

It is always important to explore the strengths of a child with autism spectrum disorder or developmental delays. Parents and clinicians may become so focused on the deficits and in some cases the behavioral issues that a child is having, that they aren't able to notice what the child does well. By asking a family about what a child is good at, and what their positive traits are, one is able to frame recommendations for intervention and treatment in the context of these strengths. In addition, asking about what a child likes can be used when discussing next steps. Finally, in addition to exploring the strengths of the child, it is helpful to think about the strengths of the family and how these can be used when discussing options and next steps for treatment. If parents are unable to offer strengths and positive attributes of the child, it is important to acknowledge how difficult and stressful things seem for them at this time. It is always helpful for clinicians to take the time to note changes and improvements in functioning and positive features of the child and narrate these observations to parents.

- The child has made progress since he began to receive EI services.
- He is beginning to use language functionally.
- He is described by his mother as a sweet and loving boy.
- He is pairing language and gesture when he points to the ball and vocalizes.
- He displays some capacity for shared pleasure when the examiner throws him the ball and he laughs and briefly makes eye contact.

# Making an Autism Spectrum Disorder Diagnosis

## Case Study Part III

You share your concerns about the things Billy's mother has told you and about what you have observed during the visit. You tell her that Billy shows some characteristics of a child with autism spectrum disorder. He exhibits decreased eye contact, lack of joint attention, hand flapping, resistance to transitions, and atypical exploration of objects. You recommend she take Billy for additional evaluations. Together, you agree to proceed with a referral for a multidisciplinary evaluation for the presence of autism spectrum disorder, including an audiologic assessment. You ask Billy's mother to return for a follow-up appointment to ensure the evaluation is proceeding as it should.

Distribute Case Study Part III

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## Case Study Part III: Discussion Question

What would you do next?

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## Case Study Part III: Potential Prompts

3.1 What are the usual components of a diagnostic evaluation for ASD?

:30

3.2 What is the medical/genetic workup for a child with a suspected ASD?

3.3 What are the DSM-5 criteria for autism spectrum disorder?

:30

## Supporting Information for Potential Prompts

3.1 *What are the usual components of a diagnostic evaluation for ASD?*

:30

- A positive screening result does not mean that a child has been diagnosed with ASD. In the case of a positive screening test, or when two risk factors are identified on surveillance (see "AAP Surveillance and Screening Algorithm: Autism Spectrum Disorders") the child should be referred for a comprehensive ASD evaluation. Simultaneously, the child should be scheduled for complete audiologic testing (if not recently performed) and referred to early intervention/early childhood education to prevent a delay in receipt of services, if indicated. Pediatricians should become familiar with ASD evaluation sites and specialists in their community. The evaluation may be performed by a clinician with expertise in the diagnosis of ASD, or by a team of specialists that may include developmental-behavioral pediatricians, child neurologists, child psychiatrists, psychologists, speech and language pathologists, occupational or physical therapists, educators, and social workers.
- According to the AAP clinical report "Identification and Evaluation of Children with Autism Spectrum Disorders," a comprehensive evaluation for the presence of ASD

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should accomplish the following three goals: 1) determine the child's overall level of functioning, 2) make a diagnosis of ASD, and 3) attempt to determine the etiology of the ASD. To that end, the evaluation should include the following components:

- **Detailed history from primary caregiver, addressing the following:**
  - **Medical history** – significant pre- and perinatal problems, medical issues, surgeries or hospitalizations, seizures, ear infections
  - **Developmental history** – language, social, and motor milestones; history of any developmental regression; current communication abilities
  - **Behavioral history** – current behavior, socialization, odd or stereotypical behaviors, play interests
  - **Family history** – ASD, language disorders, intellectual disabilities, learning disabilities, ADHD, depression, schizophrenia or other mental illnesses, obsessive-compulsive disorder, genetic disorders
- **Physical examination** – general examination, growth parameters including head circumference, neurological exam, skin examination, search for dysmorphic features
- **Developmental and/or psychometric evaluation** – assessment of functioning across all developmental domains. Common tests in use (depending on child's age and abilities) that may be performed by a variety of specialists in an interdisciplinary team include:
  - **Cognitive**
    - Bayley Scales of Infant Development
    - Mullen Scales of Early Learning
    - Wechsler Preschool and Primary Test of Intelligence
    - Wechsler Intelligence Scale for Children
    - Stanford-Binet Intelligence Scales
  - **Speech and Communication**
    - Preschool Language Scale
    - MacArthur Communicative Development Inventory
  - **Motor**
    - Peabody Developmental Motor Scales Gross Motor Scale
  - **Adaptive**
    - Vineland Adaptive Behavior Scales
    - Sensory profile
- **Determination of the presence of an ASD diagnosis**, preferably with standardized tools that operationalize the DSM criteria. Clinical expertise with review of the DSM-5 criteria must be used to interpret the results of the objective tests. Commonly used tools include the following:
  - **Autism Diagnostic Observation Schedule, Second Edition (ADOS-2)**
    - The examiner observes the child through a series of structured and semi-structured scenarios, and rates the child based on his or her social interaction, communication, and stereotyped behaviors. The module to be administered is selected according to the child's verbal ability.
  - **Autism Diagnostic Interview-Revised (ADI-R)** – This is a comprehensive, structured interview administered by a trained clinical interviewer to the

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parent or caregiver. It includes 92 questions about the child's language and communication, social interaction, and behavior/interests.

- The ADOS-2 and ADI-R both require extensive training and clinical expertise.
- Other tools may include the **Childhood Autism Rating Scale, Second Edition (CARS-2)** and **Gilliam Autism Rating Scale, Third Edition (GARS-3)**. These tools are often used in conjunction with other clinical assessment tools to support diagnosis.
  - **CARS-2** is a 15-item scale that assesses for clinical symptoms of autism. It is completed by the examiner based on obtained history and observation. Resulting scores are categorized as “no autism,” “mild to moderate autism,” or “severe autism.”
  - **GARS-3** assists teachers, parents, and clinicians in identifying autism in individuals and estimating its severity. It consists of 56 clearly stated items describing the characteristic behaviors of persons with autism.
- Assessment of parents' knowledge of ASD, coping skills, and available resources and supports.
- A laboratory investigation to search for a known etiology or co-existing condition. (See question 3.2 for more information).

