

# Autism Spectrum Disorder Diagnoses: A Comparison of Countries with Different Income Levels

Marilia B Matos <sup>1,2</sup>, Tiago S Bara <sup>1,2</sup>, Mara L Cordeiro <sup>1-3</sup>

<sup>1</sup>Faculdades Pequeno Príncipe, Curitiba, Brazil; <sup>2</sup>Instituto de Pesquisa Pelé Pequeno Príncipe, Curitiba, Brazil; <sup>3</sup>Department of Psychiatry and Biobehavioral Sciences, University of California Los Angeles, Los Angeles, CA, USA

Correspondence: Mara L Cordeiro, Instituto de Pesquisa Pelé Pequeno Príncipe, Av. Silva Jardim, 1632, Curitiba, 80250-200, Brazil, Tel +5541-3310-1035, Fax +5531-3322-1446, Email mcordeiro@mednet.ucla.edu; mara.mcordeiro@professor.fpp.edu.br

**Purpose:** This study aimed to assess whether high-income countries have a lower mean age at the time of diagnosis of autism spectrum disorder (ASD) than low- and middle-income countries.

**Method:** We reviewed studies related to ASD diagnoses and the time of first concerns in low-, middle-, and high-income countries, published in PubMed, SciELO, Lilacs, and ScienceDirect. Thirty articles were included: 13 from low- and middle-income countries and 17 from high-income countries.

**Results:** The average delay between initial concerns and diagnosis was 32.33 months, with initial concerns averaging 23.64 months and diagnosis at 55.97 months. No statistical differences were found between countries with low-, middle-, and high-income.

**Conclusions:** This review found a considerable delay in ASD diagnosis despite an early presence of recognized signs and symptoms. It highlights the urgent need for standardized tools for early ASD diagnosis.

**Keywords:** autism spectrum disorders, low-income countries, diagnosis, first signs

## Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by differences in social interaction, communication, and unusual repetitive behavior that is self-stimulatory.<sup>1,2</sup> ASD is associated with substantial social and economic burdens. ASD diagnosis rates have risen rapidly in recent decades, with 1 in 44 children being diagnosed with ASD as of 2018 in the United States (US).<sup>3,4</sup>

The heightened awareness of ASD is mainly a feature of high-income countries, where epidemiological data are widely available.<sup>5-7</sup> Few studies on the prevalence of ASD have been conducted in low- and middle-income countries, with rates varying from 0.09 to 1.2%; however, no significant epidemiological study has been conducted in Africa.<sup>8-13</sup>

The relative lack of ASD awareness in low- and middle-income countries may be due to insufficient knowledge about the disorder, lack of trained health professionals, poor awareness of diagnostic tools, and low government and private resources.<sup>10</sup> The cultures, education systems, and economies of low- and middle-income countries vary greatly, with incomes ranging from low to lower-middle, middle, and upper-middle levels,<sup>14</sup> which frequently results in a pronounced disparity in healthcare access across different populations.<sup>13</sup>

Healthcare research and discourse in developing countries have focused primarily on infectious diseases, with relatively little attention to mental and behavioral health issues. The recognition of ASD may also be constrained due to stigma against mental health problems and behavioral disorders, particularly in children.<sup>13</sup>

Currently, ASD diagnosis is based exclusively on clinical observations, and ASD treatment involves intensive and individualized early therapeutic interventions.<sup>15</sup> The lack of recognition of the early signs of ASD, typically occurring within the first two years of life when intervention is recommended to start, leads to delayed diagnosis and

treatment.<sup>15</sup> As early diagnosis is associated with a better prognosis,<sup>5</sup> studies examining the prevalence and early signs of ASD are essential for the development and evaluation of screening tools. Additionally, there is a need to identify the reasons for delayed diagnosis and develop new strategies for pediatric primary care to promote timely diagnoses and intervention.

