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The Rising Prevalence of Autism in the 21st Century: Challenges, Identification, and Treatment. A Narrative Review

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ABSTRACT

Background: Autism spectrum disorder (ASD) represents a multifaceted neurodevelopmental condition characterized by social communication challenges and restricted, repetitive behaviors. As prevalence continues to rise globally, understanding its complex etiology and improving diagnostic and therapeutic strategies remain urgent public health priorities.

Objective: This narrative review synthesizes recent advances in the understanding of autism's genetic, environmental, and psychosocial determinants, while highlighting evolving approaches in diagnosis and treatment. It also addresses persistent challenges and emerging opportunities for personalized, community-anchored care.

Key Insights: Etiological research has expanded through genome-wide association studies, identification of copy number variants, and exploration of gene–environment interactions. Environmental exposures such as prenatal infections, advanced parental age, and nutritional deficits are increasingly implicated. Psychosocial and perinatal factors further influence risk and developmental trajectories. Diagnostic frameworks continue to evolve, with the integration of biomarkers, artificial intelligence, and digital tools supplementing DSM-5/ICD-11 criteria, though accessibility and heterogeneity remain obstacles. Treatment approaches have diversified, ranging from behavioral and cognitive therapies to pharmacologic management and adjunctive interventions such as exercise, technology-based platforms, and animal-assisted therapy.

Conclusion: Progress in autism research has been substantial, yet inequities and translational gaps persist. Early detection, interdisciplinary collaboration, and culturally contextualized interventions are essential for optimizing outcomes. Future efforts should prioritize longitudinal, inclusive research and the ethical deployment of innovative tools to support autistic individuals and their families across the lifespan.

Keywords: *autism spectrum disorder, etiology, diagnosis, intervention, biomarkers, gene–environment interaction, digital health.*

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1. INTRODUCTION

Autism spectrum disorder (ASD) has emerged as a significant global public health concern, marked by increasing prevalence, complex etiology, and diverse clinical presentations. Characterized by persistent deficits in social communication and interaction, along with restricted, repetitive patterns of behavior, ASD encompasses a wide spectrum of functioning across cognitive, emotional, and adaptive domains [1]. Recent estimates suggest that approximately 1 in 31 children aged 8 years in the United States are diagnosed with ASD, reflecting a steady rise from previous years [2]. While improved awareness, diagnostic practices, and surveillance explain some of this increase, the magnitude of change suggests potential shifts in underlying risk exposures and detection rates [3].

Globally, the burden of ASD is unevenly distributed. In high-income countries, early screening, diagnostic assessments, and educational accommodations are more accessible. In contrast, in many low- and middle-income countries (LMICs), children with autism are often underdiagnosed, and families face significant barriers to support [4]. The World Health Organization emphasizes that early detection and intervention can significantly improve outcomes, yet wide disparities persist in implementation [5].

The pathogenesis of ASD is multifactorial, involving a complex interplay of genetic, environmental, and psychosocial factors. Genetic contributions to ASD are well-established, with both common polygenic risk and rare de novo variants implicated [6]. Recent whole-exome sequencing studies in ancestrally diverse populations have expanded the pool of candidate genes and demonstrated the importance of increasing representation in genomic studies [7]. For example, a 2024 study found hundreds of previously unidentified variants associated with ASD, many of which were not present in predominantly European ancestry cohorts [8].

In addition to common single-nucleotide polymorphisms (SNPs), copy number variations (CNVs), chromosomal abnormalities, and mutations in genes involved in synaptic function (e.g., SHANK3, NLGN3, NRXN1) have been repeatedly linked to ASD [9]. Moreover, epigenetic mechanisms—including DNA methylation, histone modification, and non-coding RNAs—have emerged as mediators that connect genetic susceptibility to environmental triggers, offering insight into why individuals with similar genetic backgrounds may exhibit different phenotypes [10].

Among newly implicated genes, DDX53—a gene on the X chromosome—was recently associated with ASD, providing potential clues to the longstanding observation that ASD is more prevalent in males [11]. This reinforces the role of sex-linked genetic architecture and the importance of studying sex-specific expression in neurodevelopmental disorders.