## 3.2 *What is the medical/genetic workup for a child with suspected ASD?*

There is no laboratory or radiologic test that will diagnose ASD. Instead, medical evaluations can aid in ruling in or out other medical disorders on the differential, or once a diagnosis of ASD is made, searching for a known etiology or determining the presence of a co-existing condition. At this time, there is no standard battery of tests recommended in the evaluation of a child with possible ASD. Evaluations vary according to location and the clinician's experience. To help guide clinicians, a tiered evaluation strategy is often recommended by experts in the field.

The medical workup of a child with suspected ASD should always begin with a thorough medical history, review of symptoms, and physical examination. It is important to ask about the prenatal history, as some teratogens have been associated with ASD including rubella, cytomegalovirus (CMV), and fetal exposure to alcohol. As previously stated, all children with a history of speech delay or suspected of having ASD should undergo a complete audiologic evaluation. Results of the newborn screen should be reviewed. A lead level should be obtained if it has not been done recently, or if the child is reported to mouth objects frequently. Currently, there is no evidence to support routine EEG testing in children with suspected ASD, but it should be considered for children with clinical histories that may represent seizures and for those with a clear history of language regression. While a number of findings on neuroimaging studies have been associated with ASD, none are diagnostic. The decision to perform neuroimaging studies should be guided by the clinical history and examination. Likewise, metabolic testing should be considered in children with suggestive findings on history and physical exam.

The approach to the genetic workup of a child with suspected or confirmed ASD has become increasingly complex as the diagnostic options available have rapidly evolved. With the introduction of newer technologies, the reported “yield” rates of genetic evaluations have increased and are currently estimated to be about 15% (with some reports suggesting rates as high as 40%). Benefits of testing may include helping the patient acquire needed services, empowering the family with knowledge about the

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underlying disorder, providing more specific genetic counseling, identifying associated medical risks, and in limited cases, possibly pursuing new or developing therapies. As knowledge about genetic etiologies of ASD continue to advance, targeted treatments for specific genetic diagnoses may become available, such as those currently in clinical trials for targeted treatments for fragile X syndrome. Evaluations should always be customized, taking into account the clinical findings, family interest, cost, and practicality.

- In the past, high-resolution karyotype and DNA testing for fragile X syndrome (fragile X) were the first-line tests to be performed when a diagnosis of ASD was made. Some more recent guidelines recommend that a technology known as array comparative genomic hybridization (aCGH, may also be called microarray or chromosome microarray) should replace the karyotype as a first-line test. This test uses computer chip technology to screen multiple segments of DNA simultaneously, allowing for the detection of tiny microdeletions and microduplications in the genome (also known as copy number variants). Many of the currently available chips test for most of the known microdeletion syndromes, the subtelomeric regions, and other ASD “hot spots.” Testing for genetic causes is often performed after the ASD diagnosis is made, but in some cases the testing may be performed during the initial ASD evaluation, particularly when co-existing intellectual disability is present.

In addition to high-resolution chromosome testing/aCGH and DNA testing for fragile X, additional tests may be performed based on the clinical presentation. A select few include:

- MECP2 DNA sequencing for Rett syndrome in females with ASD, especially if they are microcephalic
- PTEN gene testing for Bannayan-Riley-Ruvalcaba syndrome in children with ASD and head circumference >2.5 SD above mean
- Genetic evaluation for tuberous sclerosis or neurofibromatosis in children with abnormal skin pigmentation (ash leaf or café au lait macules respectively)
- Fluorescence in situ hybridization (FISH) may be ordered when a specific diagnosis caused by a microdeletion syndrome (e.g., Angelman syndrome) is being considered.

Finally, mitochondrial disorders and dysfunction as well as other metabolic disorders should be considered. One neurometabolic disorder that has an autistic phenotype is phenylketonuria (PKU).

### 3.3 What are the DSM-5 criteria for autism spectrum disorders?

The diagnostic criteria for autism and related disorders have undergone many revisions since the term “infantile autism” first appeared in the DSM-III in 1980. In 1994, the DSM was revised to include five diagnostic categories under the umbrella term “pervasive developmental disorders”: autistic disorder (AD), Asperger syndrome (AS), pervasive developmental disorder – not otherwise specified (PDD-NOS), Rett syndrome, and childhood disintegrative disorder. In recent years, clinicians and researchers began referring to autistic disorder, Asperger syndrome, and PDD-NOS together as “Autism Spectrum Disorders” or “ASDs”. The DSM-5, released in May, 2013, uses the term “Autism Spectrum Disorder” to refer to these conditions, and the criteria for making the diagnosis of autism spectrum disorder were adjusted. Individuals with an existing PDD diagnosis are now considered to have ASD.

These criteria encompass clinical signs pertaining to the two primary areas of impairment seen in ASD. While reviewing the criteria, it is important to keep in mind the wide heterogeneity of symptoms, severity, and clinical presentations that characterize children with ASD.

#### IV. DSM-5 ASD Checklist



# Making an Autism Spectrum Disorder Diagnosis

The core domains of ASD:

- **Impairments in social interaction and communication** – All children on the autism spectrum share an inherent difficulty in their ability to relate socially to or connect with others. Children with ASD may prefer to be alone, make poor eye contact, and have difficulty interpreting the facial expressions of others. They often don't respond to bids for their attention, and conversely, may make rare attempts to gain the attention of another. Deficits in joint attention are characteristic of children with ASD, as is a lack of “shared affect” (sharing one's emotional state with another, e.g., through a smile) and “showing” behaviors (bringing an object over to another to share their interest in it with them). Although delayed speech is often the first concern to be raised by parents, it is not a primary diagnostic characteristic of ASD. Instead, if the social use of communication is lacking, it would be important to evaluate for ASD. At any level of verbal language, the child usually has challenges in nonverbal or social use of language. For example, he or she may not use gestures or eye contact to regulate social interaction. Language may be atypical, and lacking in communicative intent. Because of their difficulties with these basic building blocks of social behavior, children with ASD often have great trouble in forming relationships and making friends.
- **Restricted and repetitive interests and behaviors** – Children with ASD often demonstrate a range of behaviors that are atypical, appear purposeless, and tend to be performed in a repetitive fashion. Motor stereotypes include behaviors such as hand flapping, unusual finger movements, rocking, and spinning. Language may be characterized by abnormal tone and prosody (pitch, intonation, stress, and rhythm used in speech “echolalia” (repeating or “echoing” words for phrases), or “scripting” (e.g., repeating lines from a favorite TV show). Play is often perservative in nature and may be limited to lining toys up or spinning or mouthing objects. Children with ASD may adhere to strict routines in their daily lives and will often have a tantrum when the routine is disrupted. They may develop preoccupations and attachments with atypical objects, such as a piece of paper or string. For some children, restricted interests are often manifested in their obsession with certain topics (e.g., dinosaurs or the solar system).

