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# A road map for identifying autism spectrum disorder: Recognizing and evaluating characteristics that should raise red or "pink" flags to guide accurate differential diagnosis

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#### ABSTRACT

**Objective:** Given the high population prevalence of Autism Spectrum Disorder (ASD) and overlapping symptoms with medically complex groups, ASD is a common rule out diagnosis for neuropsychologists even when not identified in the referral or initial presenting concerns. This paper presents practical guidance to support neuropsychologists in their ability to accurately assess, diagnose, and/or rule out ASD, especially in patients with more subtle presentations. Method: This paper combines clinical experience and empirical literature to highlight important assessment measures and related considerations, differential diagnostic considerations, common misconceptions about ASD and person/ family characteristics, as well as variability in presentation and comorbidities that can obscure the diagnosis. Characteristics that may be considered "red flags" (clearly diagnostic, classic symptoms) and "pink flags" (associated features and symptoms that are suggestive of ASD but not guite definitive and that may overlap with symptoms seen in other neurodevelopmental or psychiatric diagnoses) will be discussed. **Conclusions:** Neuropsychologists in all clinical settings should be able to effectively screen for and/or diagnose ASD, even when its presentation is more subtle and/or when symptoms are masked by patient strengths in a way that makes their clinical presentation less obvious. Practical strategies for communicating the diagnosis and next steps/recommendations for interventions are reviewed.

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#### Introduction

The current prevalence of Autism Spectrum Disorder (ASD) in the United States is approximately 1 in 54 (Maenner et al., 2020) with similarly high rates seen internationally. Given this relatively high base rate, clinicians and neuropsychologists across all specialties are highly likely to see patients who have ASD, regardless of the official reasons for referral. Therefore, it is incumbent on clinicians in our field to have a strong appreciation for the differential diagnostic process in ASD whether they decide to confirm a diagnostic conceptualization themselves, or refer a patient on for additional assessment. Many clinicians identify as specializing in a specific population (an age group, a set of disorders, a form of treatment) and autism spectrum disorder (ASD) may not be a common primary differential diagnosis in general practice. If clinicians do not feel confident in recognizing the signs to further explore the possibility of an ASD diagnosis, they may fail to make referrals for further evaluation in subtle presentations or may unnecessarily delay diagnosis in clearer cases. These patients may be sent to specialty clinics at diagnostic centers and although they are well equipped to diagnose and provide guidance for individuals with ASD, these centers often have long waitlists (Penner et al., 2018). We believe that psychologists and neuropsychologists are well positioned to evaluate and diagnose individuals with ASD given their expertise in: intellectual and language functioning; comorbid neurodevelopmental, psychiatric and medical conditions and other aspects of functioning (e.g., eating, sleeping, maladaptive behaviors, motor skills, and psychosocial challenges); and diagnostic assessment processes that include interviews with collateral informants around complex medical conditions (Board of Directors, 2007).

In this article we provide a roadmap that outlines a number of considerations and tools that can be used to determine whether an ASD diagnosis may be warranted. We discuss clear and classic symptoms of ASD ("red flags") and associated features, as well as more easily missed subtle signs and symptoms of ASD that warrant further investigation due to their relevance but decreased diagnostic specificity ("pink flags"). We also review important considerations for differential diagnosis, including comorbidities, the variable presentation of ASD, and important considerations when gathering information from informants. The last section addresses pragmatic issues for the clinician, including an overview of screening and diagnostic tools and procedures, as well as how to best communicate the diagnosis and recommendations to the family. **Note to readers**: many of the statements made in this article are supported by the research literature and include citations. However, other statements are solely based on the clinicial experience of the authors. Please read the suggestions and guidance that follows with this in mind.

#### Using red flags and pink flags to recognize and diagnose ASD

The Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association, 2013) and the International Statistical Classification of Diseases and Related Health Problems (11th ed.; ICD-11; World Health Organization, 2020) describe ASD as a neurodevelopmental disorder with symptoms of impaired social communication and restricted/repetitive behaviors that result in clinically significant

functional impairment. ASD is an overarching diagnosis that encompasses individuals who may have previously been diagnosed with Autistic Disorder, Asperger Syndrome and, in some cases, Pervasive Developmental Disorder Not Otherwise Specified. While all psychiatric and neurodevelopmental conditions can present in various ways, ASD is rather extreme in its **variability**. Overall cognitive functioning in this population can range from severe intellectual disability to highly gifted (Robinson et al., 2014). Core social symptoms can range from a fairly complete disinterest in other people except for immediate need fulfillment to (1) having successful interactions with adults and/or much younger children but not same age peers; (2) having brief social interactions with peers but an inability to maintain them; and/or (3) strong social motivation to be accepted and valued by others, including success in forming bonds with other people who may have similar interests and sometimes common limitations. If a clinician is unaware of this variability in the presentation of ASD, it can lead to delays in early detection, misdiagnosis, and lack of access to evidence-based treatments.

Individuals with more subtle symptom presentation and intact or above average cognitive abilities are often informally referred to as "high functioning." However, this term can be confusing since "high functioning" in the autism research literature often only indicates that a person does not meet criteria for intellectual disability (Ameli et al., 1988; Szatmari et al., 1989). Perhaps more importantly, even when individuals present with more subtle symptoms and require less support (often in a way that hinders the diagnostic process), their pattern of social communication difficulties and restricted/repetitive behaviors still contributes to very significant and functional impairment in adaptive, educational and/or vocational settings. Thus, we recommend refraining from using this term.

There are no pathognomonic signs of autism; no one symptom unequivocally indicates that ASD is present (or absent). However, research and clinical practice do highlight a number of "red flags" especially in individuals more severely impacted by the diagnosis (Jensen et al., 2011). We conceptualize that some characteristics may be considered "red flags" (clearly diagnostic, classic symptoms) or "pink flags" (more subtle associated features and less definitive symptoms) for ASD depending on their intensity, atypicality, prevalence, and specificity (See Table 1). Red flags represent the more highly conspicuous characteristics or exemplar ASD symptoms, such as absent or markedly reduced eye contact from a very young age that occurs across all settings. Some additional, but perhaps less common, examples of "red flag" symptoms (i.e., those with higher specificity for ASD) include (1) longstanding patterns of frank visual regard (i.e., when individuals seek out visual stimuli in atypical manners) such as repeated and close inspection of an item or fingers out of the corner of one's eye; (2) using another person's hand as a tool without eye contact; and (3) intense and early attachment to atypical objects (e.g. sleeping with a spatula versus a stuffed animal).

While the presence of red flags facilitates the diagnostic process, maintaining an awareness of and actively looking for a history of "pink flags" can also be instrumental when evaluating for the possibility of ASD. Pink flags are the more subtle, but still potentially diagnostic features of ASD that should raise an evaluator's concern for the diagnosis. Examples of pink flags include a pervasively rigid cognitive thinking style, as well as difficulties with transitions, and low daily living skills despite high intellectual

Symptom Type	Red Flag	Pink Flag
<b>Restricted, Repetitive Patterns of</b> Restricted Interests and Play	f Behavior, Interests or Activities Exhaustive and obsessive interest in highly specific, atypical topics. For example, dishwasher models, electric blanket controls, state license plates, WWII war planes, recites the Latin names of dinosaurs to strangers at the grocery store, carries doorstopper with them at all times or memorizes bus routes as a hobby.	Really likes to learn about and talk about certain niche topics. For example, Minecraft, Dinosaurs, Thomas the Train, Five Nights at Freddy's, US History, Aviation , My Little Pony or Psychology.
Repetitive Movements	Stereotyped pacing that wears a route into the carpet due to frequency, whole body spinning and/or rocking in conjunction with head banging when content or bored or to wind down or pink flag movements combined with associated visual regard.	Non-specific pacing, toe walking, head banging when upset or frustrated, shaking legs up and down, wringing hands, hand flapping (not uncommon in young children), subtle finger posturing while talking or completing tasks.
Sensory Seeking Behaviors	Licking sandpaper, cannot go for walks on rainy days because child lies face down in puddles to feel water on lips, repeated smelling of items with no odor (e.g., puzzle pieces). Lining up items –and looking along the line (gets down on the floor to look at objects at eye level), peering out of corner of eyes (visual regard). Backing one's body into another to request frequent and intense squeezing.	Likes rolling down hills, rollercoasters, always wants to spin in tire swings or office chairs, loves water play, seeks out spicy or crunchy foods, seeks out mirrors or bright lights, prefers tight clothes, likes tight hugs/squeezes, heavy blankets or weighted vests, likes walking barefoot, likes to stroke or rub hair.
Sensory under sensitivity, over sensitivity (sensory avoidant behaviors)	Under responsive: Major injury occurred without display of pain or sharing with adult (burned hand on stove, broken toe, needed stitches when closed hand in car door). Oversensitive: Avoids favorite places because cannot stand the hum of neon lights, extreme distress with daily noises these cannot occur in their presence (e.g., vacuum), repulsed by the smell of people who are eating mints or have recently bathed and smell of soap, since infancy has avoided or resistedall physical contact (touch).	Under responsive: High pain tolerance for minor injuries (skinned knee, bruises). Oversensitive: Picky eater, dislikes soft texture or mixed texture food, refuses hot or cold food (insists on room temperature), dislikes tags in clothes, hates having hair washed or cut, refuses to wear jeans, shoes, or jackets, resists change of clothes with change of seasons. Dislikes or is distressed by loud noises (fire alarm, sirens), covers ears with blender.Likes to be squeezed or tapped but not touched softly or stroked. Will initiate touch with others but dislikes others to initiate touch
Difficulty with Transitions and Change, Rigidity or Inflexibility	Severe distress with trivial changes (e.g., home décor is moved, need to take alternate route due to roadwork), even switching from non-preferred to preferred activities is hard (e.g., Let's skip teeth brushing tonight and read an extra book instead). Refuses to eat from bowls, always walks on the left side of sidewalk.	Adjusting to new teachers (or substitutes or returning to school after a holiday) is stressful, switching from preferred to non-preferred activities is hard (e.g., time to turn off TV and get ready for bed), has to complete activities (TV program, game, worksheet). Needs special lovey to fall asleep, preference for a certain seat in the car or favorite plate.

