Autism Spectrum Disorder

CHAPTER 18

Prof Kerim M. Munir[1], MD, MPH, DSc, DFAACAP, DLFAPA

[1] Departments of Pediatrics and Psychiatry, Harvard Medical School, Developmental Medicine Center, Boston Children's Hospital

Definition and Aetiology

Autism spectrum disorder (ASD) is a neurodevelopmental condition defined by persistent difficulties in social communication and interaction together with restricted, repetitive patterns of behaviour, interests, or activities, including sensory hyper- or hypo-reactivity[1,2]. Symptoms arise in early development but may become apparent only when social demands exceed capacity, or may be masked by learned compensatory strategies.

The DSM-5-TR and ICD-11 share these core features; the DSM-5-TR specifies three severity (support) levels (**Table 1**), whereas the ICD-11 separately classifies intellectual and language level and loss of skills[1,2].

Social-communication difficulties must not be better explained by intellectual developmental disorder (IDD), with which ASD frequently co-occurs.

Contemporary practice increasingly favours dimensional thinking and identity-first language, reflecting a neurodiversity framework that regards some presentations of ASD as a natural variation rather than solely a disorder to be cured[3,4].

Table 1. *DSM-5-TR severity (support) levels for ASD across the two core domains (adapted from DSM-5-TR).*

Severity (support) level	Social communication	Restricted, repetitive behaviour
Level 1 Requires support	Without support, deficits cause noticeable impairment; reduced initiation and atypical responses to social overtures.	Inflexibility causes interference in one or more contexts; difficulty switching activities; problems with organisation and planning.
Level 2 Requires substantial support	Marked deficits in verbal and non-verbal social skills, apparent even with support; limited initiation and reduced/abnormal responses.	Inflexibility, difficulty coping with change, and other restricted/repetitive behaviours obvious to the casual observer; distress when redirected.
Level 3 Requires very substantial support	Severe deficits cause severe impairment; very limited initiation and minimal response to social overtures.	Extreme inflexibility, great distress at change, and restricted/repetitive behaviours that markedly interfere with all spheres of functioning.

ASD is among the most heritable neurodevelopmental conditions, with twin- and population-based heritability estimates of roughly 70–90%[5,6]. Its genetic architecture is mixed: a polygenic burden of common variants of small effect[7] combines with rare, high-impact *de novo* and inherited variants in synaptic and chromatin-regulating genes (e.g., CHD8, SCN2A, SHANK3) and recurrent copy-number variants (e.g., 16p11.2, 15q11.2, 22q11.2)[8,9]. Syndromic forms — fragile X, tuberous sclerosis complex, Rett and Phelan-McDermid syndromes, among others — account for a minority of cases but illuminate convergent synaptic biology.

Gene–environment interaction and epigenetic mechanisms modulate expression; replicated prenatal risk factors include advanced paternal age, prematurity, and fetal valproate exposure[10]. The historically alleged link between MMR vaccination and ASD has been comprehensively discredited, and the original report retracted[12].

Work over the past two years reframes ASD as a family of overlapping neurodevelopmental pathways rather than a single entity[11]. Phenotypically anchored genomic analyses of large cohorts resolve reproducible, clinically recognisable subgroups carrying different mixtures of liability — some enriched for *de novo* protein-truncating variants in constrained neurodevelopmental genes, others loading more heavily on polygenic risk shared with ADHD, depression and educational attainment[12]. Consistent with this, early- and late-diagnosed follow partly distinct developmental trajectories and polygenic signatures, so later diagnosis reflects a different liability profile rather than simply "missed" early autism[13]. Polygenic scores robustly index ASD at the group level but explain little individual variance (meta-analytic $r \approx 0.16$) and are not yet clinically predictive[14]; rare damaging variants contribute disproportionately to ASD co-occurring with IDD[15], and these architectures converge on shared synaptic and prenatal gene-regulatory pathways that partly distinguish ASD from overlapping conditions[16].