Co-existing conditions, while not part of the core features of ASD, may be seen frequently in children with ASD. Some of these include (see module of “Autism Spectrum Disorder-Specific Anticipatory Guidance” for more information):

- Cognitive abnormalities, such as global developmental delay, intellectual disability, uneven cognitive abilities (sometimes referred to as splinter skills)
- Sensory symptoms, such as hyper/hyposensitivities to touch, taste, smell, and sound
- Atypical motor development, poor coordination, or deficits in praxis
- Co-morbid symptomatology of other DSM-5 disorders, such as ADHD and anxiety disorders
- Sleep problems
- Gastrointestinal disorders
- Seizure disorders

Approximately 25% to 30% of children with ASD initially develop some language, and then experience a regression, often between 15 and 24 months of age. This regression may also be accompanied by a loss of gestures and social skills. Regression of skills should always serve as a red flag to pediatricians of a child in need of further evaluation.

For a diagnosis of ASD, impairments must be present across the two core categories:

# Making an Autism Spectrum Disorder Diagnosis

- **Category 1: Social communication and interaction (Social)**

Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history

1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back- and- forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absences of interest in peers.

- **Category 2: Restricted, repetitive patterns of behavior, interests, or activities (RRBs)**

Restricted, repetitive patterns of behavior, interests, or activities (RRBs) as manifested by **at least 2 of 4 symptoms** currently or by history

1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g. extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).
3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or preservative interest).
4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement)

At least five DSM-5 criteria must be met either by history or current behavior. All three criteria must be met from category 1, and at least two criteria must be met from category 2. In addition, symptoms must be present in the early developmental period; cause clinically significant impairment in social, occupational, or other important areas of current functioning; and not be better explained by intellectual disability or global developmental delay.

New to the DSM-5 diagnostic criteria for ASD are severity ratings of the two symptom domains and the inclusion of clinical specifiers. The severity ratings for the Social and RRB domains are based on the type and degree of impairments and level of support needed in these areas. Specifiers provide more clinically-relevant information about the child's history and functioning; they include information about etiology, co-morbidities (e.g. intellectual disability, language delay, medical conditions such as seizures), and pattern of onset.

# Making an Autism Spectrum Disorder Diagnosis

## **Case Study Part IV**

Six months later, you review the results of Billy's evaluation with his mother. His hearing evaluation, consisting of behavioral audiometry and tympanogram testing, was normal. Billy's comprehensive evaluation included assessments by a developmental-behavioral pediatrician, a psychologist, a speech-language pathologist, and an occupational therapist.

The report from the developmental-behavioral pediatrician details Billy's medical history, developmental history, current behavior, and family history, as well as findings on physical and neurological examination. Billy meets the DSM-5 criteria for ASD diagnosis. He has persistent deficits in social communication and social interaction across contexts, and he has two or more repetitive and restrictive behaviors. According to the report he has a severity level of 2 for social communication and a severity level of 3 for restricted and repetitive behaviors and interests.

The report also mentions that blood was drawn at that visit for a karyotype and molecular test for fragile X, but the results are still pending as Billy only saw the specialist last week. The psychologist's report reviewed Billy's performance on cognitive testing and revealed below-age-level skills in all areas, with the most pronounced weakness in the language domain.

On formal language testing, Billy's receptive and expressive skills were at the 15-to 18-month level. The occupational therapist's report described Billy's strengths and weaknesses in fine motor skills and adaptive functioning and detailed some of his sensory issues that impacted his day-to-day life. All of the clinicians who evaluated Billy thoroughly described their observations of Billy's social interactions and behaviors during their sessions. As part of the comprehensive evaluation, Billy also underwent ADOS-2 (Autism Diagnostic Observation Schedule, Second Edition) testing, which supported the diagnosis of ASD. Observations included Billy's wanting to play with a wind-up toy; he threw himself on the ground when the examiner tried to take the toy away. One clinician also mentioned that when his name was called, he did not answer.

Billy's mother informs you that she took a copy of the reports to Billy's school. A meeting has been scheduled to re-assess Billy's educational plan. She has also been reading some information on autism and is looking into a parent support group in her community. Billy's mother tells you that two other families they know have sons with ASD. She asks why there seem to be so many more children diagnosed now than in the past.

Distribute Case Study Part IV



# Making an Autism Spectrum Disorder Diagnosis

## Case Study Part IV: Discussion Question

**Has your opinion changed with this new information?**

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## Case Study Part IV: Potential Prompts

- 4.1 What is the current estimated prevalence of ASD? What are the thoughts as to why it appears to be increasing?
- 4.2 What evidence supports the major role of genetics in the etiology of autism?
- 4.3 What would you do to support the patient and parents while awaiting an official diagnosis?

### Supporting Information for Potential Prompts

- 4.1 *What is the current estimated prevalence of autism? What are the thoughts as to why it appears to be increasing?*

The most recent studies have reported current prevalence estimates in the United States to be approximately 1 in 59. This represents a greater than twentyfold increase from studies done 50 years ago. Great controversy has surrounded the so-called “autism epidemic” and whether or not the current rates reflect a true increase in incidence. Some factors believed to contribute to the increased rates include the following:

- Greater awareness of autism in both the medical community and the general public has led to increased screening and diagnosis.
- AAP recommendations have led to increased screening.
- Broadened definitions – Earlier studies predominantly included only those with autistic disorder, while the more recent studies reflect the full spectrum.
- Better diagnostics – Children who had been diagnosed with other disorders (e.g., intellectual disability, language impairment) in the past are now being diagnosed as having ASD (this applies to individual children who receive a new diagnosis and also reflects changing diagnostic patterns in the population over time).
- Eligibility for services under the Individuals with Disabilities Education Act (IDEA) – in 1990, autism became a diagnosis for which children became eligible for special education services under the IDEA law.
- There are likely unidentified factors associated with the increase in prevalence. Current epidemiologic studies, such as the Study to Explore Early Development (SEED), are looking at risk and protective factors. (See <http://www.cdc.gov/SEED> for more information.)
- Diagnosis of ASD in children with genetic syndromes may be associated with features of autism.

- 4.2 *What evidence supports the major role of genetics in the etiology of ASD?*

There is compelling evidence that autism has an underlying genetic etiology. It is considered to be a multifactorial inherited disorder with a calculated heritability of around 90%.