The objectives of this study were to conduct a systematic review of published research related to ASD diagnosis delays in low- and middle-income countries and compare the findings with those from high-income countries. We hypothesized that high-income countries have a lower mean age of diagnosis than low- and middle-income countries. To verify this hypothesis, we focused our analysis on the following: age at the time of assessment related to first concerns, early signs, and the time interval from concerns to a final diagnosis. We also explored the reasons for delayed diagnosis and discussed the importance of early ASD screening.

## Materials and Methods

### Data Sources and Search Strategies

This systematic review was conducted and written according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.<sup>16</sup> The study was registered with the International Prospective Register of Systematic Reviews (PROSPERO identifier CRD42020158996) before data extraction and analyses. We searched the PubMed, SciELO, LILACS, and ScienceDirect databases for scientific literature related to ASD delayed diagnosis. We searched using the keyword search strategies as follows. In PubMed, we searched for the following: autism[Title] OR autistic[Title] OR autism spectrum[Title] OR autistic spectrum[Title] OR autism spectrum disorders[Title] OR autistic spectrum disorders[Title] OR Asperger[Title] OR Asperger's[Title] OR Asperger's syndrome[Title] OR ASD[Title] OR Pervasive developmental disorders[Title] OR Disintegrative disorder[Title] AND Sign[Title] OR Signs[Title] OR Early signs[Title] OR Symptom[Title] OR Early symptoms[Title] OR Concerns[Title] OR First concerns[Title] OR Concern[Title] OR Diagnostic[Title] OR Diagnosis[Title] OR Diagnoses[Title] OR Age[Title] OR Age of first concerns[Title] OR Age of first symptoms[Title] OR Age of first signs[Title] OR Age of diagnosis[Title] OR Age of diagnoses[Title] OR Recognition[Title] OR Delay[Title] OR Delayed diagnosis[Title] OR Delayed diagnoses[Title] OR Identification[Title]. In SciELO we searched for the following: (ab:(\*autism)) OR (ab:(asd)) OR (ab:(autistic)) AND (ab:(age)) OR (ab:(time)). In Lilacs, we searched for the following: Autism AND age. Finally, in ScienceDirect we searched for the following: Autism AND age of diagnosis. There were no date limitations on the searches.

### Study Selection

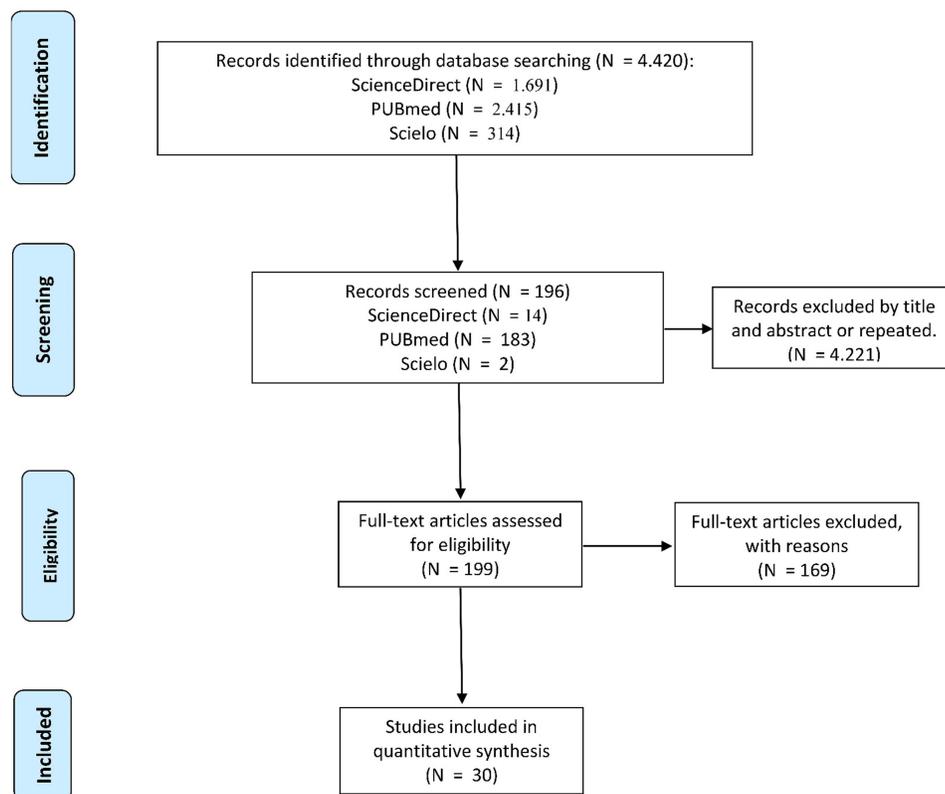
First, two of the authors separately reviewed the titles and abstracts for all the studies during the period January to August 2020. Second, full texts were obtained for final selection. When a consensus could not be reached on the eligibility of any article, the third author was involved in the discussion (Figure 1).