Aetiology is sex modulated. Autistic females carry a higher burden of *de novo* protein-truncating variants, and within families, the male relatives of female probands show the greatest social-communication difficulty — with genomic support for a "female protective effect"[17]. Population-register data estimate higher heritability in males (~87%) than in females (~76%), with negligible shared environment, implying a sex-differential genetic architecture rather than a single liability threshold[18]. Genomic studies nonetheless remain heavily skewed toward European ancestry: whole-genome work in East African families identifies risk loci on African haplotypes poorly captured by European datasets[19], yet no African ASD genome-wide association study exists[20] — reflecting an equity gap that limits the generalisability of current aetiologic models.

Environmental contributions are real but modest and are best framed within a gene–environment model. Quasi-experimental and negative-control analyses of population registers support a cautiously causal, small effect of severe maternal infection and immune activation in pregnancy, with estimates attenuating after control for familial confounding[21]; maternal pre-pregnancy obesity and diabetes confer similarly small increases, chiefly for ASD co-occurring with IDD[22]. Critically, many maternal-health associations attenuate substantially once shared familial liability is accounted for, cautioning against overinterpreting observational links [23]. Folate sufficiency supports fetal neurodevelopment, but this does not justify high-dose folinic acid as a general autism "treatment" outside well-defined cerebral folate deficiency[11].

Epidemiology

Global prevalence is estimated at approximately 1 in 100 children (median ~1.0%), although estimates vary widely and remain sparse in many low- and middle-income countries (LMICs) [24]. United States surveillance by the Centers for Disease Control and Prevention Autism and Developmental Disabilities Monitoring (ADDM) Network reports a substantially higher figure of about 1 in 36 eight-year-olds, with marked site-to-site variation[25], and the Global Burden of Disease (GBD) 2021 analysis ranks ASD among the leading neuropsychiatric contributors to disability in children and adolescents worldwide[26].

ASD is diagnosed about four times more often in boys, but this ratio narrows when co-occurring IDD is present and is inflated by the under-recognition and later diagnosis of girls, whose presentations are frequently subtler and more often "camouflaged"[27].

The steep rise in recorded prevalence over four decades is driven mainly by broadened diagnostic criteria, greater awareness, earlier and more equitable case-finding, diagnostic substitution from IDD, and improved service access[28]. A genuine increase in incidence underlying these trends remains possible and unlikely to be explained by genetic factors; nevertheless, epidemiological signals are difficult to separate from ascertainment.

Recent data show the largest increases among children without IDD and, for the first time in some US sites, higher recorded rates among Black, Hispanic and Asian/Pacific Islander than White children — reversing earlier disparities and consistent with improved detection rather than changing biology[25].

In most LMICs, by contrast, prospective surveillance is rare, and identification typically occurs late, so recorded prevalence understates the true burden, and the clinically visible population is skewed towards more severely affected, often non-verbal children[29].

Pathophysiology

No single lesion characterises ASD; rather, convergent genetic risk perturbs synaptic development and the balance of cortical excitation and inhibition[30]. A replicated, though not universal, finding is early brain overgrowth in the first years of life — particularly in the frontal and temporal cortices and the amygdala — followed by a relative plateau [31].

Functional and diffusion imaging suggest atypical connectivity, classically local/short-range hyperconnectivity with long-range hypoconnectivity, altered default-mode-network activity subserving social cognition, and white-matter microstructural differences [32].

At the synaptic level, an excitatory–inhibitory imbalance involving glutamatergic and GABAergic signalling is proposed to underlie sensory differences and repetitive behaviour[30].

Crucially, these differences precede behavioural diagnosis: longitudinal infant-sibling studies detect atypical functional connectivity within default-mode and social-brain networks by 12–24 months in children who later meet diagnostic criteria, and composite infant markers of attention and social orienting carry moderate — not deterministic — predictive value[33,34].