- Recurrence risk for siblings is reported to be between 2% and 18%. If a second child

# Making an Autism Spectrum Disorder Diagnosis

- has autism, the recurrence risk for a subsequent child is on the order of 25% to 35%.
- Studies show a concordance rate of 70% in monozygotic twins (90% if a broader ASD definition is used), in contrast to a 3% concordance rate in dizygotic twins.
- ASD occurs four times more often in males than in females.

## 4.3 What would you do to support the patient and parents while awaiting an official diagnosis?

Wait times between referral and diagnosis may vary. The process for Billy took six months. What would you do while parents are waiting for diagnosis results?

- Maintain frequent contact with the family.
- Monitor early intervention services to advocate for appropriate intensity of services.
- Refer the family to parent support groups, such as Family Voices ([www.familyvoices.org](http://www.familyvoices.org)).

### Case Study Part V – Epilogue

A few days later, you receive a call from the developmental-behavioral pediatrician who evaluated Billy. He informs you that chromosomal testing was normal, but fragile X testing revealed 383 CGG repeats, consistent with a diagnosis of fragile X syndrome. He says that he has discussed the results of the test with Billy's mother and has scheduled an appointment with a geneticist to address the issue of testing other family members and to discuss possible enrollment in clinical trials.

Distribute Case Study Part V - Epilogue

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### Case Study Part V – Epilogue: Discussion Questions

How would you apply the information in this case?

What did you learn through this case?

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### Case Study Part V – Epilogue: Potential Prompts

- 5.1 What is the relationship between fragile X syndrome and ASD?
- 5.2 What causes fragile X syndrome? What are some of the clinical manifestations?

### Supporting Information for Potential Prompts

5.1 *What is the relationship between fragile X syndrome and ASD?*

- Between 2% and 6% of all children diagnosed with autism have the fragile X gene mutation. Between 16% and 43% of children diagnosed with fragile X syndrome also have ASD.
- Fragile X syndrome is the most common known single-gene cause of ASD.
- For more information, see <http://www.cdc.gov/ncbddd/fxs/index.html>

# Making an Autism Spectrum Disorder Diagnosis

## 5.2 What causes fragile X syndrome? What are some of the clinical manifestations?

V. Fragile X Syndrome  
Fact Sheet



Fragile X is the most common cause of inherited mental impairment. This impairment can range from learning disabilities to more severe cognitive or intellectual disabilities. It is caused by a mutation in the FMR1 gene found on the X chromosome, which causes methylation of the gene and turns off production of FMR1 protein. The number of CGG repeats on the FMR1 gene determines the diagnosis. A permutation is diagnosed if there are 55-200 CGG repeats. People with a permutation are often asymptomatic or have mild symptoms.

A full mutation is diagnosed when more than 200 CGG repeats are present. Males with the full mutation will have symptoms, and females will often have milder symptoms. Both males and females can have fragile X syndrome. Males and females can also both be “carriers” of the fragile X gene. The classic triad of long face, prominent ears, and macroorchidism is present in just 60% of cases, and some boys may present with only intellectual impairment.

- <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=fragilex>  
Denmark JL, Feldman MA, Holden JJA, MacLean WE Jr. Behavioral relationship between autism and fragile X syndrome. Am Journal Ment Retard 2003;108:314-26.

### Potential Next Case: “Early Intervention and Education”

Appropriate early intensive educational therapies greatly improve long term outcomes for children with autism spectrum disorder (ASD). Effective primary care management of ASD includes supporting families by referral for appropriate therapies and community resources.

*After completion of this module, learners will be able to:*

- Discuss the evidence base and recommended educational therapies for children with ASD.
- Provide ongoing support and management for children with ASD and their families regarding educational therapies.

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# Case Worksheet for Learners

## Case Goal

The diagnosis of autism spectrum disorder (ASD) is made on the basis of detailed information obtained from the child's caregivers, careful observation and assessment of the child, and the use of standardized tools designed to aid in the diagnosis of ASD.

## Key Learning Points of This Case

1. *Be familiar with the basic principles regarding the diagnosis and epidemiology of ASD.*

a. Describe the two domains of impairment in ASD. \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

b. Know the currently reported estimate of the prevalence of ASD in the U.S. \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

c. Describe the current evidence for the genetic etiology of ASD. \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

2. *Understand the diagnostic approach to evaluating a child with suspected ASD.*

a. Identify the important elements of a comprehensive history. \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

b. Recognize the important features to assess when observing a child's behavior. \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

c. List the aspects of the physical exam that are of particular importance when evaluating for ASD. \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

d. Describe the components of a comprehensive diagnostic evaluation for ASD. \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

# Making an Autism Spectrum Disorder Diagnosis

## Post Learning Exercise

1. Observe and participate in a team evaluation for autism spectrum disorder. Specific activities could include taking a history, doing a physical exam, and observing an Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) exam.
2. Attend a genetics clinic and observe genetic counseling for the family of a child with a genetic cause of ASD.
3. For some, it may not be possible to observe an autism evaluation. Suggest residents:
  - Talk to a parent of a child with ASD about getting a diagnosis.
  - Interview an attending about how they introduce concerns about ASD with families.

## Case Study Part I

Billy is a 3 ½ -year-old boy you are seeing for the first time in your resident practice. He was born full term following a normal pregnancy and delivery. His newborn screen and neonatal hearing test were normal. At 18 months, he underwent bilateral myringotomy tube placement following repeated bouts of otitis media. His mother also had concerns that he was not speaking any words, and his doctor said, “Let’s wait and see.” A follow-up appointment was scheduled for when he turned 2. At his 2-year well-child check, because of the history of global developmental delay, he was referred to early intervention (EI) services.

Three months ago, Billy began attending a specialized preschool in the local school district; there, he receives speech, physical, and occupational therapies. This is the third preschool Billy has attended. He was asked to leave his previous schools because of behavioral problems. Billy’s mother reports that his current preschool teacher recommended that she take him to the pediatrician given concerns about his behavior. Since he began preschool, his teachers have reported that he is extremely hyperactive, does not follow directions, and largely ignores the children in the class.

Billy’s mother reports that he has been in good health recently. She tells you that all of his milestones were delayed, particularly his language. She denies any history of developmental regression. She adds that Billy has made some nice progress since he began receiving EI services. He will now use single words like “juice” and “cookie” to make requests. At home, Billy is a “handful,” but he will usually calm down when she turns on his favorite cartoon. She describes him as a sweet and loving boy, but she also shares that he will have prolonged tantrums when denied what he wants and that tantrums will often occur when they are attempting to leave their house. During these tantrums, he will frequently bang his head and bite his hand, which frightens her. For some time now she has been concerned that Billy does not like to play with his similar-aged cousins during family get-togethers, but she thought this was because he was an only child and didn’t like to share. She had been eagerly awaiting his first day of preschool so that he could spend more time around other children.