### Inclusion and Exclusion Criteria

The following inclusion criteria were applied for retrieved studies: published in English, Portuguese, or Spanish; case series, cohort, or survey study design; and studies related to the age of initial concerns and age of ASD diagnosis data reported. This study included published articles and excluded reviews. We aimed to determine the prevalence of ASD or validate an instrument, including individuals diagnosed after screening or represented by only a published abstract.

### Data Extraction

Data related to the following items were extracted: first author, year of publication, study location, population/sample size, sex distribution, age at first concern, age at the time of ASD diagnosis, and instruments used for diagnosis. If present, the first ASD signs, the first person to suspect (FPS), and factors related to delayed diagnoses were also extracted. Studies were divided by location and income for further statistical analyses.



**Figure 1** Records identified through a database search.

## Bias and Quality Assessment

Quality assessment of the included studies was conducted independently by two reviewers. Any discrepancies were resolved by consensus with a third reviewer. For the bias assessment, we used the Newcastle scale,<sup>17</sup> which is a checklist of three types of bias most often associated with observational studies (selection, comparability, and outcome).

## Statistical Analysis

The results were synthesized in a narrative format, and summary tables were used to compare the results across the included studies. Due to the limited number of studies published, combined with the heterogeneity of study populations and outcomes, the data were not pooled or subjected to a meta-analysis. A standardized summary of the evidence table was used to assess the overall strength of the evidence. This summary of evidence table included the number and design of included studies, sample size, a summary of findings by outcome, consistency or precision of results, potential reporting bias, study quality summary, body of evidence limitation, and applicability of the findings.

Articles were divided into groups regarding the country where the study was performed and publication age for further comparison. The year 2014 was used as a cut point since there were changes in the ASD diagnosis criteria published in 2013 with the DSM 5.<sup>1</sup>

The grouped variables “period of time” (studies before 2014 and after) and “level of development of the countries in the studies” (“low- and middle-income” countries and “high-income” developed countries) were analyzed using the Mann–Whitney test. The null hypothesis of the test was that age values differ in terms of their distribution. All analyses were performed using SPSS for Windows® software version 21.0, with a significance level of 0.05.

## Results

### Articles Retrieved

The database search yielded 4420 records identified in PubMed, ScienceDirect, Lilacs, and SciELO. Based on a review of the titles and abstracts of these records, 199 articles were considered potentially relevant and were further reviewed. After full-text assessments, 169 articles were excluded because they did not meet the inclusion criteria, and 30 were included. The third reviewer's intervention was required for the decision regarding 50 articles. (Figure 1).