Table 1. Symptoms of autism spectrum disorder: real life examples of red flags and pink flags from expert clinicians.

(continued)

### Table 1. Continued.

Symptom Type	Red Flag	Pink Flag
Play, whole and part relationships	Little functional use of toys as they are intended to be used (e.g., exclusively spins wheels on cars but never "drive them"). Interest in objects to the exclusion of people or the social world.	Poor quality pretend play (pretend play by him/herself but not with others, pretends same scenario over and over), wants others/caregiver to participate in play but only in certain ways (e.g., may be very directive).
Social Communication and Social Social Relationships	Interaction Seeks out relationships for primarily rational reasons (e.g., cites tax benefits of marriage). Talks incessantly about preferred topics regardless of partner's interest. Not easily comforted by caregiver, and distress may have no obvious cause.	Trouble understanding and expressing feelings or emotions (e.g., alexithymia), trouble reading the tone of a room, gravitates to adults or much younger children. May be difficult to comfort but caregivers usually know what the trigger for distress is. A history of difficulties maintaining friendships (often without understanding why they end)
Verbal Social Communication	Asks perseverative questions he/she already knows the answer to (not reassurance seeking), pronoun reversal (e.g., says "she wants water" instead of "I want water"). Immediate and delayed echolalia of content and tone (e.g., parroting repetitively without context, responds to "How are you?" with "Whenever you're in trouble, just yelp for help!") Pervasive atypical prosody with combinations of ASD specific patterns (mid-word dysfluencies/breathy breaks, poor inflection, mis-assigned stress) present since early childhood or marked language regression (loss of skill)	Scripted questions of others (asks new people same set of questions: What do you like to do? Did you have a nice weekend?), pedantic, overly formal speech (e.g., like a little professor). Immediate echolalia of content (e.g., responds to other's comment of "I like cows" with "cows", can be common in language delays). Subtle vocal quality differences or atypical prosody (e.g., tends to be flat, often exaggerated or frequent sarcastic tone). Speaks too loud or too soft for the social context, language delay with plateau of skills.
Nonverbal Social Communication	Using another person's hand as a tool (e.g., manipulates another's hand to operate a toy without eye contact), does not point to items just to show and share (e.g., point and look to airplane, then looks to parent with smile, then looks to airplane), regularly avoids eye contact and does not smile with eye contact to share enjoyment, even with preferred adults.	Leads others by the hand to what they want. Limited gestures, variable or poorly modulated eye contact. Does not respect the usual personal space boundaries. Has flat or inappropriate facial expressions.
Social Responsiveness, Social Initiation and Social Maintenance	Poor reciprocity (does not roll ball back and forth or respond to name when younger), never responds to comments made by others only direct questions, does not even notice if others are in obvious distress. Initiates with others solely to get needs met (e.g., requests). May tolerate (or enjoy) if caregiver or others join in child's play but child does not readily seek out the caregiver to share pleasurable activities or seek to maintain interaction if caregiver stops attending.	Trouble keeping a conversation going, only understands others' emotions if obviously displayed. Passive, abrasive, aggressive or disruptive when approaching another for social interaction. Described as being ignored by peers (due to passive presentation). Difficulty with reading nuances of peer relationships (e.g., is bullied OR reports being bullied even when that is not the intent; misunderstandings related to misinterpreting others' cues)

functioning. Due to their lack of specificity, pink flags must be considered cautiously. Depending on the totality of the individual's presentation, many of these pink flag symptoms may reflect normal developmental and behavioral variability and/or are more accurately explained by other disorders. Some pink flags may be common and even developmentally appropriate for younger children (e.g. hand flapping, toe walking). However, they may also be especially striking, unusual, or even off-putting in older individuals in a way that reflects their atypicality and therefore, diagnostic relevance. Pink flags should never be used in isolation to confirm a diagnosis of ASD. They are better thought of as signs that the evaluator should take a closer look at the patient's psychosocial history and presentation to effectively determine the etiology of these symptoms. As is true when confirming any diagnosis, both red and/or pink flags must significantly impact the patient's daily functioning to meet diagnostic threshold. As there is high variability in the neurotypical population in behaviors and social communication, pink flags may be present without being functionally impairing. Table 1 refers to a number of additional real-life examples of red and pink flags that the authors have come across in their clinical practice.

#### Important factors when considering the differential diagnosis of ASD

Because social difficulties are a common presenting concern across a myriad of diagnoses, a thorough diagnostic interview by a well-seasoned clinician will frequently unearth a number of pink flags, even if they are not part of the original reasons for referral, and sometimes even when the individual or informants downplay their relevance. The clinician's role is not only to recognize these features, but to systematically determine their true source or etiology to rule out or rule in a diagnosis of ASD. Both tasks can be complicated by a number of factors including comorbidities, similar presentations across multiple diagnoses (with *differing* etiologies), diagnostic overshadowing, and specific characteristics in the patient and/or system. Having a solid understanding of each of these features can help to ensure that the diagnostic conceptualization best captures the individual's symptom presentation, profile, and etiology.

#### Clarifying the presence of comorbid disorders vs. differential diagnoses

Comorbidities are high in ASD and can make differential diagnosis especially challenging. Systematic reviews and meta-analyses show a variable prevalence of comorbidity, with up to 94% of individuals with ASD meeting criteria for at least one additional diagnosis (Hossain et al., 2020). Challenges with social communication make it difficult to form meaningful relationships (Bromfield, 2010), which can result in social isolation, reduced quality of life, and in turn an increased occurrence of anxiety and mood disorders; individuals with ASD are three times more likely to have depression than peers (Croen et al., 2015; Van Steensel et al., 2011). Looked at another way, comorbidities in ASD are especially high for psychiatric conditions that are common in the general population, such as anxiety (1.47-54% of individuals with ASD have some form of anxiety), ADHD (25.7-65%), depressive disorders (2.5-47.1%), language disorder and intellectual disability (30-70%) (Fombonne, 2009; Hossain et al., 2020). As noted above, many of the "pink flags" that raise questions about a more subtle ASD presentation commonly occur in a number of psychiatric disorders. Indeed, a generic description of "social struggles" can represent common secondary sequela of anxiety, depression, learning disorders, ADHD, and personality disorders. Therefore, differentiating the guality and source of these symptoms from the core and primary social communication deficits seen in ASD requires careful exploration. For example, individuals with ADHD may be described as having difficulties with social/emotional reciprocity associated with inappropriate initiation of social interactions, unresponsiveness to facial expressions, difficulties inferring others' emotional state, and challenges engaging in reciprocal conversations. In these patients, however, careful investigation will show that their impairments are secondary to inattention to social cues and/or impulsive and distracted behavior, rather than an *inability* to understand subtle social interactions and respond accordingly. In more severe ADHD presentations, unpredictable behavior, excessive talkativeness, tangential conversations, trouble with maintaining personal space boundaries or poor self-monitoring can also lead peers to distance themselves.

Similarly, depression and anxiety disorders can be associated with social withdrawal or avoidance, flat vocal affect, minimal facial expressions, reduced gestures and limited or avoidant eye contact, despite an *intuitive* appreciation for the utility of eye contact to elicit and maintain joint attention, as well as a history of more typical affect and vocal quality during periods of decreased anxiety or euthymic mood. In individuals with depression you may also see anhedonia leading to decreased social activities and more isolative tendencies, which in turn can lead to less practice in social situations and atrophy of skills. With anxiety you might hear reports of high variability in skills depending on the context and demands of the situation. Working with a new examiner may trigger high anxiety and lead to diminished social interactions, minimal communication and averted eye contact. Report and ideally observation of (live or recorded) interactions with a comfortable communication partner (e.g., parent, teacher or spouse) may demonstrate a broad and strong repertoire of nonverbal and verbal social communication skills, in extreme cases this pattern of presentation may align with severe social anxiety and/or selective mutism. In anxiety (perhaps most clearly seen in Obsessive Compulsive Disorder) patients can present with higher levels of rigidity and ritualized/compulsive behaviors. At first glance, these behaviors (e.g., lining things up, needing to know the plan, trouble with transitions and change, latencies to social responses due to rumination) can raise questions about a possible ASD diagnosis (i.e., "pink flags"). Looking more closely at the source and pattern of these behaviors can help to differentiate the etiology of these symptoms. Patients with anxiety/ OCD but not ASD also should have intact social pragmatics though they may experience variable social success. Finally, the developmental course of symptoms is also different in mood and anxiety disorders, please see the 'Early History' section below for additional discussion.