When asked about family history, Billy’s mother reports that her sister’s 7-year-old son is in special education, but she is not sure what kind of evaluation has been done as her sister “does not like to talk about these kinds of things.” She mentions that it has been hard for the family, and she finds Billy’s preschool reports to be embarrassing and discouraging. She is frustrated and wants the best for Billy.

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## Case Study Part II

At first, Billy clings to his mother, but as you continue to speak with her, he climbs down from her lap and runs around the room touching everything in sight. When you give him a few toys to play with, he briefly inspects them, smells them, and then throws them down. Billy spots a ball in your bag of toys. He points at it and says “ball” without looking at you or his mother. When you toss him the ball, he laughs and makes brief eye contact with you, but then proceeds to kick and chase the ball around the room, ignoring your efforts to engage him in play. You call his name several times and he doesn’t answer. When his mother begins to undress him for the exam, he begins to scream and jump up and down while flapping his hands. She says he tends to have difficulty transitioning from one activity to another. On physical examination, Billy is at the 75th percentile for weight and height, and his head circumference is at the 98th percentile. His ears are prominent, and he has a wide nasal bridge. He has mildly hyperextensible joints. The remainder of his exam is within normal limits.

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## Case Study Part III

You share your concerns about the things Billy's mother has told you and about what you have observed during the visit. You tell her that Billy shows some characteristics of a child with autism spectrum disorder. He exhibits decreased eye contact, lack of joint attention, hand flapping, resistance to transitions, and atypical exploration of objects. You recommend she take Billy for additional evaluations. Together, you agree to proceed with a referral for a multidisciplinary evaluation for the presence of autism spectrum disorder, including an audiologic assessment. You ask Billy's mother to return for a follow-up appointment to ensure the evaluation is proceeding as it should.

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## Case Study Part IV

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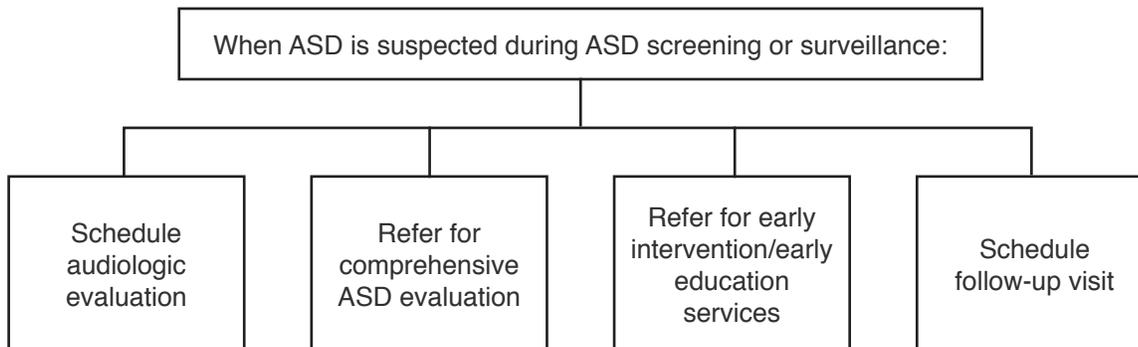
### Case Study Part V - Epilogue

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## Handout I: Components of a Comprehensive Evaluation for ASD



- Detailed history from primary caregiver
- Medical history
  - Developmental history
  - Behavioral history
  - Family history
- Physical examination
  - Growth parameters, head circumference
  - General examination with special attention to skin and neurological findings
  - Inspection for any dysmorphic features
- Observation of child
  - Social interaction, response to name, joint attention
  - Play skills
  - Use of language
  - Presence of atypical behaviors or stereotypies
- Developmental/psychometric testing
- Speech/language testing
- Determination of categorical ASD diagnosis using DSM criteria and a standardized tool
  - Autism Observation Diagnostic Schedule, Second Edition (ADOS-2)
  - Autism Diagnostic Interview–Revised (ADI-R)
- Assessment of family’s knowledge regarding ASD, coping skills, resources, and supports
- Medical/genetic workup as indicated by clinical picture
  - High-resolution chromosomes
  - Array CGH
  - Fragile X testing
  - Rett syndrome/MECP2 testing in girls
  - Additional tests to consider include: PTEN gene analysis, EEG, metabolic studies, neuroimaging

Macferran K, Major N, Fussell J, High P. Components of a Comprehensive Evaluation for ASD. Developed for the *Autism Case Training: A Developmental Behavioral Pediatrics Curriculum*. 2011.

# Handout II: Differential and Etiologic Diagnosis of Autism Spectrum Disorder

<b>Developmental delay/ intellectual disability</b>	Children with intellectual disability may have “autistic features,” but not meet criteria for autism spectrum disorder (ASD). Children with ASD may have intellectual disability or normal intelligence. Children with intellectual disability usually have better social and communication skills than do children with ASD with the same cognitive level.
<b>Fetal alcohol spectrum disorders</b>	There is an increased risk of ASD and other neurodevelopmental disorders in children exposed to alcohol in utero.
<b>Genetic syndrome</b>	<p>There may or may not be a family history, depending on the specific disorder. If dysmorphic features are present, a genetic disorder should be considered. There are certain neurogenetic syndromes that tend to be associated with ASD. These include, but are not limited to:</p> <ul style="list-style-type: none"> <li>• Fragile X syndrome – intellectual disability, macrocephaly, large ears, large testicles, hypotonia, and joint hyperextensibility</li> <li>• Tuberous sclerosis – hypopigmented macules, central nervous system hamartomas, seizures, intellectual disability</li> <li>• Angelman syndrome – global developmental delay, hypotonia, wide-based ataxic gait, seizures, progressive spasticity</li> <li>• Rett syndrome – disorder seen primarily in girls. They have apparently normal development for the first 5 months of life and have a normal head circumference at birth. Deceleration of head growth is seen from 5 to 48 months of age resulting in microcephaly. They lose previously acquired hand skills and begin to have hand-wringing stereotypes. They often develop seizures.</li> </ul>
<b>Hearing Impairment</b>	There may be a history of recurrent otitis media or fluid. Children with hearing impairments often have speech delays, but will typically use compensatory nonverbal forms of communication. They make eye contact and use facial expressions. Children with ASD may be described as having “selective hearing” (i.e., may not respond when their name is called, but are oversensitive to other noises). Children with a hearing impairment will usually be underresponsive to all noises, although this will be somewhat variable depending on the degree of hearing loss.