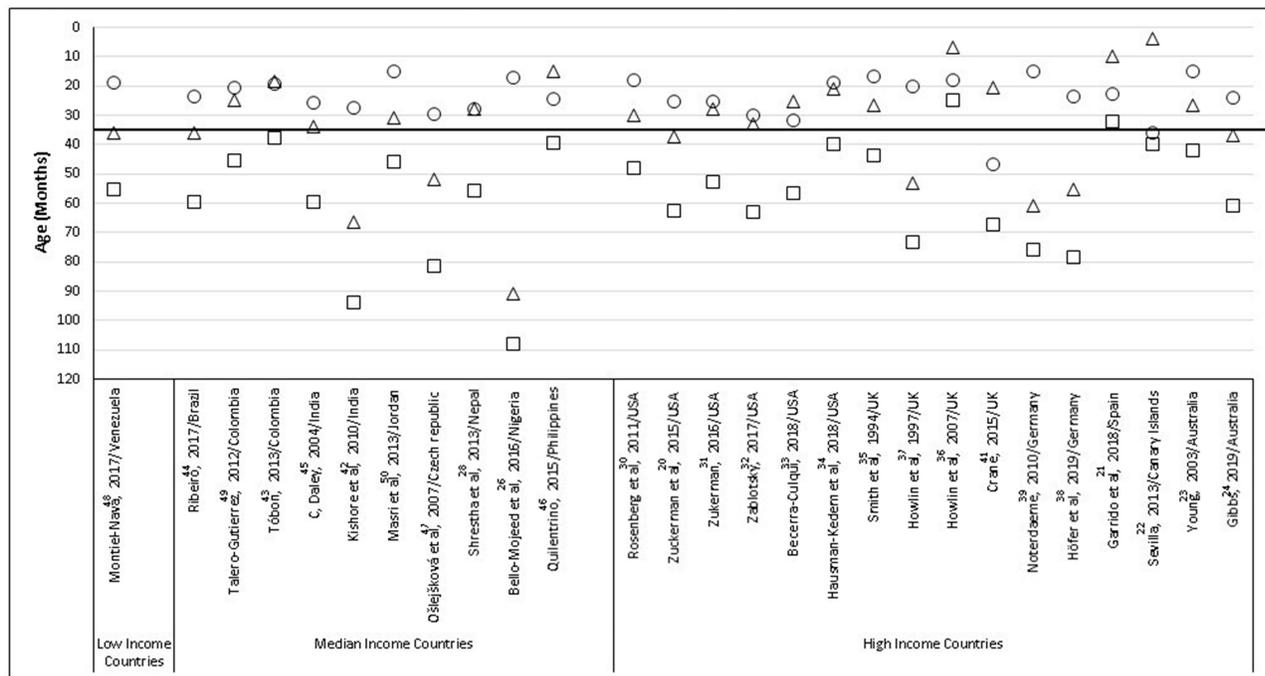
Quality assessment was performed in all articles without high bias in one or more parameters. At this stage, the third reviewer's intervention was necessary to evaluate five articles. The summary scores of the selected studies are reported in Table 1.

Figure 2 shows the distribution of means according to the level of development of the different countries. As shown in Figure 2, 13 of the 30 included studies were conducted in upper-, middle-, and lower-income countries.<sup>18–29</sup> The other