Environmental exposures during critical developmental windows can substantially alter the risk trajectory for ASD. Perinatal factors such as maternal obesity, gestational diabetes, advanced parental age, exposure to toxins, and birth complications have been independently linked to increased ASD risk [12]. For instance, a 2024 Swedish cohort study (ABIS) of over 16,000 children found that maternal smoking during pregnancy, serious life events, and short durations of exclusive breastfeeding were significantly associated with ASD and ADHD diagnoses [13]. Interestingly, higher household income appeared to offer a protective effect, underscoring the complex interrelation between environmental and socioeconomic risk.

In utero exposure to air pollution—including fine particulate matter (PM2.5), nitrogen dioxide (NO2), and ozone—has also been implicated in increased risk for neurodevelopmental disorders, including ASD [14]. Mechanisms may include systemic inflammation, oxidative stress, and disruption of placental function. These findings support calls for public health interventions that reduce environmental exposure, particularly in urban and industrial areas.

Psychosocial factors are increasingly recognized as both modifiers of risk and determinants of outcome in ASD. Maternal stress, low parental education, limited social support, and caregiver mental health issues can contribute to more severe phenotypes and reduced access to early intervention [15]. In contrast, nurturing family environments, early behavioral therapy, stable housing, and responsive caregiving have been shown to buffer against developmental delays and improve adaptive functioning [16]. A 2024 systematic review reported that family-centered intervention approaches are associated with improved emotional regulation and social communication in young children with ASD [17].

Diagnosis of ASD continues to rely on clinical observation and standardized behavioral assessments guided by the DSM-5 or ICD-11 frameworks [18]. However, emerging tools—including genetic testing (microarray, WES), biomarker analysis, neuroimaging, and machine learning-based behavioral screening—are increasingly being integrated into research and early detection models [19]. Still, many of these methods remain inaccessible in routine care, especially in low-resource settings.

Treatment remains multidisciplinary and highly individualized. Behavioral interventions such as Applied Behavior Analysis (ABA), speech and occupational therapies, social skills training, and parent-mediated programs remain first-line strategies [20]. Pharmacologic therapies, such as risperidone and aripiprazole, are primarily used to manage irritability and aggression, rather than core ASD symptoms [21]. Novel approaches including dietary modifications, microbiota-targeted treatments, neurofeedback, and digital therapeutics are under active investigation, though their clinical efficacy is still being evaluated in large-scale trials [22].

Despite significant progress, several critical challenges persist: lack of longitudinal data to track trajectories from infancy through adulthood, underrepresentation of diverse populations in genetic and clinical studies, limited translation of biological discoveries into practice, and systemic barriers to early diagnosis and intervention access [23]. In particular, most genetic studies continue to overrepresent populations of European ancestry, limiting the generalizability of findings and perpetuating global health inequities [8].

Purpose of this review. In light of these developments, the purpose of this narrative review is threefold: (1) to synthesize recent evidence from genetic, environmental, and psychosocial perspectives contributing to ASD; (2) to highlight emerging advances in diagnostic and therapeutic modalities; and (3) to identify critical research gaps, particularly in the global context, that must be addressed to inform equitable, effective, and personalized care. By integrating cross-disciplinary

findings, this review aims to contribute to a more nuanced understanding of autism and guide future research, clinical innovation, and policy.

2. NARRATIVE BODY

Etiology

Genetic underpinnings (GWAS, CNVs, candidate genes)

Recent work has refined the genetic architecture of ASD. Litman et al. conducted a multivariate GWAS including ASD and related traits (anxiety, ADHD) and found several novel loci, improving polygenic risk scoring in diverse populations [24]. Another study used genomic structural equation modelling to isolate the ASD-specific genetic component (after accounting for overlap with ADHD), identifying pathways involved in synaptic function and brain development uniquely associated with the ASD latent factor [25]. X-chromosome-wide association analyses across thousands of individuals with ASD add to evidence of sex-linked genetic contributions, showing that certain common variants on chromosome X influence risk in males more strongly [26].