## Handout II: Differential and Etiologic Diagnosis of Autism Spectrum Disorder

<p><b>Mental health disorders</b></p>	<p>This is a broad category of differential diagnoses with variable symptomatology depending on the specific diagnosis.</p> <ul style="list-style-type: none"> <li>a. Obsessive compulsive disorder (OCD) – The obsessive thoughts and repetitive actions seen in OCD can appear very similar to the ritualistic behaviors and motor stereotypes seen in ASD.</li> <li>b. Anxiety – Children who have problems with anxiety may be hesitant to interact with others. They may have difficulties with transitions. Children with anxiety are still socially related and have appropriate social insight.</li> <li>c. Depression – Depression in children can present in a variety of ways. Children may be withdrawn and isolate themselves. They may have a blunted affect and avoid eye contact.</li> <li>d. Attention deficit-hyperactivity disorder (ADHD) – Children with ADHD may have impairments in their social skills due to their hyperactivity and impulsivity. They may have difficulty sustaining a conversation because of inattention. Children with ASD often have problems with hyperactivity, impulsivity, and inattention.</li> <li>e. Oppositional defiant disorder (ODD)/behavior problems – The behavior problems seen in children with ODD are usually intentional. Most children will have temper tantrums at some point. Children with ASD are more likely to have tantrums associated with transitions or “for no apparent reason.”</li> <li>f. Tourette syndrome – Tics seen in Tourette syndrome may appear similar to motor stereotypes associated with ASD. Children with Tourette syndrome will usually not have the social or communication impairments seen with ASD. However, there may be some social isolation due to embarrassment or peer avoidance.</li> </ul>
<p><b>Psychosocial (e.g., neglect)</b></p>	<p>Children who have a history of significant abuse or neglect may be withdrawn and hesitant to interact with others. They may also have regression of skills, such as loss of language, and behavior problems.</p>
<p><b>Sensory problems</b></p>	<p>Children with ASD often have sensory issues such as being hypersensitive to loud noises or avoiding certain food textures. A child that has sensory impairments but is not on the autism spectrum will not have the core features of ASD (impairments in social communication, etc.).</p>
<p><b>Speech/language disorder</b></p>	<p>Children with speech/language disorders will compensate with nonverbal forms of communication such as pointing and gestures. They lack severe social deficits, although there may be some social impairment due to the communication difficulties.</p>

Suggested Citation: Macferran K, Major N, Fussel J, High P. Differential and Etiologic Diagnosis of Autism Spectrum Disorder. Developed for the Autism Case Training: A Developmental-Behavioral Pediatrics Curriculum. 2011.

## Handout III: AAP Screening Guidelines

Surveillance and Screening Algorithm: Autism Spectrum Disorders (ASDs)