Tics and Tourette Syndrome both involve habitual, non-goal directed behaviors that can mimic the repetitive behaviors seen in ASD. However, the motor stereotypies that are often present in ASD differ from tics in that stereotypies are often more rhythmic and typically occur for a longer duration (e.g., hand-flapping or finger-flicking) and are more likely to involve the hands, arms or the entire body. This is in contrast to tics, which are much more likely to take place in the eyes, face, head, and shoulders and to be briefer, very rapid and fluctuating (Singer, 2013). Also, tic disorders can be comorbid with ASD, where an individual may demonstrate both discrete tics and complex motor stereotypies.

In addition to the stereotyped repetitive movements that are a hallmark of ASD, children and adolescents with autism often present with a range of motor-based difficulties including: hypotonia, apraxia, clumsiness, toe walking, gross motor delay (Carbone et al., 2010; Ming et al., 2007), incoordination, reduced grip strength, poor balance, postural stability, abnormal gait, joint flexibility, and manual dexterity (Abu-Dahab et al., 2013), as well as difficulties with balance, slowed speed, dysrhythmia with timed movements of the hands and feet, and greater overflow during timed movements and stressed gait maneuvers (Jansiewicz et al., 2006).

Motor impairments appear to carry prognostic value for an individual child with ASD, even beyond social language functioning. For example, Sutera et al. (2007) demonstrated that motor functioning in early childhood was a better predictor of outcome two years later than any other factor measured. On the Physical and Neurological Exam for Subtle Signs (PANESS, Denckla (2008) and Denckla et al. (1985)), boys with autism were highly discriminated from controls using balance and gait, slower and dysrhythmic movements of the hands and feet, and greater overflow movements (Jansiewicz et al., 2006). Additionally, Mostofsky et al. (2006) showed children with ASD demonstrated impairment in all conditions (performing skilled gestures to command, to imitation, and with the actual tool) that were not fully explained by basic motor impairment. Notably, these motor difficulties do not explain the decreases in imitation also commonly seen in this population (Vivanti & Hamilton, 2014), especially for non-meaningful actions.

It has been postulated that motor differences may impact social communication, social success and opportunities. Motor differences may lead to impaired or slowed development of gesture, which may also exacerbate communication impairments in autism (Mostofsky et al., 2009). More generally, early motor impairments lead to reduced ability to participate successfully in child and teen activities, such as pretend play, games and sports, impair the acquisition of daily living activities, restrict vocational possibilities, contribute to an awkward impression among peers, and deprive the individual of social opportunities (Bremer & Lloyd, 2016; Zeliadt, 2017).

ASD is often comorbid with Intellectual Disability (ID), and individuals with ID but not ASD also show stereotyped and repetitive behaviors, which can further confuse the differential diagnosis. The most widely used questionnaire for characterizing repetitive behaviors is the Repetitive Behavior Scales – Revised (RBS-R; Bodfish et al., 2000), which is organized into six scales: stereotypic, self-injurious, compulsive, ritualistic, sameness, and restrictive behavior. This questionnaire can be very helpful when assessing individuals who are known to have an intellectual ability/IQ in the ID range. Several studies with the RBS-R (Martínez-González & Piqueras, 2019) or the similar Repetitive Behavior Questionnaire (Moss et al., 2009) found that adults with ID with or without ASD show elevated scores on all subscales, with minimal differences attributable to ASD except for overall greater severity; most research shows the severest stereotypies in ASD + ID, followed by ASD, followed by ID. These comparisons reinforce the idea that elevated repetitive behaviors cannot clearly distinguish ID from ASD + ID. One possible exception is a study of individuals with ID and 7 specific genetic syndromes (Moss et al., 2009), which revealed some syndrome-specific behaviors that may be helpful in a neuropsychological assessment of individuals with one of these known or suspected genetic etiologies.

As mentioned above, typically developing toddlers frequently present with repetitive behaviors and restricted interests, which makes distinguishing these behaviors in typical development, ASD, and ID especially difficult in very young children. To facilitate this process, the Repetitive Behavior Scale for Early Childhood was recently developed, pulling from the RBS-R, and validated for children aged 17 to 25 months of age (Wolff et al., 2016). This will no doubt help to differentiate repetitive behaviors in typical development from those in ASD, and – the more difficult differential – to compare RRB's in ASD vs. other developmental disorders. One other measure that should be helpful in this comparison is the repetitive behavior portions of the Toddler Autism Symptom Inventory, for children 12 – 36 months (Coulter et al, in press). Early validation of this measure indicates that higher prevalence of repetitive behaviors, restricted interests and unusual sensory behaviors, but not insistence on sameness, characterized the ASD group compared to both the typical toddlers and those with other developmental disorders, including Global Developmental Delay. Specifically, inflexible play, unusual body movements, strong specific interests, carrying around atypical objects, sensory seeking, and sensory hyperarousal were found in more than 50% of the ASD toddlers and distinguished them from those with typical development and other developmental disorders. In older children (mean age 9 years), Joosten and Bundy (2010), similarly, found that oversensitivity and sensory avoidance were more common in ASD with ID than in children with ID alone.

A theoretical distinction, useful in conceptualizing repetitive behaviors in neuropsychological assessments, has been drawn between repetitive motor behaviors/ unusual sensory responses, and an insistence on sameness (both in rituals and in the environment). Repetitive behaviors and sensory sensitivities are seen throughout childhood and correlate with IQ such that children with lower IQ and younger children with ASD typically show these behaviors. The second category, insistence on sameness, requires higher cognitive functioning (i.e., the child must be aware of these changes before he/she can respond adversely to them). Once the requisite age or cognitive level is reached, insistence on sameness does not tend to be correlated with IQ (Bishop et al., 2013). This is consistent with findings that insistence on sameness was the only feature not shown by a majority of ASD toddlers on the Toddler Autism Symptom Inventory (Coulter et al., in press).

It is not unusual for typically developing children and adults to have intensive interests and/or passions. These also need to be distinguished from the intense interests seen in patients with ASD that are *atypical* in their focus and/or strength. One key factor is the ability to actively engage in reciprocal conversations on topics *outside* of their interests. Patients with ASD often have greater difficulties with this task, and they typically try to redirect the conversation to their interests and/or disengage from the discussion when it veers outside of their interests. Individuals with ASD may also be more likely to "talk at" versus "talk with" a conversation partner, especially related to their restricted interests and may have trouble gauging when a conversation partner loses interest. The focus of their interests is also frequently atypical. For example, a client may appear to have an age-appropriate passion for sports, but if you dig deeper you may discover the individual is more interested in the statistics of the game or obscure details about the players, while having little to no investment in whether their team wins the game. (See Table 1 for additional examples).

Because of the overlap in symptoms across diagnoses, it is not unusual for an individual with ASD to be misdiagnosed with multiple disorders *rather than* ASD. A concept that may be helpful in clarifying the assessment in these cases is the notion of *parsimony*. For example, if a clinician finds themselves diagnosing or evaluating a patient previously diagnosed with ADHD, Social Anxiety Disorder, Language Disorder, Developmental Coordination Disorder *and* sensory processing differences, it may be worth reassessing the constellations of symptoms and considering if ASD is a more overarching, accurate and parsimonious diagnosis.

#### The role of diagnostic overshadowing

Diagnostic overshadowing is the tendency to assess individuals with developmental disabilities less accurately due to co-occurring and moreobvious medical, genetic, psychiatric, and/or learning disorders (Jopp & Keys, 2001; Reiss & Szyszko, 1983). These other diagnoses can lead clinicians to overlook the possibility of ASD (and other conditions), which in turn leads to the absence or delay of treatment. For example, Jónsdóttir et al. (2011) compared children diagnosed with ASD before 6 years of age to those diagnosed after 6 years and found that half of the latter group received a different developmental diagnosis (often language disorder) before their ASD diagnosis. Similarly, Hinnebusch et al. (2017) followed a sample of children at approximately 2 years of age with symptoms of ASD and severe developmental delays in all domains. They speculated that low cognitive functioning explained some of their ASD characteristics, and that at a later point in childhood, they might meet diagnostic criteria for an intellectual disability (ID) but not ASD. Contrary to expectation, almost every child at age four still amply met criteria for ASD, in addition to their significant developmental delays. Individuals with medical conditions are also especially at risk for diagnostic overshadowing, as their known etiology is easily (and frequently) used to explain their complicated psychosocial presentation. Focusing on their medical condition without conducting a careful differential diagnostic interview around ASD symptoms often fails to consider well documented risks for ASD comorbidity both in the literature and in the patient's developmental/psychosocial history. Indeed, there is ample evidence that complicated birth history (including prematurity), neurological disorders (e.g., epilepsy), GI issues and sleep difficulties are common in individuals with ASD (Bauman, 2010; Tye et al., 2019). For example, while specific rates vary widely across studies, approximately 25-30% of individuals with ASD experience seizures; patients with both ASD and ID show the greatest risk for epilepsy (21.5%; Amiet et al., 2008). Additionally, up to 60% of individuals with ASD have abnormal EEGs in the absence of clinical seizures (Kim et al., 2006; Tye et al., 2019).