Multimodal models that combine exome variant burden with resting-state connectivity are beginning to predict social adaptability, illustrating a gene–brain–behaviour pathway that may eventually inform stratification[35]. These mechanisms are heterogeneous and overlapping, supporting a view of ASD as a disorder of neural connectivity and synaptic function rather than of any single region or transmitter (**Figure 1**).

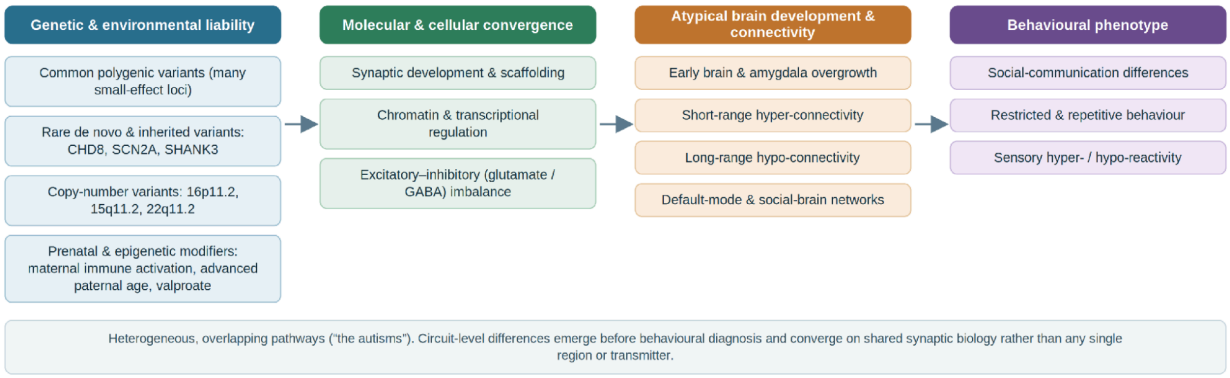


Figure 1. *Convergent neurobiology of ASD: from polygenic and rare genetic variation, through synaptic dysfunction and excitatory–inhibitory imbalance, to atypical short-range hyper- and long-range hypoconnectivity and the behavioural phenotype.*

Presentation and Course of the Disorder

The two diagnostic domains and their earliest signs can be remembered with the mnemonic **AUTISM** (**Table 2**). The restricted/repetitive domain is itself usefully summarised as the "4 S's": **S**tereotypies, **S**ameness (insistence on), **S**pecial (restricted) interests, and **S**ensory differences.

Prospective sibling ("baby-sibs") studies show that overt signs are usually absent before six months, with non-specific motor delays appearing first, followed by emerging deficits in joint attention, gaze-following, and gestures over the second year [36,37]. Updated consortium data place the sibling recurrence risk at about 20% — higher in boys, in multiplex families, and when the first affected child is a girl — supporting intensive developmental surveillance of infant siblings[38]. The course is highly variable. A minority of children — typically those with early intervention and higher cognitive ability — improve to the point of no longer meeting criteria ("optimal outcomes"), whereas others, particularly those with co-occurring IDD or minimal language, require lifelong support[39].

Table 2. *The AUTISM mnemonic for core features and early red flags.*

Letter	Clinical feature / early red flag
A	Atypical social reciprocity and reduced eye contact
U	Unusual sensory responses (hyper- or hypo-reactivity)
T	Talking — difficulty in social use of language, pragmatics, poor-turn taking, idiosyncratic speech/echolalia
I	Insistence on sameness and inflexible routines/rituals
S	Stereotyped/repetitive movements and restricted, intense interests
M	Missing joint attention — reduced pointing, showing and response to name

In girls and in cognitively able individuals, camouflaging can delay recognition into adolescence or adulthood and is linked to later mental health burden[40]. Co-occurring conditions are the rule rather than the exception — IDD, ADHD, anxiety, epilepsy, and sleep and gastrointestinal disorders.