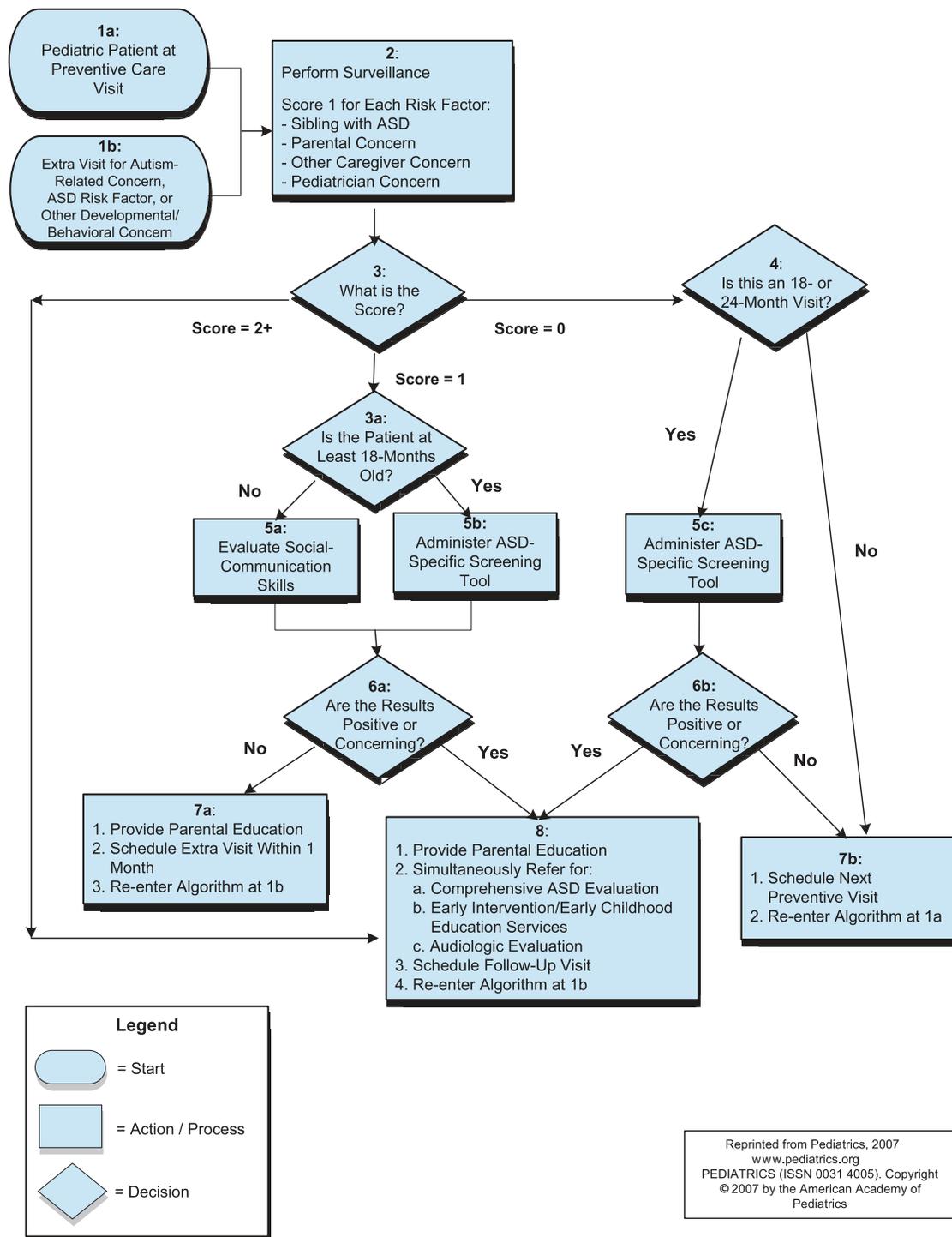
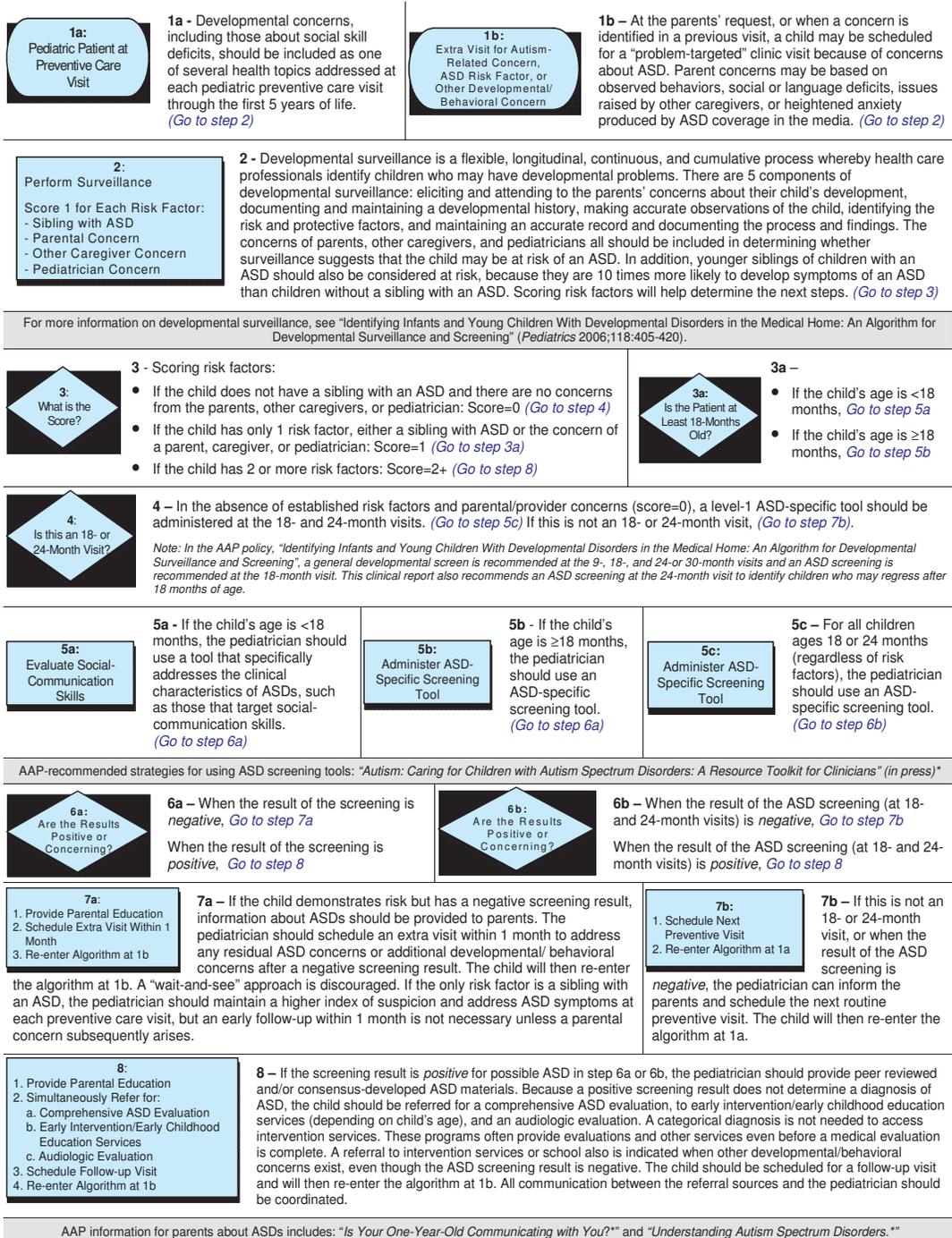


FIGURE 1  
Surveillance and screening algorithm: ASDs.

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## Handout III: AAP Screening Guidelines

### Surveillance and Screening Algorithm: Autism Spectrum Disorders (ASDs)



\*Available at [www.aap.org](http://www.aap.org)

## Handout IV: DSM-5 ASD Checklist

- \_\_\_\_\_ **A.** Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history
- A1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back- and- forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
  - A2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
  - A3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absences of interest in peers.
- \_\_\_\_\_ **B.** Restricted, repetitive patterns of behavior, interests, or activities as manifested by at least 2 of 4 symptoms currently or by history
- B1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
  - B2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g. extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food everyday).
  - B3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or preservative interest).
  - B4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement)
- \_\_\_\_\_ **C.** Symptoms must be present in the early developmental periods ( but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life)
- \_\_\_\_\_ **D.** Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning. (minimum = level 1)
- \_\_\_\_\_ Social Communication Severity Level (1, 2, or 3)
- \_\_\_\_\_ Restricted Repetitive Behavior Severity Level (1, 2, or 3)
- \_\_\_\_\_ **E.** These disturbances are not better explained by intellectual disability (intellectual development disorder) or global developmental delay.

Patient meets criteria for ASD  
(criteria A-E satisfied)

Severity Level for ASD	Social Communication	Restricted Interests & Repetitive Behaviors
<p><b>Level 3</b> <b>‘Requiring very substantial support’</b></p>	<p>Severe deficits in verbal and nonverbal social communication skills cause severe impairments in functioning, very limited initiation of social interactions, and minimal response to social overtures from others. For example, a person with few words of intelligible speech who rarely initiates interaction and, when he or she does, makes unusual approaches to meet needs only and responds to only very direct social approaches.</p>	<p>Inflexibility of behavior, extreme difficulty coping with change, or other restricted/repetitive behaviors markedly interfere with functioning in all spheres. Great distress/difficulty changing focus or action.</p>
<p><b>Level 2</b> <b>‘Requiring substantial support’</b></p>	<p>Marked deficits in verbal and nonverbal social communication skills; social impairments apparent even with supports in place; limited initiation of social interactions; and reduced or abnormal response to social overtures from others. For example, a person who speaks simple sentences, whose interaction is limited to narrow special interest, and who has markedly odd nonverbal communication.</p>	<p>Inflexibility of behavior, difficulty coping with change, or other restricted/repetitive behaviors appear frequently enough to be obvious to the casual observer and interfere with functioning in a variety of contexts. Distress and/or difficulty changing focus or action</p>
<p><b>Level 1</b> <b>‘Requiring support’</b></p>	<p>Without supports in place, deficits in social communication cause noticeable impairments. Difficulty initiating social interactions, and clear examples of atypical or unsuccessful response to social overtures of others. May appear to have decreased interest in social interactions. For example, a person who is able to speak in full sentences and engages in communication but whose to-and-fro conversation with others fails, and whose attempts to make friends are odd and typically unsuccessful</p>	<p>Inflexibility of behavior causes significant interference with functioning in one or more contexts. Difficulty switching between activities. Problems of organization and planning hamper independence.</p>

