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# **Autism spectrum disorder: definition, global epidemiology, prevalence in Poland and worldwide, and heredity**

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## ABSTRACT

**Introduction:** The understanding of autism spectrum disorder (ASD) has evolved significantly. First mentioned in 1911, autism was described as "early childhood autism" by Leo Kanner in 1943, and a milder form, Asperger syndrome, was outlined by Hans Asperger in 1944. Expanding diagnostic criteria have led to increased recognition, with prevalence rising from 1 in 2,000 children in the 1980s to about 1 in 100 today. This growth is attributed to improved diagnostics, awareness, and healthcare access. While its exact causes remain unknown, ASD risk is influenced by genetic, environmental, prenatal, and perinatal factors, with genes like *SHANK3*, *CHD8*, and *FMRI* playing key roles.

**The aim of the study:** This study aims to provide a comprehensive overview of autism spectrum disorder by examining its definition, historical context, epidemiology, and heredity. Special attention is given to global prevalence rates, with a focus on comparative trends in Poland, as well as genetic advancements shaping our understanding of this condition.

**Material and method:** In our article we used English databases such as PubMed and Google Scholar. We selected the articles according to keywords such as "ASD", "autism", "history of

autism”, “epidemiology”, “inheritance”, “genetic”. The articles we used were published from 1943, mainly 2019-2024.

**Conclusions:** ASD is a complex condition influenced by genetic and environmental factors. Advances in diagnostics and awareness have led to increased prevalence rates globally. Genetic studies highlight key hereditary components, offering insights for early intervention. Ongoing research and culturally tailored strategies are essential to improve diagnosis, support, and quality of life for individuals struggling with this condition.

**Keywords:** autism spectrum disorder, history of autism, epidemiology, inheritance, genetics

## INTRODUCTION

The concept of “autism” first appeared in the early 20th century, but it wasn’t until several decades later that it acquired its contemporary meaning [1,2]. According to the DSM-5 and ICD-11 diagnostic criteria, the terms "early childhood autism" and "Asperger's syndrome" are no longer used; instead, a broader category known as "autism spectrum disorders" has been adopted [3,4]. Over the years, there has been a noticeable increase in the number of ASD diagnoses. This rise is likely attributed to a better understanding of the disorder, enhanced environmental awareness, and expanded diagnostic capabilities. Increased access to information, the availability of screening tests, and a growing number of public awareness campaigns have contributed to heightened sensitivity to the issue [5,6]. Today, various diagnostic tools and questionnaires allow for the early assessment of autism, even in young children. It is not the actual prevalence of ASD that has grown, but rather the advancement in diagnostic practices that has resulted in a larger number of diagnoses [7]. In the 1980s, the incidence of this neurodevelopmental disorder was reported to be 1 in 2,000 children (0.05%) [8]. However, current estimates suggest that the global prevalence of ASD has risen to approximately 1%, with a male-to-female ratio of 4:1 [9]. The occurrence across different continents is estimated to range from 0.4% to 1.7% of the population, although some studies report much lower frequencies, as low as 0.007%, while others suggest that it could be as high as over 30% [5,6,10,11].

## **BRIEF HISTORICAL OUTLINE OF AUTISM**

The term “autism” first appeared in the context of schizophrenia in pediatric patients in 1911, introduced by the Swiss psychiatrist Eugen Bleuler [1]. Derived from the Greek word *autos*, meaning “self”, the term was initially used to describe a condition in which individuals appeared inwardly focused and detached from social interactions [12]. In 1943, the Austrian-American psychiatrist Leo Kanner published his landmark work *Autistic Disturbances of Affective Contact*, in which he described a group of 11 children (8 boys and 3 girls) exhibiting a shared set of symptoms. He characterized them as having "an inability to relate themselves in the ordinary way to people and situations from the beginning of life," while also noting traits such as "extreme [autistic] aloneness," "excellent rote memory," "personal pronouns repeated just as heard," "fear of loud noises and moving objects," "monotonous repetitiveness," "anxious obsessive desire for maintenance of sameness," and others. A common feature among these children was their inability to create emotional contact, a fundamental trait for neurotypical people [2].

Initially, Kanner defined autism as a specific disorder, but over time it became evident that the spectrum of symptoms was much broader. As a result, the definition was expanded. Kanner is considered the creator of the definition of early childhood autism, and the condition was named “Kanner syndrome”. At almost the same time, in 1944, Austrian psychiatrist Hans Asperger described a milder form of autism, now known as “Asperger syndrome”, characterized mainly by difficulties in social interaction but with preserved cognitive and linguistic abilities and minimal developmental delays [13].