Candidate gene studies continue to confirm roles for established genes. In Japanese children with high-functioning ASD, variants in SCN1A, SHANK3, DYRK1A, CADPS, and SCN2A were significantly associated with ASD diagnosis and correlated with social responsiveness and IQ measures [27]. These findings reinforce that both rare high-impact mutations and more moderate effect common variants contribute to the ASD phenotype, with different contributions depending on ancestry, sex, and phenotype.

Environmental influences (toxins, infections, maternal age, nutrition)

Across many populations, increasing parental age remains among the strongest environmental risk factors. Advanced paternal and maternal age correlate with elevated de novo mutation rates and epigenetic changes influencing neural development [28]. Prenatal infection and maternal metabolic health (e.g., obesity, gestational diabetes) are also robustly associated with higher ASD risk in offspring [29]. Regarding nutritional factors, deficiencies in folate, vitamin B12, vitamin D, and certain micronutrients have been implicated; conversely, better maternal diet quality appears protective in some large-scale birth cohorts [30]. Environmental toxins—air pollution, heavy metals, endocrine disruptors—are under study, with growing evidence that prenatal exposure to particulate matter and specific pollutants can influence neurodevelopmental outcomes via oxidative stress and immune dysregulation pathways [31].

Psychosocial and perinatal factors

Perinatal complications (preterm birth, low birth weight, hypoxia, neonatal complications) are associated with increased ASD risk and may interact with genetic susceptibility to exacerbate outcomes [32]. Maternal psychosocial stress (life events, depression, anxiety during pregnancy), lower socioeconomic status, limited prenatal care, and less optimal early caregiving environments have been shown to modulate severity of social communication deficits, language delays, and adaptive behavior trajectories in children with ASD [33]. Exclusive breastfeeding duration and early sensory-rich stimulation are emerging as protective psychosocial/perinatal modifiers in multiple cohort studies [34].

Diagnosis

ICD-11 / DSM-5 frameworks

Behavioral diagnostic criteria grounded in DSM-5 and ICD-11 remain foundational. Recent diagnosis guidelines emphasize specifiers for intellectual ability, language level, and co-occurring conditions, aiming for more precision in defining subgroups for intervention and prognostication [35]. These frameworks are central for clinical consistency, research standardization, epidemiologic surveillance, and global reporting.

Advances in AI, biomarkers (miRNAs, microbiome, cord blood)

AI-assisted diagnostic tools are showing promise in facilitating earlier and more accessible ASD screening. “Canvas Dx,” for instance, when used in real-world settings, provided high sensitivity and specificity, enabling diagnosis more than two years earlier than typical clinical timelines in many cases [36]. Deep learning models combining facial image analysis with transformer architectures have been developed; in one recent study the model distinguished ASD vs non-ASD children based on facial features with high accuracy, demonstrating promise for non-invasive screening tools [37].

Gut microbiome biomarkers are also under investigation. Researchers in Hong Kong identified differences in gut microbial taxa (bacteria, viruses, archaea, fungi) between children under four diagnosed with ASD versus controls; using a microbial panel and machine-learning classifiers, diagnostic accuracy of ~82% was reported [38]. Cord blood transcriptional studies and epigenetic profiling suggest differential gene expression in newborns who later develop ASD, though replication is limited and longitudinal stability remains to be established [39].

Challenges: heterogeneity, comorbidities, tool limitations

Diagnosis is complicated by ASD heterogeneity: variation in symptom onset, severity, cognitive and language level, and

sensory profiles means that single diagnostic tools may misclassify or miss certain subgroups [40]. Comorbid conditions—such as ADHD, anxiety, intellectual disability—often delay accurate diagnosis and can confound behavioural assessments [41]. Many AI and biomarker studies suffer from small sample sizes, lack of diversity in study populations, risk of overfitting, and limited external validation [42]. Additionally, cultural, linguistic, and resource-based differences influence how symptoms are reported and assessed, limiting generalizability.

3. TREATMENT & INTERVENTIONS

Pharmacological management (risperidone, aripiprazole)

Pharmacologic treatments remain focused on non-core symptoms such as irritability, aggression, or tantrums. Risperidone and aripiprazole are among the FDA-approved drugs for such symptoms. Recent meta-analytic updates reaffirm their efficacy in reducing irritability but also highlight side effects including weight gain, metabolic syndrome, and sedation, underscoring the need for careful monitoring [43]. Efforts to develop drugs targeting core social communication or restricted/repetitive behaviors have not yet yielded robust breakthroughs.