Family history is also pertinent, given that ASD has strong genetic links. Genetic mutation is common in ASD, up to 25% of diagnosed cases have genetically identifiable causes (Huguet & Bourgeron, 2013). Other studies have shown that 5% to 15% of individuals with ASD have inherited copy number variations (CNVs) in some affected genes (Devlin & Scherer, 2012). Rare *de novo* mutations are identified as risk factors for ASD and may account for 2.6% of the variance in liability to autism, in addition to inherited common variation (Gaugler et al., 2014). Further, it is estimated that up to 1,000 genes are potentially implicated in autism, making it one of the most complex disorders (Ramaswami & Geschwind, 2018). Certain defined genetic conditions have also been associated with greater rates of ASD. For example, approximately 50% of individuals with Dravet Syndrome and tuberous sclerosis complex (TSC) meet ASD criteria (Strasser et al., 2018; Wong, 2006). Finally, despite the stereotype of individuals with Down Syndrome being overly friendly, ASD has also been found to occur more frequently in these individuals than in the general population (Dressler et al., 2011).

#### Individual factors

*Early history.* Early psychosocial and developmental history should be carefully explored when considering a diagnosis of ASD. Symptoms of this disorder can be evident as early as 12 months in some children, allowing for a reliable diagnosis in children as young as 14-16 months of age (Pierce et al., 2019). Even in children with more subtle presentations, nuanced symptoms are often evident from a younger age, even if it is difficult to document full criteria until many years later. In this sense, some individuals are said to "grow" into their deficits as their social environments become more graded and complex, thereby unmasking their underlying challenges (Ozonoff et al., 2015).

The developmental trajectory of social struggles (even if symptoms are not functionally impairing until later) can be useful to differentiate the source of pink flags that can be seen across multiple diagnoses. For example, patterns of later emerging social difficulties can be seen in ADHD secondary to peer rejection and missing social cues. Similarly, patients with generalized and social anxiety disorder can present with a history of typical social interactions and relationships in early childhood, followed by social withdrawal as their anxiety heightens. A careful analysis of when a patient's social difficulties emerged and their intact skills relating to social reciprocity can therefore help to clarify the source of their current impairments. The absence of other pink and red flags in a patient's developmental history can also help with differential diagnosis. For example, restricted and repetitive patterns of behavior and interests are typically notable from an early age in ASD (though the behavioral manifestations and foci often change over time). Similarly, the motor stereotypies associated with ASD typically develop before age 3, while tics usually emerge in early school years (estimated mean ages 4 - 7 years) (Singer, 2013). Compulsive behaviors, extreme rigidity and consuming thoughts usually develop at later ages in patients with anxiety disorders including obsessive compulsive disorder (Shulman et al., 2020). Finally, when patients present with primary deficits in language pragmatics (e.g., overly literal language, trouble changing communication to fit the context, difficulties utilizing intact language for social purposes) in the absence of restricted and/or repetitive behaviors a diagnosis of Social (Pragmatic) Communication Disorder may be considered. However, this diagnosis is new to DSM-5 and remains somewhat contentious as the prevalence appears low and the current criteria have been conceptualized by some as, "lying on the borderlands of the autism spectrum" (Mandy et al., 2017). Relatedly, clinical experience suggests that this diagnosis is frequently given without a thorough assessment for "pink flags" and other symptoms that would support the diagnosis of ASD had the evaluator asked about them/tested them as part of their assessment and diagnostic interview process.

Trajectory of skill development. The patient's developmental acquisition and implementation of social skills can also be a significant factor for ruling in or out ASD. A neurotypical child intuitively acquires social pragmatic skills in a natural, fluid, and generalizable fashion. The effortless mirroring and social learning of these children differs significantly from the more structured, repetitive, overlearned and often explicitly taught patterns of social behavior in patients with ASD. For example, clinicians should distinguish between a person's intuitive ability to connect with peers in a developmentally appropriate way and the application of *learned* social scripts and heuristics to interact with others. In fact, a review of the literature by Vanvuchelen et al. (2011), did not find that imitation deficits are universal in or specific to ASD and individuals with intact imitation skills can present with a more subtle presentation. It is especially important to understand that some individuals with ASD and high cognitive abilities can compensate for a less intuitive understanding of social relationships and pragmatics by imitating others and developing complex sets of social rules that can yield an intact social veneer. These systems provide them with structures to navigate social situations in a way that can camouflage their social impairments, at least until social expectations become more nuanced and complex. However, even when these systems are still relatively effective these individuals may become confused when confronted with novel social conflicts and may struggle to intuit people's motives and anticipate the reactions of others. They can also report feeling that their own actions are often misunderstood.

The capability of individuals with autism to develop and maintain both friendships and intimate relationships can vary greatly. The social communication deficits in ASD (e.g., poorly modulated eye contact, difficulties initiating and maintaining conversations, challenges expressing feelings) can propagate a misconception that people with ASD "do not want" friends. However, research shows that many individuals with ASD genuinely desire social interactions, despite often having difficulties initiating and maintaining friendships (Bottema-Beutel et al., 2016). When working with individuals with a high suspicion of autism who do report having friends, it is important to explore the quality, reciprocity and duration of these relationships. It is not unusual for individuals with more subtly presenting ASD to be able to play with unfamiliar children on a playground, and even to initiate friendships while having difficulties maintaining them. Finally, some individuals with more subtle ASD presentations can develop sustained friendships. At times, these friendships are with others who share the same interest or same set of social skills weaknesses or they may develop exclusively online relationships with connections made through videogames or similar means.

It is also important for clinicians to understand that individuals with ASD can both desire and successfully establish more intimate or romantic relationships. Historically, the study of sexual and romantic relationships was once excluded in this population (Torisky & Torisky, 1985). When it was studied, papers previously characterized this group as asexual, and/or largely heterosexual (Van Bourgondien et al., 1997). However, more recent studies have suggested that many individuals with ASD seek romantic and sexual relationships, and similar to the general population have great diversity of sexual experiences and behaviors. In terms of romantic relationships, up to 73% of individuals report intimate relationships (Strunz et al., 2017), although their level of experiences with sexual intimacy varies, and ranges from limited partners to extensive experiences with a large number of partners (Hancock et al., 2020).

In addition, individuals with ASD may experience greater levels of non-heterosexual attraction (Strunz et al., 2017) and some may display hypersexual behaviors compared to the general population (Schöttle et al., 2017). Although research is limited, evidence suggests a co-occurrence between gender diversity and autism. A number of studies have identified increased rates of gender variance in individuals with ASD using a single item (110: "wish to be opposite sex") on the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001), a caregiver-report measuring behavioral difficulties. Studies show that between 4% and 5.4% of youth with autism may potentially identify as gender diverse, compared to 0.7% of youth without ASD (Janssen et al., 2016; Strang et al., 2014). Additionally, de Vries et al. (2010) reported a prevalence rate of 7.8% of youth with autism and gender diverse expressions, which is notably ten times higher than the general population. Between 2.3% and 9.3% of youth with gender diverse identities referred to a pediatric medical center also had a diagnosis of autism spectrum disorder (Spack et al., 2012). Finally, Warrier et al. (2020) reported higher rates of ASD in transgender and gender-diverse youth (not limited to individuals with gender dysphoria) using a large, cross-sectional dataset. Within this study, transgender and gender-diverse individuals with and without ASD scored higher on self-report measures of autism-related traits, systemizing (analyzing, extracting and constructing rules that govern behavior of a system), and sensory sensitivity, and lower on selfreport empathy measures than cisgender individuals.

#### The role of eye contact in ASD assessment

Eye contact rarely falls into a simple "present" or "absent" categorization, well-modulated eye contact is a very nuanced and highly contextual skill that in typical development is socially learned through complex implicit shaping and generalization processes. Also, it should be explicitly noted that poor current or historical eye contact is not required for an ASD diagnosis. However, given the early emergence of the use of eye contact to elicit and sustain social engagement and reciprocity in typical development, the quality of eye contact can differentiate young children with global developmental challenges or language specific delays from ASD. In fact, difficulties making eye contact is often an early indicator of autism (Chawarska et al., 2014; Szatmari et al., 2016) and may be detected as young as 2 to 6 months of age (Jones & Klin, 2013). In early development, eye contact serves to regulate face-to-face social interactions (Baron-Cohen & Hammer, 1997) and helps coordinate visual attention (Arnold et al., 2000). Several models have been used to help explain atypical eye contact in ASD. Some suggest that individuals with autism are very sensitive to eye contact and actively avoid eye contact to prevent high levels of arousal (Senju & Johnson, 2009). Others indicate that social stimuli, specifically eyes and faces, are less informative or rewarding to look at for individuals with ASD (Chevallier et al., 2012). Additionally, differences related to attentional states and associated constructs may contribute to differences in the subtle regulation of eye contact (Tager-Flusberg, 2007).

Even when patients do not exhibit frank impairments with eye contact, a more thorough assessment of their developmental history and presentation may reveal more significant historical impairments. Children diagnosed with ASD receiving early intervention services typically engage in numerous hours of intensive behavioral therapies and increasing eye contact is often an early common goal (Carbone et al., 2013). As compensation or explicit instruction in regulating eye contact can occur over time, evaluators should explore if eye contact has ever been poor or if the person has received specific intervention to facilitate eye contact.