Some of the early signs of autism typically appear before a child reaches 3 years of age, with a diagnosis often made between 18 and 24 months. Family members report that they often notice certain abnormal social communication behaviors even before a child's first year [9,15]. Currently, in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), the disorder is described as involving two domains of impairment: social communication and interaction and restricted, repetitive behaviors [3,14]. According to the previous edition, DSM-IV, patients with autistic disorders were assigned one of five diagnoses, including “autistic disorder”, “Asperger syndrome”, “childhood disintegrative disorder”, “Rett syndrome”, or “other pervasive developmental disorders not specified elsewhere”. In the outdated ICD-10, there was a classification that included “childhood autism”, “atypical autism”, “Rett syndrome”, “Asperger syndrome”, and “other childhood disintegrative disorders” [4]. In the latest revision of ICD-11, the term “autism” has been

replaced by the concept of autism spectrum [16]. However, in this paper, the terms “autism”, “autism spectrum disorder”, and “ASD” will be used interchangeably.

Various screening and diagnostic tools have been utilized across different continents. In the United States, the IQ scale was predominantly employed, while in Australia, the SDQ was commonly used. In Europe, tools such as ADOS, SCQ, and ADI-R were the most frequently applied, whereas in Asia, instruments like M-CHAT, DOS, ISAA, AQ-10, and others were utilized. Globally, diagnostic criteria have been based on DSM-IV or DSM-V, as well as ICD-9 through ICD-11, depending on the time periods during which the studies were conducted [6].

## **EPIDEMIOLOGY OF AUTISM SPECTRUM DISORDER**

### **1. Incidence of autism in Europe: insights into its distribution in Poland**

According to current data, the occurrence of autism spectrum disorder in Europe is estimated at approximately 0.5% (50 per 10,000) [6]. A landmark review published by Fombonne in 2009, which analyzed 43 studies conducted in Europe and the United States since 1966, highlighted significant variability in ASD prevalence across countries. Among the studies, the highest rates were reported in central Sweden (Karlstad), with a proportion of 72.6 per 10,000 [5]. A subsequent study from 2015 indicated a prevalence as high as 154 per 10,000 in Sweden [17]. This research involved a large cohort of 735,096 individuals aged 0–27 years, observed between 2001 and 2011. The prevalence of autism within pediatric age groups was found to increase significantly with age: 40 per 10,000 (ages 0–5 years), 174 per 10,000 (ages 6–12), and 246 per 10,000 (ages 13–17). Moreover, this study documented a 3.5-fold rise in diagnoses over the study period. Similar findings were observed in a 2017 Swedish study, reporting an incidence rate of approximately 115 in 10,000 people [5,17,18]. In contrast, the lowest rates among European countries were reported in Croatia, with an incidence of only 2–3 per 10,000 at that time [18].

A comprehensive study conducted in Germany from 2006 to 2012, involving a sample of 6.4 million individuals aged 0–24, observed a growth in diagnosed ASD cases from 0.22% to 0.38% during that period [19]. Similarly, data from Norway collected between 2008 and 2010 using the Norwegian Patient Register estimated the occurrence of this neurodevelopmental disorder at 0.7% in 11-year-old children, based on a sample of 731,318 individuals [20].

In a more recent study from 2019, the incidence rate of autism in Portugal was found to be approximately 0.12% (1 in 806 people) [21]. Meanwhile, a study in Greece covering 182,879

children aged 10–11 found rates varying between 0.59% in the western part of this country and 1.50% in the North Aegean, with an average prevalence of 1.15%, exceeding the global average [22]. In Spain, a 2020 study from Gipuzkoa calculated ASD rates at 0.59% in a group of 9,177 schoolchildren aged 7–9 years, lower than the global average of 1%, yet higher than the European mean of 0.5% [23]. A systematic review published in 2020 highlighted disparities in ASD occurrence across Europe, ranging from 0.42% in Piemonte, Italy (children aged 6–8 years), to as high as 3.13% in Iceland (children aged 8 years) [24,25].