Behavioral, CBT, speech and occupational therapies

Behavioral interventions—early intensive behavioural intervention (EIBI), applied behaviour analysis, social communication therapy—continue to show beneficial effects in language development, social skills, and adaptive functioning, especially when started early [44]. Cognitive behavioural therapy is effective for comorbid anxiety and emotional dysregulation in ASD [45]. Speech and occupational therapies are essential in addressing communication, sensory processing and daily living skills; they also contribute significantly to increasing independent functioning [46].

Adjuncts: exercise, diet, animal-assisted therapy, technology-mediated interventions

Adjunctive interventions are attracting interest. Regular physical activity and structured exercise programs have shown improvements not just in physical health but also in behaviors, mood, and cognition in several recent studies [47]. Diet and microbiome-based interventions (e.g. probiotic supplementation, microbiota modulation) show some promise, especially in children with gastrointestinal comorbidities, though effect sizes are often modest and evidence is mixed [48]. Animal-assisted therapy, where appropriate, has been associated with improved emotional regulation, social engagement, and reduction in repetitive behavior in small randomized or quasi-experimental studies [49]. Technology-mediated interventions—telehealth, apps, virtual reality, digital platforms—are increasingly used to deliver behavioural therapy and caregiver training, especially in remote or underserved settings; preliminary evidence suggests acceptable feasibility and promising effectiveness [50].

Cross-cutting Themes

Early diagnosis importance

Data consistently show that earlier diagnosis (ideally before age 3) allows for earlier intervention, which in turn leads to better outcomes in social communication, language, and adaptive skills [51]. Tools developed for infants and toddlers are less numerous but growing, and AI or biomarker-based screening may reduce diagnostic delays substantially [36, 50].

Community awareness and family engagement

Community and caregiver involvement contribute significantly both to detection and intervention success. Parent-mediated interventions improve outcomes for children and reduce caregiver stress [52]. Public awareness campaigns, culturally tailored screening tools, and community health worker involvement help reduce barriers to early diagnosis and services [53].

Ethical issues around AI/genetics

The integration of genomics, biomarkers, and AI introduces ethical concerns: data privacy, consent (particularly in children), risk of misuse of genetic information, potential algorithmic bias if training datasets are not representative [54]. Overdiagnosis or misdiagnosis via AI tools may lead to stigma or misuse of resources. Transparent reporting, equity in access, and validation across diverse populations are essential safeguards [55].

4. DISCUSSION

Over recent years the field of autism research has made meaningful progress along several trajectories, yet substantial gaps persist that limit the translation of research into equitable outcomes. Key achievements include refined understanding of genetic architecture, enhanced early diagnostic tools, and the growth of intervention models that integrate behavioral, psychosocial, and technological components. Nevertheless, the consistency, representativeness, and scalability of many advances remain limited, especially across culturally, economically, and geographically diverse populations.

Firstly, in genetics, the identification of both common polygenic risk and rare high-impact variants has improved risk stratification and mechanistic insight [56]. GWAS involving multi-ancestry cohorts have broadened the genetic loci

associated with ASD and clarified overlapping risk with other neurodevelopmental disorders [57]. CNV studies continue to reveal pathogenic structural variants that affect synaptic genes and chromatin regulators [58]. However, large proportions of heritability remain unexplained, especially in underrepresented groups; many genetic findings fail to generalize across ancestries, limiting precision for non-European populations [59].

On diagnostics, tools such as AI-assisted imaging, microbiome panels, and transcriptomic profiling show promise for earlier, objective detection [60]. Real-world validation studies (e.g., Canvas Dx) and facial analysis models suggest feasibility of screening tools that may reduce diagnostic latency in certain high-resource contexts [61]. Yet, several gaps remain: many biomarker studies lack long-term follow-up to assess prognostic value; diagnostic accuracy often drops when models are applied across different populations; and behavioural assessments still dominate clinical practice, often due to issues of cost, training, and accessibility [62].