How patients use eye contact can also be informative. For example, some individuals with ASD have learned to look at other facial features or slightly to the side of, between, or slightly above someone's eyes in response to frequent reminders or other shaping. Eye contact may be present but not utilized in a nuanced way or may be merely tolerated, and even tiresome or effortful to maintain over a more extended interaction. Clinicians should also consider the social situations in which the patient uses eye contact. For example, does the individual make eye contact only when they want something or when they are speaking? Or do they use it to elicit joint attention and engage nonverbally while listening to their speaking partner? Is their eye contact appropriately integrated with verbal and nonverbal modes of communication? Are they able to modulate eye contact intensity across a variety of situations (e.g., avoiding overly intense eye contact in the elevator or when on a first date)?

#### Gender considerations in ASD presentation

While gender differences in autism are noted in the DSM-5, distinguishing factors have not been clearly outlined (APA, 2013). Historically, ASD has been perceived to be a predominantly male diagnosis, with a male to female ratio of 3:1 (Loomes et al., 2017), while for individuals with profound intellectual disabilities, the ratio is closer to two males for each female (Dworzynski et al., 2012). While these prevalence rates highlight the etiology of ASD, they may also reflect gender biases in diagnosing autism. Gender bias may be attributed to the poor inclusion of female samples, standardized diagnostic instruments which may not be sensitive to a possible he differing distribution of symptoms between genders (Young et al., 2018), and misconceptions held by healthcare providers regarding autism expression in females. Studies indicate that even in females who showed clear signs of autism, some did not fully meet formal ASD criteria given that their symptoms were not based on traditional descriptions of ASD (Kopp & Gillberg, 1992). Others have shown that when intelligence is intact, females were significantly less likely to be diagnosed with autism (Dworzynski et al., 2012). Even with comparable levels of symptom severity (Geelhand et al., 2019) and

similar ages of first concern (Rutherford et al., 2016), females are less likely to receive a diagnosis than males. Additionally, misconceptions held by some healthcare providers may lead to underdiagnosing in females. In one study (Watson, 2014), caregivers perceived healthcare professionals as hesitant in providing their daughters an ASD diagnosis, and instead, opted for other conditions. Further, Cridland et al. (2014) included reports of healthcare professionals feeling reluctant to diagnose a female with ASD due to lack of awareness of autism presentation in this group, and a perceived higher incidence of ASD in males.

The quality of social skills in girls with ASD, especially those with intact cognition, may at least on the surface, *resemble* neurotypically developing girls (Dworzynski et al., 2012), even when closer evaluation can document sufficient impairments to meet diagnostic criteria. The *Camouflage Hypothesis* has been used to describe girls with autism who blend in or camouflage within social settings through the use of imitation or compensation through cognitive skills (Attwood, 2008). This social veneer and the more subtle difficulties exhibited within older and cognitively intact females, as well as the bias of autism rarely occurring in girls, can obscure a provider's diagnostic and clinical impressions.

Bargiela et al. (2016) identified four key characteristics to help describe symptom presentation in females with autism (Hull et al., 2020). First, females with ASD often exhibit greater social motivation and interest in developing relationships compared to boys with ASD (Sedgewick et al., 2019). Second, the camouflage hypothesis (discussed above), can include such strategies as practicing gestures, facial expressions, and eye contact (Hull et al., 2020). Third, co-occurring emotional and behavioral difficulties may be partially influenced by gender. For example, males with ASD generally demonstrate greater externalizing behaviors, such as aggression, hyperactivity, and/or attention deficits (Giarelli et al., 2010) while females with autism are more likely to develop internalizing difficulties such as anxiety (Westwood et al., 2016). This suggests that in order to receive a diagnosis, females may require a more severe and externalizing symptom presentation (Lundström et al., 2019). Lastly, repetitive behaviors and interests may be influenced by gender and societal gender norms (Hiller et al., 2014). Generally, males tend to exhibit more frequent restricted and repetitive behaviors and interests than females (Duvekot et al., 2017), and these symptoms were more predictive of an ASD diagnosis in males compared to females. Additionally, intense interests observed in males often focus on mechanics and mathematics, while females are more likely to indicate socially focused interests (e.g., other peers, novels) and/or more normative interests (e.g., animals, pop stars; Bargiela et al., 2016; Hiller et al., 2016 ). To help improve clinical decision making, healthcare professionals may need to further assess the quality and quantity of presenting symptoms as well as differences in social communication and presence of restricted and repetitive behaviors in females with suspected autism, as this group may exhibit a more nuanced clinical presentation.

#### Variability can be seen across settings

Finally, it should be acknowledged that it is not unusual for patients with ASD to present differently across settings. For example, teachers may report that a child has difficulty with peer interactions as well as with attention, compliance, and/or emotion regulation, while a parent may deny these challenges at home. In this case, it is possible that the parents are consciously or unconsciously making fewer demands on the child and are accommodating their lives to the child's needs. It is also not unusual for people with ASD to show relative strengths with familiar interaction partners, when comfortable and within less stressful environments, which can further account for this discrepancy. The opposite scenario may also occur in which the child is better requlated at school, only to demonstrate more problematic behaviors at home. Children in these situations may be demonstrating their need for reliability and structure as well as an attempt to "hold themselves together" at school, only to engage in repetitive or stimulatory behaviors at home to "blow off steam." A similar pattern can be observed during a neuropsychological evaluation, giving clinicians another tool to evaluate the child's social skills. For example, some children with ASD exhibit improved eve contact and less discrepant social skills during structured cognitive testing and more impairments during casual conversation or other non-goal directed activities. They may also engage more successfully with tests that are clearly structured and struggle with more open ended, imprecise questions and directions, particularly if they include nonliteral, abstract or metaphorical language.

#### Family/collateral informant factors that can delay diagnosis

When evaluating for ASD, it is not only critical to assess the individual's social interactions while they are in our offices and/or their performance on social pragmatic measures, we must also consider the patient's social skills (and impairments) from a psychosocial and contextual perspective. Although information from caregiver(s) is commonly sought, the type of collateral informant will necessarily vary depending on the age the patient and the availability of the informants (e.g., parents, caregivers, significant others, roommates, etc.). This is especially true when considering assessment in adults where caregivers may be less a part or unavailable for the assessment. Assessment of context requires carefully targeted interviews with an awareness of (1) how some parents or partners may inadvertently (or intentionally) make up for the patient's social impairments; (2) how parent or partner characteristics may make it challenging for them to recognize and therefore report social deficits; (3) how family structures can hide social delays; and (4) how parents may unintentionally provide inaccurate details regarding their child's development. Clinicians who do not take these factors into consideration may inadvertently rule out the diagnosis, even when a more careful interview can document a robust psychosocial history consistent with ASD. Caregivers who are well intentioned, and especially those who have the privilege, ability, time and socioeconomic options to find and take advantage of community resources, may develop and implement a number of strategies that can help younger children make up for social impairments. For example, if their child is not being invited to play with other children and/or has been unable to get through playdates without emotional outbursts, they may create supervised, carefully structured social opportunities and offer highly valued experiences as incentives (e.g., going to the pool, lunch at Chucky Cheese). With this support, and a great deal of instruction, their child may in fact be able to develop friendships and engage in reasonably successful peer-to-peer interactions. Thus, if asked whether their child has friends and can play successfully with others, they would say "yes," but they may not spontaneously explain how much work has gone into this process, or that they worry their child would be unable to maintain these relationships without their support. Similarly, when one or more of a child's caregivers are mental health providers, they may provide more explicit social skills training that can hide the child's impairments, at least until the level of social sophistication expected by their peers becomes too complicated for the child to keep up with the social demands of complex unstructured interactions (e.g., high school locker rooms). Often, if enough pink flags are evident to direct a clinician to ask these same parents more explicit questions, it becomes clear that the child is not *spontaneously* generalizing skills, and that their parents have to provide an unusually high level of instruction on a constant basis rather than providing occasional check-ins and explanations, which the child then uses to apply to future interactions.

Considerable evidence from family and twin studies indicate that the etiology of autism is largely genetic (Bourgeron, 2016; Steffenburg et al., 1989). Concordance rates range from 60-96% in monozygotic (MZ) twins compared to 0-23% in dizygotic (DZ) twins depending upon the sample and diagnostic boundaries (Bailey et al., 1995); a 2009 study of 277 twin pairs (Rosenberg et al., 2009) found concordance of 31% for DZ and 88% for MZ pairs. Additionally, relatives of individuals with ASD often present with qualitatively similar though subclinical ASD characteristics, termed the broader autism phenotype (BAP; Gerdts & Bernier, 2011). Consequently, when working with individuals with more subtle presentations, it is also not unusual for an affected parent to remain undiagnosed and have a limited awareness of his or her own social challenges. Even when they are aware of their child's difficulties, they may normalize them, because they had (or have) them as well. For example, parents will sometimes dismiss social or other difficulties by saying "he's just like his father was at that age". In these circumstances it can be difficult for clinicians to formally document the full range of symptoms needed to confirm the child's diagnosis. Similarly, in the adult population, partners may be attracted to one another due to shared interests and therefore a spouse may not report any history of intensive/restrictive interests as it is a family or shared interest. Alternatively, a more gregarious adult may be attracted to their partner's more reserved nature, and therefore may not recognize and/or highlight the patient's introverted and socially awkward characteristics. Family structure can also make it challenging for parents to accurately describe a child's psychosocial delays and/or emotional and behavioral challenges. For example, when parents have only one child, they are often better able to accommodate a child's atypically rigid needs for predictability and structure. If their child struggles with transitions, these families may be able to avoid these triggers altogether (e.g., one parent can stay home with the child while the other takes care of weekly errands). Their home can also be better tailored to the child's preferences (e.g. unusual sensory needs). For example, there would be no siblings making loud noises or objecting to the child's rigid behaviors or insistence on sameness. From a psychosocial perspective, only children frequently spend more time interacting with adults. When these children have high cognitive abilities and more subtle social impairments, they can look extremely bright and are often described as "mature" based in large part on their ability to discuss intensive interests with sophisticated and detailed knowledge. When these

children struggle to connect with same age peers, parents may report that they are only struggling socially because their classmates have different interests and/or cannot "keep up" with their child's intellect; they fail to recognize that successful interactions with adults who accommodate to a child's preferred topics of interest does not rule out difficulties with social reciprocity and an inability to engage in shared conversations on topics outside of their choosing.