Reliable data on the prevalence of autism spectrum disorder in Poland remain scarce. However, a study conducted by Skonieczna-Żydecka et al. estimated the prevalence at 0.35% among children aged 0–16 in Pomerania and West Pomerania between 2010 and 2014. This study involved a cohort of 707,975 children, of which 344,506 were male and 363,469 were female. Diagnostic tools such as ADOS, Q-CHAT, and STAT were used, with the highest prevalence (0.53%) observed in children aged 4–7 years [6,18,25]. Data from the Polish Supreme Audit Office further indicate an upward trend in ASD diagnoses. During the 2018–2019 academic year, 54,404 students (0.86%) out of a population of 6,361,246 were identified with autism. This marks an increase compared to 47,834 students (2017–2018) and 39,752 students (2016–2017) [8].

The wide variations in reported ASD rates across Europe can largely be attributed to differences in sample sizes, screening methods, and diagnostic tools. Studies involving smaller sample groups often reported higher rates of occurrence compared to those conducted with larger populations. Fombonne noted: “Prevalence was negatively correlated with sample size, and small-scale studies tended to report higher prevalence proportions” [5]. For example, in Sweden, where the sample comprised 826 individuals, the prevalence was calculated at 0.73%, whereas in the United States (Wisconsin), a study with 899,750 participants reported a significantly lower rate of 0.007%, more than 100 times lower than in Sweden. Additionally, a systematic increase in ASD rates has been observed within the same countries over time. These findings underline the importance of standardized diagnostic criteria and methodologies to obtain more reliable and comparable data.

## **2. Prevalence of ASD in the United States of America**

Based on several studies, the average rate of autism spectrum disorder in North America has been estimated to range from 0.007% to 4.49%, with the mean figure in America standing at 1%, consistent with global estimates of autism occurrence [2,6,26].

From the 1960s to the 1980s, the rate of autism diagnoses in the United States was estimated at 5 per 10,000 children. Following the revision of diagnostic criteria through the introduction of the DSM-IV and ICD-10, the incidence of ASD was reported at an average of 60-70 per 10,000 children [27]. In 2007, the Autism and Developmental Disabilities Monitoring (ADDM) Network published its initial reports based on data collected from 2000-2002. These investigations aimed to assess the occurrence of autism spectrum conditions among 8-year-old children across the United States. In 2000, the sample included 187,761 children from six states: Arizona, Georgia, Maryland, New Jersey, South Carolina, and West Virginia. By 2002, the research expanded to 14 states—Alabama, Arizona, Arkansas, Colorado, Georgia, Maryland, Missouri, New Jersey, North Carolina, Pennsylvania, South Carolina, Utah, West Virginia, and Wisconsin—covering 407,578 children. This dataset suggested a rate of 0.66% for autism spectrum disorder. The findings demonstrated substantial regional variability, with occurrence rates ranging from 33 to 106 per 10,000 children. These early reports served as key benchmarks for future studies, many of which reflected a continuing rise in the disorder's identification [28,29]. In 2008, a study of 337,093 children recorded a rate of 1.13%, or 113 per 10,000, with some areas reaching 212 per 10,000 children [30].

A decade later, in 2018, the monitoring extended to 220,281 children, reporting an estimated rate of 236 per 10,000, marking a significant rise compared to earlier findings. This upward trajectory was seen not only in the United States but also globally, pointing to improvements in diagnostic procedures, increased public awareness, and enhanced detection methods [31]. A 2023 report, based on data from 2020, revealed continued growth in the incidence of autism spectrum disorder within the U.S. The figures from 11 states monitored by the ADDM Network indicated that the overall rate stood at 276 per 10,000 children (1 in 36 children). The data further highlighted notable disparities between states, with Maryland reporting a rate of 231 per 10,000, while California recorded a significantly higher rate of 449 per 10,000 [32]. These findings represent the most recent data from the ADDM Network.

In a 2009 independent analysis, based on 43 studies conducted across various European countries and the United States, the lowest incidence of autism was observed in Wisconsin, USA, at a rate of 0.7 per 10,000 children. The study included a sample of 899,750 children aged 3-12 years [5].

The rising number of diagnoses in the United States may be attributed to a variety of factors, including enhanced accessibility to diagnostic resources, modifications in diagnostic guidelines, and greater public awareness regarding developmental disorders. However, some

researchers argue that the apparent increase in cases may not be indicative of a true surge, but rather reflect more accurate identification and categorization of individuals who might have been previously overlooked [33].

While this upward trend in the identification of autism spectrum conditions is likely a result of improvements in healthcare systems, it is essential to avoid over-simplifying the issue. Continued research is necessary to better understand the contributing factors behind these shifts and their potential consequences for future healthcare policies.