Across the lifespan, ASD is associated with premature mortality (roughly twofold or higher), driven by epilepsy, accidental injury and, in more able individuals, suicide — underscoring the need for vigilant physical and mental-health care[41].

Assessment and Diagnosis

Diagnosis is clinical, resting on developmental history and direct observation across more than one setting, ideally by a multidisciplinary team[42].

Standardized instruments support but do not replace clinical judgment: the parent-completed M-CHAT-R/F is the most widely used screen at 18–30 months, while the Autism Diagnostic Observation Schedule (ADOS-2), the Autism Diagnostic Interview-Revised (ADI-R), the 3Di and the CARS aid characterisation[43,44]. Notably, experienced clinicians reach diagnoses concordant with the ADOS in about 90% of young children, so its absence should not delay diagnosis in low-resource settings[42].

Most screening and diagnostic tools were developed and validated in high-income, Western contexts; uncritical importation risks cultural bias, and contextually adapted instruments and developmental-surveillance systems are needed for equitable case-finding in LMICs[29, 45].

Differential diagnosis includes IDD or global developmental delay alone, developmental language disorder, social (pragmatic) communication disorder, hearing impairment and selective mutism — conditions that frequently co-occur with, rather than exclude, ASD.

The formulation should profile strengths as well as impairments across communication, social interaction, behaviour, cognition and adaptive functioning (**Figure 2**). NICE, AAP and AACAP guidance converge on observation in both structured and unstructured settings and on formal measurement of adaptive behaviour (e.g. Vineland-3), which predicts support needs more reliably than IQ alone.

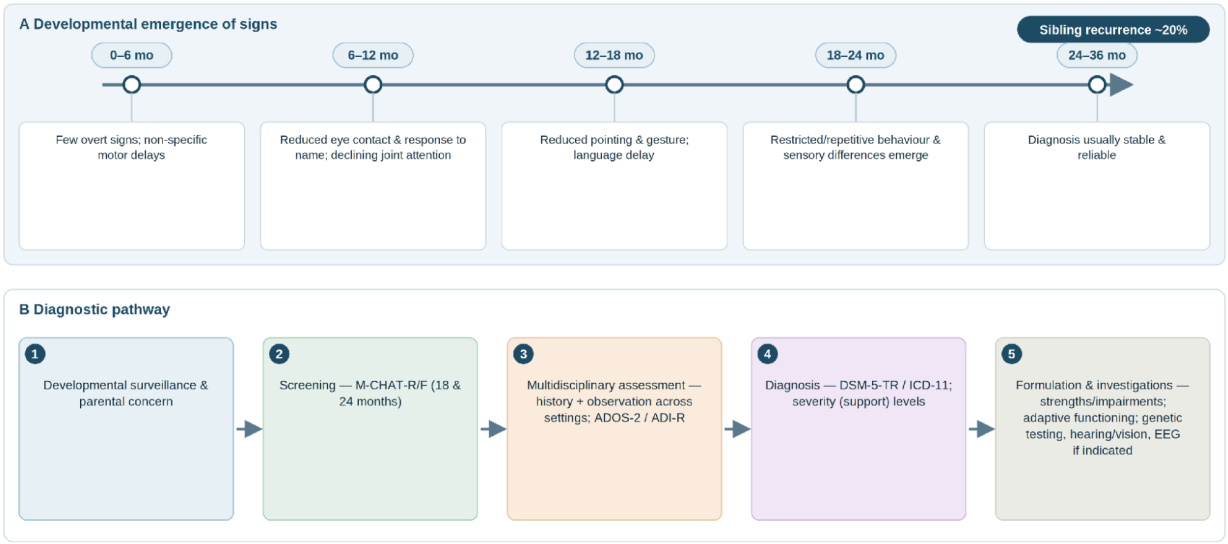


Figure 2. *The unfolding of ASD across early development — emergence of signs from infancy through the second year (sibling-study trajectory) — and the multidisciplinary diagnostic pathway from screening to formulation.*

Investigations

There is no biological or imaging test for ASD; investigations target aetiology and co-occurring conditions rather than the diagnosis itself. Physical examination should look for neurocutaneous stigmata (tuberous sclerosis, neurofibromatosis type 1), dysmorphism, and abnormal head circumference[46].