On the other hand, when children have siblings, this can also lead to inaccurate assumptions regarding the source of the individual's challenges. For example, parents frequently explain that their child's language skills emerged late, because their sibling "talked for him." Many of these children can also successfully and happily engage in simplistic joint imaginative or symbolic play with siblings, but not with other children. Thus, if asked about this skill set, a parent may report that they play imaginatively "all the time." However, further investigation may show that the child is simply following the sibling's lead (or direct instruction) and is unable to initiate or maintain this form of play independently or with other children who may not be as understanding about the identified patient's rigidity or other difficulties. Alternately, individuals with ASD may be described as highly imaginative based on play with their often younger siblings, when further questioning reveals the patient is highly directive and/or their play is considerably limited in variability or repetitive in nature.

Finally, one of the biggest challenges when collecting psychosocial history is that collateral informants can inadvertently provide inaccurate information in ways that lead to incorrect diagnostic conclusions. This is not to say that they are intentionally attempting to obfuscate relevant details. Rather, it is because they are unaware of the clinical distinctions in many of the key words we use, and because they frequently make inaccurate assumptions regarding the *source* of a child or adult's presentation. Thus, it is incumbent on neuropsychologists to ensure that we offer enough instruction (and seek out sufficient clarification) during our interviews to ensure that we are speaking the same language and addressing the person's developmental presentation through the same lens. For example, it is not unusual for parents of children with more subtly presenting ASD to emphatically describe their child as empathetic. However, when asked to clarify what they mean by this term, and when parents are asked for specific examples, it becomes clear that they are describing characteristics of generosity and caring about others and sometimes even a tendency to almost rigidly follow rules of "fairness" (e.g., "if I have a cookie, my sister should have one too"), rather than an ability to intuitively infer another person's social/emotional experiences without explicit instruction. Similarly, these parents will often report that their child is able to understand nonverbal social cues. Often, they will add examples, noting that their child can understand "If I'm mad at him or if his sister is upset." When clinicians fail to ask clarifying questions, this information can be used to incorrectly rule out an ASD diagnosis, even when further investigation can show that these children are responding to overtly obvious cues (e.g., yelling or crying), but they are unable to understand more subtle interactions (e.g., being more guietly frustrated or withdrawn). Their child may also struggle to *infer* why someone might be mad without direct observation of the trigger or clear verbal labeling. Finally, parents may also report that their child is capable of engaging in reciprocal conversations. If not asked, they may not share that this typically occurs only when discussing their own intensive interests, or that they may initiate conversations well but then struggle to maintain them or tend to end conversations inappropriately (e.g., simply leave the room when the conversation turns to a topic they find uninteresting). In each of these instances the child's parents are being truthful in their report, but their lack of awareness of our clinical and developmental expectations may prevent them from sharing the most relevant details regarding their child's social development without explicit questioning and clarification.

#### Screening and diagnostic instruments for evaluation of ASD

Given the variability in an informant's ability to recognize and accurately report the full range of psychosocial difficulties in the patients we evaluate, it should be no surprise that the diagnosis of ASD is generally more reliable across providers and over time, if they are based on direct and structured observation of a skilled clinician as well as history obtained from a knowledgeable informant (Gabrielson & Young, 2015; Kim & Lord, 2012). The following is a brief summary of some screening and diagnostic instruments for evaluation of ASD. The reader is directed to additional resources, articles and tables that describe diagnostic tools for ASD in the literature in more detail (Brian et al., 2019; Shulman et al., 2020). The most well-studied assessment methods are the Autism Diagnostic Interview-Revised (ADI-R; Rutter et al., 2003) and the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2; Lord et al., 2012). Other standardized instruments include the Screening Tool for Autism in Two-Year-Olds (STAT; Stone et al., 2004), Childhood Autism Rating Scale (CARS; Schopler et al., 1980, 1988), Social Communication Questionnaire (SCQ; Rutter et al., 2003) and Social Responsiveness Scale, Second Edition (SRS-2; Constantino & Gruber, 2012). Finally, as noted above, the Toddler Autism Symptom Interview was recently designed to structure parent report for diagnostic criteria in children aged 12 to 36 months (Coulter et al., 2020; https://mchatscreen.com/TASI). The pros and cons of these measures will be described in more detail below.

When a clinician is asked to evaluate for possible ASD, use of standardized instruments may facilitate more certainty and often, more satisfaction from the family or referral source and may be necessary to qualify individuals for services. When full clinical samples of referrals (including younger and more impaired individuals who might never be referred to a neuropsychologist) were studied retrospectively, clearly valid cut-offs on the ADOS-2 could be set, reflecting a very high likelihood that a person had autism with a particularly high score and very likely did not if they received a very low score. Only about 30 percent of cases were uncertain and required additional information (Kim & Lord, 2012; Zander et al., 2015). This fits with the fairly well-established data, even across countries, of about 80 percent sensitivity of the ADOS-2 (higher in less verbal children age 3 or older and a little lower in adults with average intelligence) and similar level of specificity (which is lower in very young children and in adolescents and adults with comorbid conditions such as ADHD). It is important to note that how well an instrument performs depends on the sample population being evaluated. For example, when the M-CHAT has been used as a population screener in young children, its sensitivity is limited but its specificity for developmental disorders is higher (Guthrie et al., 2019). In contrast, when it is used with a clinical sample of children suspected of having developmental disorders, the sensitivity is stronger but the specificity for autism is not as good (Yuen et al., 2018). This is likely true for almost all instruments though many have not been studied in both kinds of samples.

The ADI-R is easily combined with a Vineland Adaptive Behavior Scales (Sparrow et al., 2016) which reduces the time the Vineland takes. The structure of the measure also provides an opportunity for clinicians to discuss the caregivers' goals and fears for their child, and the potential differential diagnostic considerations (e.g., intellectual disability, ADHD, learning disorders and/or language impairments). A briefer ADI (one hour), organized in modules by age, language level, and purpose of the evaluation, is being developed, and is expected to be published in 2022. Despite their strengths, these instruments do have some disadvantages including a need for extensive training and practice. For example, the ADOS-2 should not be administered by clinicians who only use it a few times a year and/or without regular practice. Indeed, while this measure is often referred to as the "gold standard" instrument used to detect the presence of ASD, the possibility of false positives due to patient characteristics and/or inaccurate administration and scoring by a clinician without sufficient training or practice may create difficulties. As noted above, false positives may occur when scores are elevated due to other emotional, behavioral, and/or psychiatric conditions with similar behavioral presentations and symptoms (Renno & Wood, 2013; Schwenck et al., 2014) and/ or intellectual impairment. Shyness or frank social anxiety, or clinical depression, for example, may be accompanied by avoidant eye contact, flat affect, and restricted reciprocal conversation during testing, leading to elevated ADOS-2 scores.

False negatives can also occur, especially when scores fall in the borderline/subthreshold range, and are used to inaccurately rule out autism. Given that the coding of the ADOS-2 is derived from a single approximately hour-long observation, it does not include information regarding a child's early developmental history or yield information about how a child performs with peers or with other familiar or unfamiliar adults. Moreover, the ADOS-2 provides information only on current behaviors and was not developed to measure changes over time. The domain or total scores on the ADOS-2 are therefore not always an accurate measure of response to treatment or of developmental gains, especially in the higher modules (Lord et al., 2012). In some cases, it may be appropriate to place less emphasis on ADOS-2 scores and cutoffs, and instead use the rich observations and clinical information obtained from the ADOS-2 to map onto the DSM-5 or ICD-11 diagnostic criteria in concert with information gathered from collateral sources and early history.