### **3. Occurrence of autism in Africa**

There is a limited number of studies examining ASD across the African continent, and the considerable variation in results suggests that further research is essential to gain a more consistent understanding of the issue. Based on four published studies involving a total of 54,326 individuals, the estimated prevalence of autism in Africa stands at approximately 1%, consistent with the global average [9,10].

In the KwaZulu-Natal, region of Republic of South Africa, a study conducted on 2,036 children under the age of 10 identified a disability rate of about 6%, which included diagnoses of ASD. The findings were published in 2002 [34]. Between 2012 and 2016, studies emerged from countries including Nigeria, Uganda, Libya, and Somalia, each providing unique insights into the occurrence of autism spectrum disorder in the African context [35,36,37,38]. In Nigeria, a sample of 2,320 children aged 1–10 years revealed a prevalence rate of 2.3%, with earlier studies from the region indicating figures ranging from 0.8% to 2.3%, depending on geographical and cultural contexts [35]. Furthermore, 22.6% of 54 children diagnosed had a positive family history of autism, shedding light on potential genetic or familial patterns of the disorder [39]. Despite these valuable data, the true prevalence may be far greater due to underreporting, stigma, and limited access to diagnostic tools in many areas. It is estimated that as many as 600,000 children in Nigeria may be affected by ASD, but the underdiagnosis remains a major issue [40]. In Uganda, the incidence rate was found to be 0.68%, based on a study of 1,169 children aged 2–9 years [36]. In Libya, between 2005 and 2009, a study involving 38,508 children and adolescents aged 0–16 revealed a prevalence rate of 0.33% [37]. Similarly, in Somalia, where 12,329 individuals, half of them boys aged 7–9 years, were studied, the prevalence rate was significantly higher at 2.07% [6,38].

More recent studies also contribute to our understanding, with reports from 2023 estimating the prevalence of autism at 33.6% in Egypt and 11.5% in Tunisia [11]. These wide-ranging



figures reinforce the need to interpret regional data with caution, considering the considerable variability due to local socio-cultural, socio-economic, and healthcare factors.

In Nepal, the situation presents challenges of a different nature. It was found that 65% of pediatricians lacked sufficient knowledge and experience in managing ASD, and only 15% of clinicians were adequately familiar with the disorder to accurately diagnose it [41]. This indicates a critical gap in medical education and clinical practice that hampers the effective diagnosis and treatment of autism.

The underdevelopment of early intervention in some parts of the world significantly limits the ability of children to integrate into society and reach their full potential. Delayed or missed diagnoses not only heighten developmental risks but also contribute to societal marginalization and stigmatization. Conversely, early identification and timely therapeutic interventions can substantially enhance social and emotional functioning, reducing the risk of long-term complications [42]. Discrepancies in reported rates of autism can be attributed to variations in diagnostic tools, research methodologies, and the absence of standardized assessment criteria. Furthermore, socioeconomic disparities, unequal access to healthcare and support systems, and diverse environmental factors play a substantial role in shaping the diagnosis and management of neurodevelopmental conditions [6,9,10].

#### **4. ASD prevalence in other parts of the world**

The reported prevalence of autism spectrum disorder in Asian countries shows significant variability, largely due to differences in the evaluation methods used. Based on 26 studies encompassing a sample size of 7,356,939 individuals, the average prevalence on this continent is approximately 0.4% [6]. A study by Chiarotti et al. (2020) demonstrated considerable regional variability, with estimates ranging from as low as 0.08% in North Bangladesh's Sirajganj district among children aged 1.5–3 years to as high as 9.3% in Japan based on teacher reports; notably, parental evaluations in the same Japanese cohort suggested a much lower prevalence of 1.9% among children aged 6–9 years [25]. Further estimates reveal diverse rates across Asian countries: 2.64% in South Korean children aged 7–12 years, identified through a population-based survey of 55,266 children; 2.62% in Shenzhen, China, among children aged 3.8–4.8 years; 0.15% in Himachal Pradesh, India, for children aged 1–10 years; 0.34% in Nepal's Makwanpur district for children aged 9–13 years; and 1.08% in northern Vietnam among children aged 1.5–2.5 years [25,43,44]. These variations underscore

the critical need for harmonized diagnostic criteria and standardized screening protocols to allow for more accurate interregional comparisons.