Aetiological genetic testing — chromosomal microarray as first tier, fragile X (FMR1) testing, and increasingly exome or genome sequencing — yields a diagnosis in roughly a quarter to a half of individuals, with higher yield when IDD, dysmorphism or congenital anomalies are present; genetic counselling should accompany testing and avoid deterministic language, since strong genetic load does not fully determine outcome[11,42].

Hearing and vision must be assessed in every child.

EEG is indicated when seizures or developmental regression are suspected, and targeted metabolic or neuroimaging studies are indicated only when history or examination points to them.

Screening for co-occurring ADHD, anxiety, mood, sleep, and gastrointestinal problems is an essential part of the work-up.

Neuropsychiatric Aspects of Treatment

Evidence supports early, individualised, family-centred intervention — for example the Early Start Denver Model and naturalistic developmental-behavioural approaches, structured programmes such as TEACCH, and social-communication and augmentative/alternative communication strategies[47,48]. Intervention should be matched to the child's developmental needs and family

circumstances; greater intensity is not reliably superior to well-targeted, lower-intensity programmes. Caregiver coaching, psychoeducation and support are central, and a neurodiversity-affirming stance — accommodation and acceptance rather than enforced normalisation — improves wellbeing and engagement[4].

Recognising and treating co-occurring conditions — anxiety, ADHD, depression, epilepsy and sleep disturbance — often yields the greatest functional gains, and timely early intervention is associated with improved communication and adaptive outcomes and potential long-term cost offset[47]. There is no medication that targets core features of ASD; the foundation of management is behavioural, developmental and educational[42]. Pharmacotherapy is currently reserved for co-occurring symptoms and challenging behaviours (**Table 3**). Risperidone and aripiprazole have been approved by the US Food and Drug Administration (FDA) for irritability, aggression and self-injury in children and adolescents, ages 6-17, but carry metabolic risk[49,50]; their regulatory status elsewhere varies. The National Institute for Health and Care Excellence (NICE) also recognizes risperidone and aripiprazole as pharmacological options for severe irritability or aggression when behavioral interventions are insufficient. Selective Serotonin Reuptake Inhibitors (SSRIs) may help anxiety based on clinical rationale; however, their efficacy to reduce repetitive behaviours in ASD lacks trial evidence and may risk behavioural activation. Stimulants, and alpha-2 agonists (guanfacine and clonidine) help address co-occurring ADHD symptoms. Melatonin has received a European Medicines Agency (EMA) authorization for treatment of insomnia in children and adolescents aged 2-18.

.

Table 3. *Pharmacological management of co-occurring symptoms in ASD. Medication treats associated symptoms, not the core social-communication features. SSRI, selective serotonin reuptake inhibitor (only representative agents are noted under atypical antipsychotics and SSRIs).*

Medication	Class	Target	Evidence
Risperidone	Atypical antipsychotic	Irritability, aggression, self-injury	RCTs; FDA-approved for autism-related irritability
Aripiprazole	Atypical antipsychotic	Irritability, aggression, self-injury	RCTs; FDA-approved; lower metabolic load than risperidone
Fluoxetine / sertraline	SSRI	Anxiety, repetitive behaviours	Mixed; used for co-occurring anxiety/OCD-like symptoms
Methylphenidate	Stimulant	Co-occurring ADHD symptoms	RCTs support use; more irritability than in non-ASD ADHD
Guanfacine / clonidine	Alpha-2 agonist	Hyperactivity, impulsivity, sleep	RCT support (guanfacine); clonidine off-label
Melatonin	Chronobiotic	Sleep-onset difficulty	RCTs support efficacy after behavioural measures

Clinicians should counsel families against unproven or harmful “treatments” — chelation, hyperbaric oxygen, secretin and facilitated communication. Globally, task-shifting to trained non-specialists, the WHO mhGAP framework, and community-based rehabilitation extend care where specialists are scarce, within a

rights-based approach grounded in the Convention on the Rights of Persons with Disabilities and the Lancet Commission's call for equitable, lifespan care [29,51].