During COVID-19, many clinicians are limited to remote assessments or evaluations conducted in masks. The ADOS-2 is not valid when either the clinician or the client is masked. Clinicians may administer selected tasks from the ADOS-2 and describe these in reports, but the scoring is not valid. Thus, a currently open-source measure was created that provides some of the same information as the ADOS-2, it is called the Brief Observation of Symptoms of Autism (BOSA; Lord et al., 2020). There are currently versions for minimally verbal adults and adolescents, a version for children with phrase speech, and two versions for verbal individuals, divided by age. These comprise

12-14-minute series of tasks using mostly ADOS-2 materials that caregivers, without masks (if COVID is still mandating mask wearing), can administer without training. Teacher, therapists or other familiar adults may also be used to help administer the BOSA. It is scored by an ADOS-experienced clinician using the ADOS-2 module that the child or adult would typically fall within. ADOS-2 scores are then mapped as examples onto DSM-5 or ICD-11 criteria to help in making a diagnosis and to provide guidance in what further information would be necessary. There are currently no psychometric data on this measure other than that our own clinicians were able to reach test-retest reliability on it relatively quickly. We also carried out an initial evaluation of where within each ADOS-2 code, individuals with autism were reliably distinauished from those without autism. We are working on psychometrics and perhaps a revision of the BOSA based on these findings at the current time. It is not intended as a long-term replacement of the ADOS-2 but as a temporary measure to gather information while COVID-19 restrictions limit the safety of standard diagnostic procedures. It may also be used to supplement the ADOS-2 to gain observations of social skills with familiar adults. We would expect the sensitivity and specificity to be lower than the regular ADOS-2, but are hopeful it can still contribute unique information to the clinical process. As with other screeners, it should not be used on its own, but along with parent or teacher report measures to contribute to the information that the clinician puts together.

The ADI-R is more structured than an informal interview, but it is time-consuming, typically requiring up to about 3 hours (with less time for younger children or minimally verbal clients). Importantly, children with multiple comorbidities (e.g., ADHD, learning disorders, and anxiety) can obtain mildly elevated scores, placing them into the clinical range, even when they do not meet ASD criteria (Grzadzinski et al., 2016; Havdahl et al., 2016). It is also less sensitive with very young children, particularly firstborns, because new parents may be less aware of ordinary social behaviors in young children. The face validity of some questions means that findings can be affected by caregivers' knowledge about autism and/or a desire for such a diagnosis. Finally, it is less specific across the age range for individuals with IQs that are lower than 50. Questionnaires such as the SCQ (Rutter et al., 2003) and the SRS-2 (Constantino & Gruber, 2012) may be helpful screeners if completed by caregivers before an assessment, though they may not add much to the differential diagnosis if ASD is already a specific concern by the parents or clinician. The specificity of the SCQ is generally guite high (few false positives), except in patients with very low IQs, so most children and adults who score within the standard range (15 or over) are very likely to have autism. However, the sensitivity (false negatives) for young children (under four years) and for verbally articulate older children and adults is not high. Because the SCQ may miss considerable numbers of very young children, as well as older and more verbal children and adolescents, various researchers have suggested lower cut-offs, going down to 11 (Corsello et al., 2007; Wiggins et al., 2007).

The SRS-2 emphasizes general behavior problems (e.g., similar to internalizing and externalizing behaviors from the Child Behavior Checklist [CBCL); Achenbach & Rescorla, 2000, 2001) more than social behaviors or ASD. Scores are also affected by impairments in intellectual ability (e.g., borderline or lower IQs), but not by subtle

differences within the average range (Charman et al., 2007; Hus et al., 2013). Thus, the SRS-2 is not a specific indicator of autism (e.g., specificity is low) nor is it really a measure of social skills. However, high scores can alert clinicians that further investigation may be warranted, particularly if there are few other issues and no intellectual disability; low scores on the SRS-2 would suggest a child is unlikely to have autism unless the case is very mild and the individual is intellectually very capable. The same issues hold true for the Pervasive Developmental Problems subscale on the CBCL. Particularly in combination with the ADOS-2, these scales may be helpful as adjuncts, but should not be used on their own.

The STAT (Stone et al., 2004) is an excellent secondary screener for young children, takes less time than an ADOS-2 and requires less clinician training, but it is limited to patients between the ages of 24-36 months and performance is highly correlated with language and intelligence. The TASI (Coulter et al., 2020) is a diagnostic interview that requires little training to administer beyond the guidelines in the manual, effectively discriminates ASD from other developmental disorders, and is relatively brief to administer, but has been validated only for ages 12-36 months. Finally, the CARS (Schopler et al., 1980, 1988) is the only instrument that allows a "clinical summary of both observations and reports." This is in contrast to the ADI and ADOS-2, as well as the SCQ and SRS-2, each of which rely on observation or caregiver report but not both together. The statistics supporting the CARS are reasonable and it can be useful diagnostically, but its items do not correspond to DSM-5 or ICD-11 and it confounds other characteristics (e.g., intelligence and the clinician's overall perceptions) in the total scoring. Nevertheless, it can be useful to confirm an autism diagnosis, in part because many individuals with autism have more co-occurring disorders such as ADHD, anxiety, intellectual disability and/or lower verbal skills, which all result in higher (more abnormal) CARS scores. As demonstrated during the time of COVID-19, the CARS can be particularly useful for clinicians who are making diagnostic decisions based on caregiver report, remote observations and remote testing. Additional information about telehealth and virtual visit considerations are outside the scope of this review but the reader is referred to separate articles (Berger et al., 2021) and in this special issue on ASD for a discussion of these factors (Lord et al., 2020).

#### Communicating with families about an ASD diagnosis

Providing diagnostic results to families is an essential but complicated component of any evaluation. When done effectively, it creates a therapeutic opportunity to provide clarity and a reasonable path forward. Providing space for the family to feel heard, to grieve (if that is their response), and begin to come to terms with their new understanding is an important and necessary component of this intervention (e.g., Postal & Armstrong, 2013; Smith et al., 2007). An ASD diagnosis can help families and partners to better understand the ways in which their loved one experiences and relates to their world. However, most individuals have an inaccurate schema of what ASD "looks like" and "means" based upon others they know with an ASD diagnosis and/or popular representations of ASD. This can lead to distress and confusion when an autism diagnosis is first presented, especially if the image they have in their minds for what

ASD "looks like" differs significantly from the presentation of your patient. Helping family members to understand the nuanced presentations of ASD (in the context of "if you know one person with autism you know one person with autism") can help them to accept your diagnosis and begin to integrate their loved one's presentation into their own ASD schema. Clinicians differ in how they prefer to support families who insist that their family member does not have autism. One approach is to explain that although ASD is a medical diagnosis, it can be thought of as a collection of characteristics and then reviewing the behaviors that led you to this diagnosis. This strategy can be especially useful when including behaviors that have been endorsed by the family members themselves. If this discussion does not to lead to an acknowledgement of the diagnosis, some feel that psychologists and neuropsychologists are like physicians, in that they must include the diagnosis in a report even if the family is not receptive. Others may attempt to meet the family half-way, explaining that they need to put enough into the report to get the patient the most beneficial and appropriate services, while noting that the family does not need to agree at present with the diagnosis. In these instances, the clinician may suggest a follow-up evaluation and discussion in six months to a year to give everyone a clearer picture of the patient's presentation and associated diagnostic profile. Another option in such a situation is to discuss with the family the option of a "provisional" diagnosis of ASD, which is allowed as a specifier in the DSM-5. The reluctant family may more easily understand and accept this diagnosis when the specifier makes it clear that the diagnosis is not definite, but that services for ASD are warranted and that delay is not wise. A reevaluation in 6 months to a year can then be planned with the goal of either confirming or disconfirming the diagnosis.

While some families are devastated by and even forcefully object to an ASD diagnosis, others may be upset and disappointed if ASD is ruled out, especially if they are hoping for services that are diagnosis-driven. In these instances, clinicians need to acknowledge the overlap in symptoms (e.g., difficulties with attention, executive function, social responsivity, and behaviors) and provide alternative conceptualizations for their loved one. Explaining the difference between core ASD symptomatology and associated features may also be helpful. The key is to affirm the challenges the family members have and reassure them that you are still able to provide them with a roadmap for success, even if it is not the path they expected to take. Neuropsychologists can also get pushback from other providers, especially if they are less experienced in the nuanced presentations of ASD, and sometimes when the provider believes their patient has ASD and the neuropsychologist does not. Again, having a strong understanding of what ASD is and is not can help clinicians to articulate conceptualizations effectively to best support the needs of the patient.

Finally, an additional complexity occurs when a patient does not clearly meet diagnostic criteria for ASD, but it also cannot be fully ruled out. Helping the family understand the nuance of this ambiguity is important to ensure they seek recommended services to manage whatever is impacting the individual's current presentation, and so they do not believe that autism is entirely "off the table." In both written and verbal communication with the family, clinicians should clearly indicate why a diagnosis cannot be confirmed at this time (e.g., another condition is making it difficult to understand the etiology of symptoms, or not enough ASD symptoms were identifiable at this time to meet full diagnostic criteria but clinical concern persists) and what steps they should take next (e.g., evidence-based treatment for confounding anxiety and re-evaluation in the future). In addition to providing the diagnosis, one of the therapeutic benefits of a feedback session is to facilitate an understanding of what the autism diagnosis means for the individual and the family. Clinicians should emphasize how to support a healthy development of sense of self in the individual. Autism selfadvocacy groups have spearheaded movements toward acceptance of neurodiversity as a positive component of identity. Diagnosed patients can now access a wealth of support within communities of neurodiverse individuals, which in turn can help them to recognize how autism shapes their personality and perspective in meaningful and valued ways. Facilitating discussion of the individual's personality as well as related and commonly positively regarded traits that are often observed in autistic individuals (e.g., truthfulness, strong capacity to learn and remember information of interest, quirky sense of humor, desire to follow rules) can help the individual and their family recognize the interplay of ASD and their loved one's unique personality.