In Oceania, limited studies exist on ASD occurrence, yet available data provide valuable insights. In Australia, a large sample size of 1,563,089 individuals yielded an estimated autism prevalence of 1.7% [9,10]. Two independent studies conducted in 2016 and 2020 investigated different cohorts. The first study, comprising 8,366 children aged 6–7 years and 6,470 adolescents from two cohorts aged 12–13 years and 16–17 years, reported a prevalence of 2.5% in the younger group and 1.5% in the older group. The subsequent 2020 study by May et al. found even higher prevalence rates, with 4.36% and 2.60% for the younger and older cohorts, respectively. Similarly, data from New Zealand, published in 2020 by Bowden et al., evaluated the prevalence of autism across five age groups: 0–4, 5–9, 10–14, 15–19, and 20–24 years. The study, which encompassed 1,551,342 individuals, estimated an overall ASD prevalence of 0.57% [10,45,46,47]. The results indicated variability in occurrence across different age groups, which may reflect the dynamic nature of the condition over the life course. This could be influenced by factors such as early therapeutic interventions, the degree of societal integration, and adaptive behaviors developed over time. For instance, individuals receiving appropriate support may show a reduction in observable autistic traits as they learn to adapt to societal expectations, whereas others may experience heightened challenges if their needs remain unmet. These findings emphasize the need for longitudinal approaches and tailored interventions to account for the evolving nature of ASD across different developmental stages [48].

Collectively, these findings illuminate substantial disparities in autism prevalence within and between regions, influenced by methodological, cultural, and socioeconomic factors. Differences in screening tools, diagnostic criteria, and public awareness contribute significantly to reported variability. Moreover, access to healthcare resources and sociocultural attitudes toward neurodevelopmental conditions may shape the landscape of early diagnosis and intervention. Continued research with standardized diagnostic protocols and region-specific data is crucial to further elucidate these disparities and improve global understanding and management of ASD [5,6].

## GENETICS AND SEX-SPECIFIC MANIFESTATION OF THE DISORDER

### 1. Genetic basis and key variants in ASD

Autism spectrum disorder exhibits a strong genetic basis, as evidenced by its recurrence in families, high concordance in monozygotic twins, and association with chromosomal abnormalities and rare genetic syndromes. Unlike single-gene disorders, ASD involves multiple genomic elements. Over 2,000 genes, nearly 3,000 single nucleotide polymorphisms (SNPs), variable number tandem repeats (VNTRs), about 4,500 copy number variations (CNVs), and more than 150 linkage regions have been linked to its features to varying extents [49]. Early discoveries of rare genetic variants involved genes associated with monogenic syndromes, which often present with intellectual disabilities and a heightened risk for social impairments [50]. Important breakthroughs in identifying ASD-related genes include *FMRI*, *PTEN*, and *TSC1/TSC2*, each contributing to conditions such as fragile X syndrome, Cowden syndrome, and tuberous sclerosis, respectively [51-54].

A commonly disrupted gene in *de novo* mutations is *CHD8*, though such variants are found in fewer than 0.5% of children with autism spectrum disorder [55,56]. Other genes implicated in the condition include *NLGN3*, *NLGN4X*, *SHANK3*, and *ADA2* [50,57,58]. Additionally, chromosomal aberrations account for around 1–3% of the cases [59]. For example, the duplication of the 15q11-q13 region is associated with autism, while deletions of the same region lead to Angelman or Prader-Willi syndrome, depending on parental origin. Other chromosomal variations linked to ASD include duplications of 17p12 and deletions in regions such as 7q11.23, 17p11.2, and 22q11.2. Furthermore, alterations in regions such as 2q31-32, 7q21-22, 16p11.2, and 20q13 have been implicated in autism susceptibility. These findings suggest the intricate genetic architecture of ASD, with multiple genetic variants, both common and rare, collectively contributing to the risk and phenotypic expression of the disorder. However, many aspects of its genetic basis remain poorly understood and require further investigation [59-63].

### 2. Heritability or *de novo* mutations?

Autism spectrum disorder has a well-established genetic foundation, as evidenced by family studies that demonstrate high heritability estimates ranging from 38% to 93% [49,64,65]. A notable 2019 study involving approximately 2 million individuals further refined this estimate to around 80% [66]. Despite these findings, the genetic factors underlying heritability remain

largely unexplained, reflecting the complexity of the disorder. This gap is attributed to the interplay of common and rare genetic variants, as well as potential gene-environment interactions. Furthermore, research shows that siblings of children with ASD are at a heightened risk of developing similar conditions, with the recurrence risk among siblings of affected individuals estimated to range between 7% and 20% [14]. Additional evidence is provided by twin studies, where concordance rates for ASD are higher in monozygotic twins compared to dizygotic twins. Concordance rates in monozygotic (identical) twins range from 60% to 92%, while dizygotic (fraternal) twins exhibit a much lower concordance of about 10%. This higher concordance in monozygotic twins is likely due to the fact that they share 100% of their genetic material, which suggests that genetic factors play a significant role in the development of ASD [60,67].