Chapter Summary

Definition and Classification. ASD is a lifespan neurodevelopmental condition defined by persistent social-communication difficulties plus restricted, repetitive behaviours and sensory differences, present from early development and graded by support needs (DSM-5-TR Levels 1–3; ICD-11).

Aetiology. Highly heritable (~70–90%); common polygenic plus rare high-impact/de novo and copy-number variants define recognisable subgroups ("genetic programs") rather than one architecture; sex-differential liability with a female protective effect; modest, partly causal prenatal influences (maternal immune activation, metabolic factors). The MMR-vaccine link is discredited.

Epidemiology. ~1 in 100 globally (1 in 36 in US surveillance) and a leading paediatric neuropsychiatric contributor to disability; ~4:1 male predominance, narrowed by female under-recognition/camouflaging. Rising rates largely reflect broadened criteria, awareness and better case-finding.

Pathophysiology. Convergent synaptic dysfunction and excitatory–inhibitory imbalance; early brain/amygdala overgrowth; atypical short-range hyper- and long-range hypo-connectivity detectable before diagnosis; serotonin, dopamine and oxytocin–vasopressin involvement.

Presentation & course. Signs emerge in the second year (sibling recurrence ~20%); highly variable course; frequent co-occurring IDD, ADHD, anxiety, epilepsy; premature mortality from epilepsy, injury and suicide.

Assessment. Clinical, multidisciplinary diagnosis from history and observation; M-CHAT-R/F screen, ADOS-2/ADI-R support but do not replace clinical judgement; culturally adapted tools needed in LMICs.

Investigations. No diagnostic test; examine for neurocutaneous stigmata; chromosomal microarray and fragile X (± exome) testing with counselling; assess hearing/vision; EEG if seizures/regression; screen comorbidities.

Management. Early, individualised, family-centred behavioural/educational intervention is foundational. No core-symptom pharmacological treatment. Medications variably target co-occurring symptoms (risperidone/aripiprazole for irritability; SSRIs, stimulants, melatonin). Neurodiversity-affirming, rights-based, globally equitable care, rather than an illness to be cured.

References

1 American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 5th ed., Text Revision (DSM-5-TR). Washington, DC: APA, 2022.

2 World Health Organization. International Classification of Diseases, 11th Revision (ICD-11). Geneva: WHO, 2019/2021.

3 Lai MC, Lombardo MV, Baron-Cohen S. Autism. Lancet 2014; 383: 896–910.

4 Kapp SK, Gillespie-Lynch K, Sherman LE, Hutman T. Deficit, difference, or both? Autism and neurodiversity. Dev Psychol 2013; 49: 59–71.

5 Sandin S, Lichtenstein P, Kuja-Halkola R, et al. The familial risk of autism. JAMA 2014; 311: 1770–7.

6 Sandin S, Lichtenstein P, Kuja-Halkola R, et al. The heritability of autism spectrum disorder. JAMA 2017; 318: 1182–4.

7 Grove J, Ripke S, Als TD, et al. Identification of common genetic risk variants for autism spectrum disorder. Nat Genet 2019; 51: 431–44.

8 Satterstrom FK, Kosmicki JA, Wang J, et al. Large-scale exome sequencing study implicates both developmental and functional changes in the neurobiology of autism. Cell 2020; 180: 568–584.e23.