The challenges that autism can bring should also be addressed. The truth is that a diagnosis of ASD necessitates clincially significant impairment, which exacts a toll even in patients with more subtle presentations. For example, these individuals are often able to successfully navigate many social settings, but this can lead to extreme fatigue, emotional distress, and difficulties with sense of self, as they may be using masking strategies to facilitate success that does not feel authentic to who they are. Validating this experience and helping the individual and family explore what strategies may be deleterious despite "success" can help the individual develop agency and a stronger sense of self as a neurodiverse person who does not always need to conform to neurotypical standards. Because many individuals with autism see the world differently than their family, the feedback session may also need to address the importance of flexibility and being open to the different ways happiness, success, and metrics of "positive outcomes" can manifest. It is important for families not to project narrow expectations of friendships, work, etc. onto their loved one, as this may not be what the individual with ASD wishes for themselves or can achieve. For example, recognizing that the social expectations of parents may not fit the social desires of the child is important to ensure that the child is not being pushed to "perform" in ways that do not feel authentic and may not be successful. Finally, neuropsychologists should address expectations for prognosis. While many families will explicitly ask for information related to their loved one's future, others do not because they may be afraid of the answers, or they think it is inappropriate to ask. Some of the most common questions are whether their child will be able to attend some sort of higher education or vocational training; will be able to have friendships and marriage; and will be able to live independently. Of course, clinicians should be mindful about any prognostic statements and will want to balance setting artificial glass ceilings for individuals and managing expectations for families. In our experience, if this is a first evaluation, the child is young, and has not yet had evidence-based intervention, parents can accept the fact that it is too early to make any prognosis if they are also given some concrete perspective (e.g. after the child has had years of intensive high-

quality therapy it may be easier to anticipate his or her developmental trajectory). If this is a follow-up evaluation or an assessment of an older child with consistent patterns of strengths and impairments as well as stable language and intellectual findings, the clinician may be able to provide some guidance about likely developmental trajectory. Be careful, however, not to state your opinions with a certainty beyond what is warranted (for example, one parent of a two-year-old shared two early prognostic opinions: one professional said the child would be institutionalized soon and for the rest of his life. The other said "Don't worry, he'll be a quirky professor"). Impressions and prognosis should be conveyed compassionately and with caveats as clinicians do not have crystal balls and cannot predict specific outcomes for any person (with or without neurodevelopmental differences), especially when they are young.

#### **Conveying key recommendations**

Medical recommendations typically include meeting with the individual's primary care provider to share results and determine what referrals must come from this provider. Consultation with a psychiatrist experienced in working with individuals with ASD may be recommended if there are co-occurring areas of difficulty that may respond well to medication (e.g., anxiety, depression, attentional challenges, behavioral outbursts, sleep difficulty). Genetic testing is a standard recommendation of the American Academy of Pediatrics for all individuals diagnosed with ASD (Hyman et al., 2020) and can be ordered by the individual's primary care provider, though sometimes this is not covered by insurance. Consultation with a geneticist can also occur, should there be atypical genetic findings or the family or primary care provider wish for this level of expertise. Depending on the age of the individual, school-based recommendations can be given to support in-class learning as well as provide guidance, structure, as well as specialized instruction to support the development of social based skills, and support during less-structured parts of the day (e.g., recess, lunch), when social challenges may result in discomfort or more significant negative social interactions (e.g., bullying). For adults, recommendations to support success within the workplace can include education around the Americans With Disabilities Act (ADA, 1990) and legal requirements for reasonable accommodations for employees. Suggestions for specific accommodations, and helping the individual articulate what is most helpful to them, can allow him or her to more successfully advocate for their needs within the workplace. Discussion of whether and when to disclose their autism diagnosis in the workplace can also be part of both the feedback process and recommendations and should include an emphasis on identifying when contextualizing the individual's behaviors and needs will facilitate communication with managers and colleagues as well as access to ADA accommodations and increased employee efficacy. There are also valuable resources aimed at healthcare providers, patients and supporters to improve the healthcare of autistic adults (e.g., Academic Autism Spectrum Partnership in Research and Education [AASPIRE], 2020; https://autismandhealth.org) that are worth reviewing and sharing. There is evidence from several research groups that some individuals receiving intensive early intervention may lose the ASD diagnosis and operate socially and cognitively within the average range of functioning, though they may still retain some features or unique traits. However, this is clearly a minority of children with ASD (perhaps on the order of 10-15%) and therefore parents should not be encouraged to think this is a likely outcome for their child (Fein et al., 2013; MacDonald et al., 2014; Rogers et al., 2014). For the remainder of individuals diagnosed with ASD there is no cure for its core symptoms (and many self-advocates strongly reject the concept of eliminating core symptoms). Nonetheless, evidencebased interventions that support flexibility, communication, social skills, and functional adaptive abilities are important recommendations to include across the lifespan. Indeed, there is a wealth of literature on evidence-based interventions to improve the lives and functioning of individuals diagnosed with ASD; Hyman et al. (2020) provide a concise summary of evidence-based treatment modalities, including the need for datadriven monitoring of progress. Indeed, there is a wealth of literature on evidencebased interventions to improve the lives and functioning of individuals diagnosed with ASD; Hyman et al. (2020) provide a concise summary of evidence-based treatment modalities, including the need for data-driven monitoring of progress. There is also a great deal of research promoting evidence-based Applied Behavior Analysis (ABA) for children with ASD. Derived from basic learning principles, ABA incorporates highly structured teaching strategies (e.g., Discrete Trial Training; Lovaas, 1987; Verbal Behavior; Sundberg & Partington, 1998) and potent rewards to promote socially significant behaviors (Baer, 1968). ABA programming is often implemented by a Board Certified Behavior Analyst (Behavior Analyst Certification Board [BACB], 2014) and tailors a treatment package based on a child's needs and skill level. Several meta-analytic studies indicate that ABA-based approaches for children with autism results in favorable long-term outcomes for improving language and communication, social skills, cognitive abilities, adaptive behavior, and reducing challenging behaviors (Dawson & Burner, 2011; Reichow, 2012; Virues-Ortega, 2010).

Other forms of ABA, such as Naturalistic Developmental Behavioral Interventions (NDBI), prioritize teaching in the context of natural environments to facilitate generalization of skills in varied situations (McGee et al., 1985).While there are several types of NDBIs, such as Incidental Teaching (IT; McGee et al., 1999), Pivotal Response Training ( PRT; Schreibman & Koegel, 2005; Koegel & Koegel, 2006), the Early Start Denver Model (ESDM; Dawson et al., 2010), and Joint Attention Symbolic Play Engagement and Regulation (JASPER; Kaale et al., 2014; Kasari et al., 2014), these models share a number of hallmark features.These include parent training, teaching functional skills, promoting child motivation, following the child's interests when selecting skill acquisition materials, incorporating natural reinforcers, and teaching in natural contexts. Research on naturalistic interventions for children with ASD has established implementation with high fidelity in clinics, homes and schools, and has resulted in consistent positive outcomes, especially for communication, language and social behavior (Kasari et al., 2014; Wetherby et al., 2014).

Finally, research supports the utility of Cognitive Behavior Therapy (CBT; Beck & Beck, 2020) with ASD specific modifications, to help reduce symptoms of anxiety in youth with autism in individual and group formats, yielding short term and longer term gains (Storch et al., 2015; Ung et al., 2015). Explicit social skills training in smalls

groups, such as the *Program for the Education and Enrichment of Relational Skills* (PEERS; Laugeson & Frankel, 2010) can help with breaking down of abstract social concepts into concrete actions and provide opportunities for practice that promote generalization in real life settings. PEERS has demonstrated immediate social skills gains for adolescents with ASD without intellectual disability (Dolan et al., 2016) and long-term treatment effects, even 1 to 5 years following the intervention (Mandelberg et al., 2014) and may even improve comorbid anxiety symptoms (Hill et al., 2017).

#### Conclusions

Psychologists provide a key role in differential diagnosis for a variety of individuals with neurodevelopment differences and medical complexity. Given the fact that the overall prevalence rate of ASD in the United States is approximately 2% (Maenner et al., 2020), a portion of individuals presenting for psychological and neuropsychological evaluations across all areas of specialty will meet criteria for this diagnosis, regardless of their presenting concern. While expertise in autism is not expected in all clinicians, a base level of knowledge is both feasible and necessary to support effective identification, supports and treatment for individuals across the lifespan. Clinicians may seek continuing education (through conferences or trainings offered by autism centers), additional training in specific measures (e.g., ADOS-2) or consultation with colleagues to refine their skills in working with individuals with ASD. Even with additional training and ongoing consultative support, however, some experts in other areas of neuropsychological assessment may not feel comfortable diagnosing ASD. In this case, it is still incumbent on clinicians to understand enough regarding the symptoms and presentation of ASD to effectively refer out for expert diagnostic evaluation. Knowing and recognizing red and pink flags (See Table 1), as well as family/informant and individual characteristics that can inadvertently hide the diagnosis will improve a clinician's ability to more effectively and accurately confirm or rule out the diagnosis, or refer to an autism specialist for additional evaluation as needed.

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