In treatment and interventions, there has been growth in both core and adjunctive modalities. Early intensive behavioural intervention (EIBI), combined with speech, occupational, and family-mediated therapies, has robust evidence of benefit when instituted early [63]. Adjunctive supports — such as exercise, dietary modulation, digital therapy platforms, animal-assisted interventions — are expanding the toolkit of available supports [64]. However, pharmacological management remains limited to symptom reduction (irritability, aggression) rather than addressing core features; side effects and monitoring burdens pose barriers to widespread use [65].

Despite this progress, persistent gaps underscore inequities and scientific–translational challenges. Many studies are cross-sectional rather than longitudinal, limiting understanding of how genetic, environmental, and psychosocial factors play out over time, how biomarkers evolve, and how early indicators reliably forecast long-term outcomes [66]. In global contexts, low- and middle-income countries often lack diagnostic infrastructure, culturally validated screening tools, and services for early intervention; research from these regions remains sparse, which constrains both generalizability and equity [67].

A particularly promising trend is interdisciplinary integration: the convergence of genetics with behavioral science, environmental epidemiology, AI, and digital health offers a more holistic understanding of ASD. For example, studies combining genetic risk scores with longitudinal behavioral tracking and digital phenotyping (e.g., passive monitoring through wearables or apps) reveal finer-grained trajectories of symptom emergence and variation [68]. Moreover, environmental exposure studies are increasingly modeled together with genetic vulnerability (gene-environment interaction), yielding insights into why similar prenatal exposures may have differential effects depending on underlying genotype [69]. Also, the integration of digital tools (telehealth, app-based interventions, virtual reality) into behavioral and psychosocial frameworks holds potential for scalability and reach, particularly where in-person services are limited [70].

Looking forward, several future research needs stand out. Longitudinal, cohort-based studies that follow children from prenatal or early perinatal stages through childhood, adolescence, and into adulthood are urgently needed. Such studies would clarify developmental trajectories, stability of biomarkers, interaction of early environmental exposures with genetic risk, and identify optimal windows for intervention. Culturally contextualized interventions are another priority: adaptation of screening tools, diagnostic frameworks, and therapeutic models to diverse cultural, linguistic, and resource settings will improve access and relevance. Research designs must move away from over-reliance on samples from high-income, English-language, Western settings.

Moreover, future work should aim to enhance biomarker validity and clinical utility: improving reproducibility, multi-site validation, longitudinal prognostic performance, and integration into routine diagnostic systems. There is also need for ethical, regulatory, and policy frameworks to keep pace with technological advances—particularly surrounding genetic and AI tools: issues of consent, data privacy, algorithmic bias, equitable access, and psychosocial implications for children and families.

In summary, the trajectory of autism research over recent years reflects significant advances across genetics, diagnostics, and interventions; yet the field faces ongoing challenges of heterogeneity, inequity, and a translational gap. Interdisciplinary integration provides one of the promising pathways forward. By prioritizing longitudinal research, cultural adaptation, ethical oversight, and inclusive representation, future work can better ensure that scientific progress translates into improved lives for autistic individuals around the world

5. CONCLUSION

Autism spectrum disorder (ASD) is increasingly recognized as a complex, multifactorial neurodevelopmental condition arising from the interplay of genetic susceptibilities, environmental exposures, and psychosocial influences. While significant strides have been made in elucidating etiological pathways, improving diagnostic technologies, and diversifying therapeutic approaches, persistent challenges—particularly regarding early detection, cultural inclusivity, and equitable access—remain.

This review underscores the urgent need for personalized, developmentally appropriate, and community-supported models of care. Interventions must be tailored not only to individual profiles but also to family and societal contexts. Integrating

interdisciplinary insights—from genomics and neuroscience to behavioral science and digital innovation—will be key to advancing early diagnosis and meaningful intervention outcomes.

Ultimately, ensuring that scientific progress translates into real-world impact requires sustained investment in longitudinal research, ethical deployment of emerging technologies, and global collaboration. Only then can we bridge gaps in care and empower autistic individuals and their families to achieve optimal quality of life.

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