**Table 1** Summary scores and correspondence level of development of the countries in the included studies

Author (Year)/Location	Diagnosis Method	Study Design	N	FSP	Age at First Concern, Mos.	Age at Diagnosis, Mos.	Delay from Concern to Diagnosis, Mos.
Low-Income Countries							
Montiel-Nava et al(2017) <sup>48</sup> /Venezuela	-	A	103	-	18.90	55.02	36.12
Medium Income Countries							
Ribeiro et al (2017) <sup>44</sup> /Brazil	DSM-IV	A	18	Parent	23.60	59.60	36.00
Talero-Gutiérrez et al (2012) <sup>49</sup> /Colombia	DSM-IV	A	138	Parent/ other	20.60	45.50	24.90
Tóbon et al (2013) <sup>43</sup> /Colombia	DSM-IV	A	42	Parent	19.08	37.58	18.50
Daley (2004) <sup>45</sup> /India	DSM-IV	-	98	-	25.7	59.4	33.7
Kishore et al (2010) <sup>42</sup> /India	ICD 10	-	50	-	27.38	93.78	66.4
Masri et al (2013) <sup>50</sup> /Jordan	DSM-IV	-	84	-	15.0	45.63	30.63
Ošlejšková et al(2007) <sup>47</sup> /Czech Republic	-	-	204	-	29.7	81.5	51.8
Shrestha et al (2013) <sup>20</sup> /Nepal	DSM-IV	-	50	-	27.9	55.6	27.7
Bello-Mojeed et al (2016) <sup>28</sup> /Nigeria	DSM 5	-	60	-	17.0	108	91.0
Quilendrin et al(2015) <sup>46</sup> /Philippines	-	-	41	-	24.42	39.39	14.97
Jayanath and Ozonoff (2020) <sup>18</sup> /Malaysia	DSM 5	-	366	Parent	24	46	22
García et al (2021) <sup>19</sup> /Chile	-	B	291	Parent	29.2	58	28.8
High-Income Countries							
Rosenberg et al(2011) <sup>30</sup> /US	-	-	6214	-	18	47.9	29.9
Zuckerman et al(2015) <sup>22</sup> /US	-	B	1420	-	25.22	62.44	37.22
Zuckerman et al(2017) <sup>31</sup> /US	-	B	722	Parent	25.20	52.80	27.60
Zablotsky et al(2017) <sup>32</sup> /US	-	B	1287	Parent	30.00	62.76	32.76
Becerra-Culqui et al(2018) <sup>33</sup> /US	DSM-IV	-	538	-	31.5	56.54	25.04
Hausman-Kedem et al (2018) <sup>34</sup> /US	DSM 5	-	67	-	18.7	39.63	20.93
Smith et al (1994) <sup>35</sup> /UK	-	-	127	-	16.8	43.5	26.7
Howlin and Moore(1997) <sup>37</sup> /UK	-	-	1200	-	20.29	73.37	53.08
Howlin and Asgharian (1999) <sup>36</sup> /UK	-	-	770	-	18.0	24.61	6.61
Crane et al (2015) <sup>41</sup> /UK	DSM-IV	B	1047	-	46.80	67.20	20.40
Noterdaeme et al, 2010 <sup>39</sup> /Germany	ICD 10	A	601	-	15.00	76.00	61.00
Höfer et al (2019) <sup>38</sup> /Germany	ICD 10	-	208	-	23.4	78.5	55.1
Garrido et al (2018) <sup>23</sup> /Spain	DSM-IV	-	48	-	22.58	32.25	9.67
Fortea Sevilla et al(2013) <sup>24</sup> /Canary Islands	-	A	72	Parent	36.10	39.70	3.60
Islands							
Young et al (2003) <sup>25</sup> /Australia	DSM-IV	-	153	-	15.1	41.82	26.72
Gibbs et al (2019) <sup>26</sup> /Australia	-	-	215	-	23.75	60.67	36.92
Alotaibi et al (2021) <sup>40</sup> /Saudi Arabia	DSM 5	B	67	Parent	20.4	34.5	14.1

**Abbreviations:** A, observational and descriptive - case series; B, survey. DSM-IV, The Diagnostic and Statistical Manual of Mental Disorders, 4th edition; DSM 5, The Diagnostic and Statistical Manual of Mental Disorders, 5th edition; ICD 10, International Classification of Diseases.



○: Time 1, FPS's initial concerns; □: Time 2, Diagnosis period; △: Time 3, Delay between FPS and diagnosis.

**Figure 2** Distribution of means according to the level of development of the countries in the studies.

**Note:** Superscript number: Reference number.

16 studies were conducted in high-income countries, including six in the US,<sup>20,30–34</sup> four in the United Kingdom (UK),<sup>35–37</sup> two in Spain,<sup>21,22</sup> two in Germany,<sup>38,39</sup> two in Australia,<sup>23,24</sup> and one in Saudi Arabia.<sup>40</sup>

## First Person to Suspect

Six studies had information on the FPS that the child's development was not typical; a family member was reported in most studies.<sup>22,23,41–43</sup> One of the studies conducted in Nigeria found that the teacher was the FPS in 51.7% of the cases.<sup>26</sup>