9 Fu JM, Satterstrom FK, Peng M, et al. Rare coding variation provides insight into the genetic architecture and phenotypic context of autism. Nat Genet 2022; 54: 1320–31.

10 Hultman CM, Sandin S, Levine SZ, et al. Advancing paternal age and risk of autism. Mol Psychiatry 2011; 16: 1203–12.

11 Munir KM. Etiology of autism spectrum disorders: recent advances and emerging directions. Curr Opin Psychiatry 2026; 39: 75–82.

12 Litman A, Sauerwald N, Green Snyder L, et al. Decomposition of phenotypic heterogeneity in autism reveals underlying genetic programs. Nat Genet 2025; 57: 1611–9.

13 Zhang X, Grove J, Gu Y, et al. Polygenic and developmental profiles of autism differ by age at diagnosis. Nature 2025; 646: 1146–55.

14 de Wit MM, Morgan MJ, Libedinsky I, et al. Systematic review and meta-analysis: phenotypic correlates of the autism polygenic score. JAACAP Open 2025; 3: 839–51.

15 Viggiano M, Ceroni F, Visconti P, et al. Genomic analysis of 116 autism families strengthens known risk genes and highlights promising candidates. NPJ Genom Med 2024; 9: 21.

16 Schaffer LS, Breunig S, Lawrence JM, et al. Characterizing genetic pathways unique to autism spectrum disorder at multiple levels of biological analysis. Mol Autism 2024; 15: 46.

17 Kim SW, Lee H, Song DY, et al. Whole genome sequencing analysis identifies sex differences of familial pattern contributing to phenotypic diversity in autism. Genome Med 2024; 16: 114.

18 Sandin S, Yip BHK, Yin W, et al. Examining sex differences in autism heritability. JAMA Psychiatry 2024; 81: 673–80.

19 Tuncay IO, DeVries D, Gogate A, et al. The genetics of autism spectrum disorder in an East African familial cohort. Cell Genom 2023; 3: 100322.

20 Hakizimana O, Hitayezu J, Uyisenga JP, et al. Genetic etiology of autism spectrum disorder in the African population: a scoping review. Front Genet 2024; 15: 1431093.

21 Gardner RM, Brynge M, Sjöqvist H, et al. Maternal immune activation and autism in offspring: what is the evidence for causation? Biol Psychiatry 2025; 97: 1127–38.

22 Li M, Fallin MD, Riley A, et al. The association of maternal obesity and diabetes with autism and other developmental disabilities. Pediatrics 2016; 137: e20152206.

23 Khachadourian V, Arildskov ES, Grove J, et al. Familial confounding in the associations between maternal health and autism. Nat Med 2025; 31: 996–1007.

24 Zeidan J, Fombonne E, Scorah J, et al. Global prevalence of autism: a systematic review update. Autism Res 2022; 15: 778–90.

25 Maenner MJ, Warren Z, Williams AR, et al. Prevalence and characteristics of autism spectrum disorder among children aged 8 years — ADDM Network, 11 sites, United States, 2020. MMWR Surveill Summ 2023; 72(2): 1–14.

26 GBD 2021 Autism Spectrum Disorder Collaborators. The global epidemiology and health burden of the autism spectrum: findings from the Global Burden of Disease Study 2021. Lancet Psychiatry 2025; 12: 111–21.

27 Lai MC, Szatmari P. Sex and gender impacts on the behavioural presentation and recognition of autism. Curr Opin Psychiatry 2020; 33: 117–23.

28 Hansen SN, Schendel DE, Parner ET. Explaining the increase in the prevalence of autism spectrum disorders: the proportion attributable to changes in reporting practices. JAMA Pediatr 2015; 169: 56–62.

29 Bakare MO, Munir KM. Autism spectrum disorders (ASD) in Africa: a perspective. Afr J Psychiatry (Johannesbg) 2011; 14: 208–10.