In simplex families (those with only one affected child), approximately 30% of ASD cases are associated with *de novo* mutations, which occur spontaneously and are not inherited [68]. Recent research underscores the significance of these *de novo* mutations in autism, with a 2021 study by Vasisht et al. revealing that such mutations are particularly prevalent in severe cases and are linked to genes involved in neuronal development. For high-risk families, including those with multiple ASD-affected members, *de novo* mutations contribute to 9-11% of cases, while in lower-risk families, the rate of mutations contributing to autism can rise as high as 52–67% [69]. While heritable genetic factors remain central to the understanding of ASD, *de novo* mutations, particularly in simplex families, emerge as significant contributors to the disorder's complexity, influencing both its development and severity. These findings highlight the importance of continued research to unravel the intricate genetic and environmental factors involved in autism [70].

### **3. Autism spectrum disorder by gender**

There is a well-established gender disparity in ASD, with males being more frequently diagnosed than females. Studies have consistently shown that boys are four times more likely than girls to develop autism. The Missouri Twin Study conducted between 1999 and 2001 found that among 788 twin pairs aged 7–15 years, 1.4% of boys exhibited traits indicative of autism, compared to only 0.3% of girls [71]. Similarly, in a dataset from the Norwegian Patient Register that included 731,318 children, the male-to-female ratio of ASD cases was found to be 4.3 among school-aged children (6–11 years old) [20]. A comparable result was observed in a large 2020 study conducted by the Autism and Developmental Disabilities Monitoring Network. This study, which analyzed 227,526 children, reported that autism

spectrum disorder was 3.8 times more common among boys than girls, with prevalence rates of 430 per 10,000 and 114 per 10,000, respectively [32].

The greater prevalence of ASD in males suggests that males are more susceptible to the genetic and environmental factors contributing to the disorder. However, the concept of a "female protective effect" has emerged, positing that females may require a higher genetic or environmental burden to exhibit autism traits at the same severity as males. This hypothesis is supported by findings indicating that girls with autism often present with more severe or broader symptoms compared to boys. Additionally, this protective effect may contribute to the underdiagnosis of ASD in females, as their symptoms tend to be subtler, leading to delayed or missed identification of the disorder [72].

## CONCLUSIONS

Autism spectrum disorder is a neurodevelopmental condition with significant variability in prevalence worldwide, shaped by cultural, socioeconomic, and methodological factors. Recent data indicate increasing diagnostic rates, partially due to heightened awareness and improved screening methods. Historically, the concept of autism emerged in the 20th century, with foundational research by Kanner and Asperger shaping modern diagnostic frameworks. Genetics plays a crucial role in ASD, with heritability estimates ranging from 80-90%. Numerous genes and chromosomal regions have been implicated, including, as well as rare *de novo* mutations, contributing to 10-30% of cases, particularly in simplex families. The remaining risk is attributed to environmental and prenatal and perinatal factors. Twin studies highlight high concordance rates in monozygotic twins (60-92%) compared to dizygotic twins (10%). Moreover, the "female protective effect" suggests that females require a higher genetic burden to develop ASD, explaining the observed male-to-female diagnostic ratio of approximately four to one. Autism research underscores the complexity of its genetic and environmental interactions, necessitating comprehensive approaches to understanding and addressing the condition globally. Accurate diagnosis, early intervention, and tailored support are critical in improving the quality of life for individuals with this developmental disorder.

## **DISCLOSURES**

### **Author contributions**

Conceptualization, MZ, PP; methodology, MZ; software, MG; check, MZ, MK; formal analysis, MZ, MG; investigation, MZ, MK; resources, MZ; data curation, PP; writing - rough preparation, MG,PP; writing - review and editing, MZ, MK; visualization, MZ; supervision, MZ, PP; project administration, MZ, PP. All authors have read and agreed with the published version of the manuscript.

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### **Conflicts of Interest**

The authors declare no conflict of interest.

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