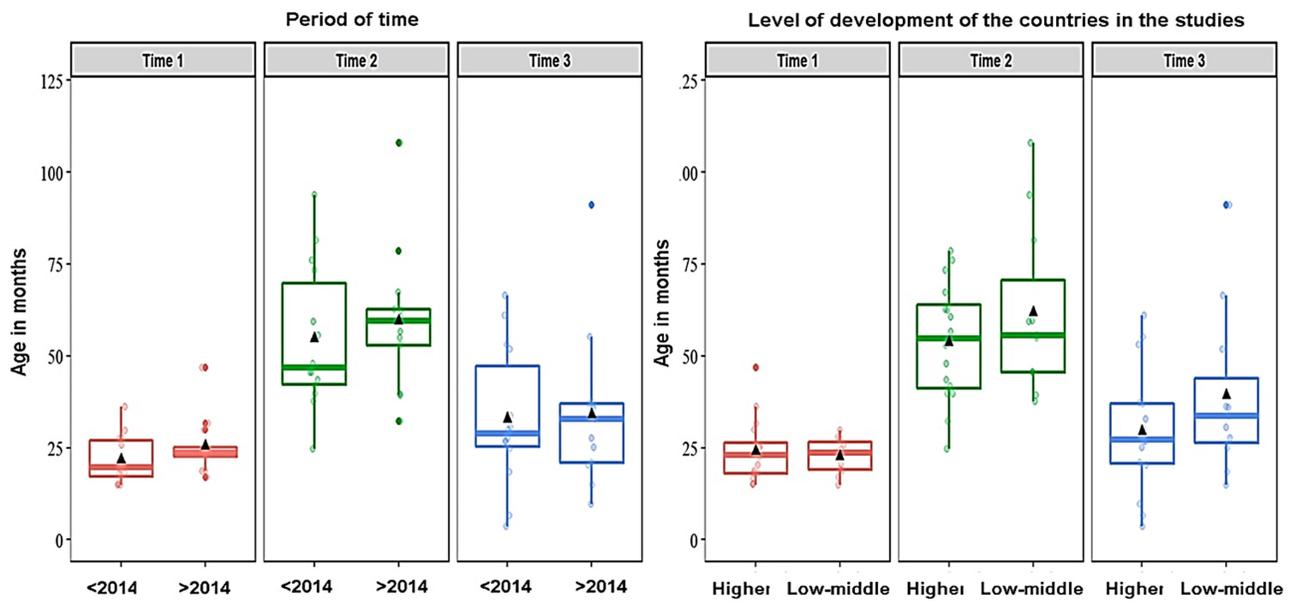
## Time Lag Between Initial Concerns and Diagnosis

For each time variable (i.e., the FPS's initial concerns [Time 1], diagnosis [Time 2], and the delay between [Time 3]), the data were grouped between "period of time" (studies before 2014 and after) and "level of development of the countries in the studies" ("low- and middle-income" countries and "high-income" developed countries). Thus, it was possible to notice similar values from the boxplots (Figure 3); in general, the median and average age values tended to be higher for studies from 2014 onward, and in the "low- and middle-income" countries. The interquartile range (third quartile minus first quartile) tended to be greater for values obtained in surveys before 2014, but there were more discrepant values for age after 2014.

The Mann–Whitney test indicated that the age distribution (Times 1, 2, and 3) between the "period of time" and "differences by the level of development of the countries in the studies" did not differ at the significance level  $\alpha = 5\%$ , as shown in Table 2. These results remained stable over time in general, even though some of the studies with retrospective cohorts reflected ASD diagnoses made almost a decade ago.

## Delay Between Initial Concerns and Seeking Help

Some studies reported the time interval between the FPS's initial concerns and parents seeking help. This delay was, on average, 3 months in a Brazilian study,<sup>44</sup> 32 months in an Indian study,<sup>45</sup> and 13.5 months in a study conducted in the Philippines.<sup>46</sup>



**Figure 3** Boxplots of the difference in period (prior to 2014) and differences by the level of development of the countries in the studies.  
**Notes:** Time 1: FPS's initial concern; Time 2: Diagnosis; and Time 3: Delay between Time 1 and 2. >2014: Studies published after 2014; <2014: Studies published before 2014; Higher: Studies from high income countries; Low-middle: Studies from low-and-middle income countries.