30 Robertson CE, Baron-Cohen S. Sensory perception in autism. Nat Rev Neurosci 2017; 18: 671–84.

31 Courchesne E, Pierce K, Schumann CM, et al. Mapping early brain development in autism. Neuron 2007; 56: 399–413.

32 Ecker C, Bookheimer SY, Murphy DG. Neuroimaging in autism spectrum disorder: brain structure and function across the lifespan. Lancet Neurol 2015; 14: 1121–34.

33 Dawson G, Rieder AD, Johnson MH. Prediction of autism in infants: progress and challenges. Lancet Neurol 2023; 22: 244–54.

34 Pruett JR Jr, Todorov AA, Hawks ZW, et al. Brain functional connectivity correlates of autism diagnosis and familial liability in 24-month-olds. J Neurodev Disord 2025; 17: 40.

35 Luo T, Zhang M, Li S, et al. Exome functional risk score and brain connectivity can predict social adaptability outcome of children with autism spectrum disorder in 4 years' follow-up. Front Psychiatry 2024; 15: 1384134.

36 Zwaigenbaum L, Bryson S, Rogers T, et al. Behavioral manifestations of autism in the first year of life. Int J Dev Neurosci 2005; 23: 143–52.

37 Wetherby AM, Woods J, Allen L, et al. Early indicators of autism spectrum disorders in the second year of life. J Autism Dev Disord 2004; 34: 473–93.

38 Ozonoff S, Young GS, Bradshaw J, et al. Familial recurrence of autism: updates from the Baby Siblings Research Consortium. Pediatrics 2024; 154: e2023065297.

39 Howlin P, Goode S, Hutton J, Rutter M. Adult outcome for children with autism. J Child Psychol Psychiatry 2004; 45: 212–29.

40 Zhuang S, Tan DW, Reddrop S, et al. Psychosocial factors associated with camouflaging in autistic people and its relationship with mental health and well-being: a mixed-methods systematic review. Clin Psychol Rev 2023; 105: 102335.

41 Hirvikoski T, Mittendorfer-Rutz E, Boman M, et al. Premature mortality in autism spectrum disorder. Br J Psychiatry 2016; 208: 232–8.

42 Hyman SL, Levy SE, Myers SM; Council on Children with Disabilities. Identification, evaluation, and management of children with autism spectrum disorder. Pediatrics 2020; 145: e20193447.

43 Lord C, Rutter M, Le Couteur A. Autism Diagnostic Interview-Revised. J Autism Dev Disord 1994; 24: 659–85.

44 Lord C, Rutter M, DiLavore PC, Risi S. Autism Diagnostic Observation Schedule. Los Angeles: Western Psychological Services, 2002.

45 Adiguzel S, Munir KM. Autism Diagnostic Observation Schedule (ADOS) in unequal and low-resource systems of care. Psychiatry Clin Psychopharmacol. 2026; 36: 322-328.

46 Volkmar F, Siegel M, Woodbury-Smith M, et al. Practice parameter for the assessment and treatment of children and adolescents with autism spectrum disorder. J Am Acad Child Adolesc Psychiatry 2014; 53: 237–57.

47 Reichow B, Hume K, Barton EE, Boyd BA. Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders. Cochrane Database Syst Rev 2018; 5: CD009260.

48 Fuentes J, Hervás A, Howlin P. ESCAP practice guidance for autism: a summary of evidence-based recommendations for diagnosis and treatment. Eur Child Adolesc Psychiatry 2021; 30: 961–84.

49 McCracken JT, McGough J, Shah B, et al. Risperidone in children with autism and serious behavioral problems. N Engl J Med 2002; 347: 314–21.

50 Owen R, Sikich L, Marcus RN, et al. Aripiprazole in the treatment of irritability in children and adolescents with autistic disorder. Pediatrics 2009; 124: 1533–40.

51 Lord C, Charman T, Havdahl A, et al. The Lancet Commission on the future of care and clinical research in autism. Lancet 2022; 399: 271–334.