American Psychiatric Association. *Pervasive developmental disorders. In: Diagnostic and Statistical Manual of Mental Disorders. 5th ed.-text revision (DSM-5). Washington, DC: American Psychiatric Association; 2013.*

# Facts About Fragile X Syndrome

## What is fragile X syndrome?

Fragile X syndrome (FXS) is the most common known cause of intellectual disability (formerly referred to as mental retardation) that can be inherited, that is passed from parent to child. It is estimated that FXS affects about 1 in 4,000 boys and 1 in 6,000 to 8,000 girls. Both boys and girls can have FXS, but girls usually are more mildly affected.

## What causes FXS?

The cause of FXS is genetic. FXS occurs when there is a change in a gene on the X chromosome called FMR1. The FMR1 gene makes a protein needed for normal brain development. In FXS, the FMR1 gene does not work properly. The protein is not made, and the brain does not develop as it should. The lack of this protein causes FXS. Other Fragile X-associated Disorders (FXDs) can be present in the extended family, even if not currently evident. Talk with a genetic counselor for more information.

## What are some signs of FXS?

### Children with FXS might:

- Sit up, crawl, or walk later than other children
- Have trouble with learning and solving problems
- Learn to talk later, or have trouble speaking
- Become very anxious in crowds and new situations
- Be sensitive about someone touching them
- Bite or flap their hands
- Have trouble making eye contact
- Have a short attention span
- Be in constant motion and unable to sit still
- Have seizures

### Some children with FXS have certain physical features such as:

- A large head
- A long face
- Prominent ears, chin, and forehead
- Flexible joints
- Flat feet
- Macroorchidism (enlarged testicles in males; more obvious after puberty)

*These physical features tend to become more noticeable as the child gets older.*

## What conditions are common among children with FXS?

Children with FXS might have learning disabilities, speech and language delays, and behavioral problems such as attention-deficit/hyperactivity disorder (ADHD) and anxiety. Some boys can develop aggressive behavior. Depression can also occur. Boys with FXS usually have a mild to severe intellectual disability. Many girls with FXS have normal intelligence. Others have some degree of intellectual disability, with or without learning disabilities. Autism spectrum disorder (ASD) occurs more often among children with FXS.

## What can I do if I think my child has FXS?

Talk with your child's doctor or nurse. If you or your doctor thinks there could be a problem, the doctor can order a blood test for FXS or refer you to a developmental specialist or geneticist, or both. Also, contact your local early intervention agency (for children younger than 3 years of age) or public school (for children 3 years of age or older) to find out if your child qualifies for intervention services. To find out whom to call in your area, contact the Center for Parent Information and Resources at [www.parentcenterhub.org/find-your-center/](http://www.parentcenterhub.org/find-your-center/).

In addition, CDC has links to information for families at [www.cdc.gov/fragilex](http://www.cdc.gov/fragilex).

Additional resources include the National Fragile X Foundation ([www.fragilex.org](http://www.fragilex.org)) and the FRAXA Research Foundation ([www.FRAXA.org](http://www.FRAXA.org)). CDC also supports the efforts of the Fragile X Clinical & Research Consortium ([www.FXCRC.org](http://www.FXCRC.org)) which can be reached through the National Fragile X Foundation.

While there is no cure for fragile X syndrome, therapies and interventions can improve the lives of those affected and of their families. It is **very** important to begin these therapies and

Interventions as early as possible to help your child reach his or her full potential. Acting early can make a real difference!

**1-800-CDC-INFO | [www.cdc.gov/fragilex](http://www.cdc.gov/fragilex)**

# Making an Autism Spectrum Disorder Diagnosis

## References

- American Psychiatric Association. Pervasive developmental disorders. In: Diagnostic and Statistical Manual of Mental Disorders. 5th ed.-text revision (DSM-5). Washington, DC: American Psychiatric Association; 2013.
- Denmark JL, Feldman MA, Holden JJA, MacLean WE Jr. Behavioral relationship between autism and Fragile X Syndrome. *Am J Ment Retard.* 2003;108:314-26.
- Fililpek PA, Accardo PJ, Ashwal S, et al. Practice parameter; screening and diagnosis of autism. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Child Neurology Society. *Neurology.* 2000;55:468-79. Available at <http://www.neurology.org/cgi/reprint/55/4/468>.
- Johnson CP, Myers SM. American Academy of Pediatrics, Council on Children with Disabilities. Identification and evaluation of children with autism spectrum disorders. *Pediatrics.* 2007;120(5):1183-214. Available at: <http://pediatrics.aappublications.org/content/120/5/1183.full.html>
- Manning M, Hudgins L Array-based technology and recommendations for utilization in medical genetics practice for detection of chromosomal abnormalities. *Genet Med.* 2010; 12(11): 742-745.
- Mefford HC, Batshaw ML, Hoffman EP. Genomics, intellectual disability, and autism. *N Engl J Med.* 2012; 366(8): 733-43.
- Pickler L, Elias E. Genetic evaluation of the child with an autism spectrum disorder. *Pediatr Ann.* 2009;38(1):26-9.
- Baio J, Wiggins L, Christensen DL, et al. Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2014. *MMWR Surveill Summ* 2018;67(No. SS-6):1–23. DOI: <http://dx.doi.org/10.15585/mmwr.ss6706a1>
- Schaefer GB, Mendelsohn, NJ. Clinical genetics evaluation in identifying the etiology of autism spectrum disorders. *Genet Med.* 2008;10(4):301-5.
- Teplin SW. Autism and related disorders. In: Levine MD, Carey WB, Crocker AC. *Developmental-Behavioral Pediatrics.* 3rd ed. Philadelphia, PA: Saunders; 1999-589-605.
- Zecavati N, Spence S. Neurometabolic disorders and dysfunction in autism spectrum disorders. *Curr Neurol Neurosci Rep.* 2009 9:129-36.