Among high-income countries, there was a 2.4 months delay in a Spanish study,<sup>22</sup> 8 months in Australia,<sup>24</sup> and 6.96 (for ASD) and 12.96 (for Asperger’s syndrome) months in a study from the UK.<sup>36</sup> The latter findings were similar to a previous study on the same group that was conducted in the last decade in the UK, where the average delay was 6–7 months.<sup>37</sup>

### Factors Associated with Child’s Age at Initial Concerns and Age of Diagnosis Clinical Characteristics

Children who were initially diagnosed with Asperger’s syndrome were diagnosed later than children diagnosed with classic autism.<sup>21,33,36,39,41,47</sup> In contrast, in the Venezuelan study,<sup>48</sup> the ages of concern and diagnosis did not differ significantly between children diagnosed with autism and those diagnosed with pervasive developmental disorder not otherwise specified.

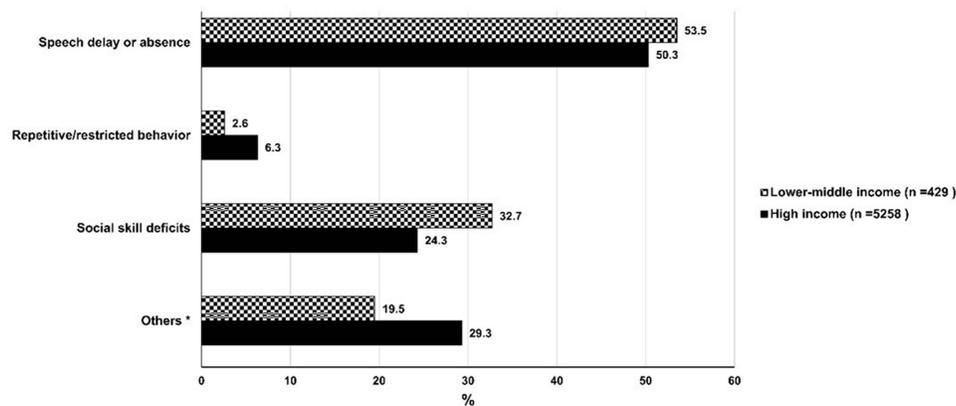
Children with an intellectual disability (ID) tended to have concerns reported earlier than autistic children without ID, along with earlier commencement of services. Impaired cognitive functioning was associated with a younger age at diagnosis.<sup>30,32,38,39,48</sup> However, Kishore and Basu<sup>42</sup> reported no association between ID and an early diagnosis.

The presence of comorbidities also showed mixed results in the studies. For example, comorbidities were associated with an earlier diagnosis in an Indian study,<sup>49</sup> but a later diagnosis in an Australian study.<sup>24</sup>

**Table 2** Comparison of p-Values of the Mann–Whitney Test Results

	Period of Time	Level of Development
	<2014 vs >2014	Higher- vs Low- and Middle-Income
Time 1	0.368	0.952
Time 2	0.960	0.849
Time 3	0.390	0.976

**Notes:** Significance level  $\alpha = 5\%$ ; >2014: Studies published after 2014; <2014: Studies published before 2014.



**Figure 4** Proportion of early signs reported by study.

**Note:** \*Lack of imagination, motor delay, general medical conditions, eating problems, excessively crying, toilet training delayed, sleeping disorders.

### Sociodemographic Characteristics

A linear regression analysis indicated that social status did not significantly affect the age of diagnosis in a German study,<sup>39</sup> and an American study also reported no differences in sociodemographic factors.<sup>33</sup> However, in the Venezuelan study, higher social and economic status and higher parental education levels were associated with earlier diagnosis.<sup>48</sup> Whereas, Jayanath and Ozonoff's<sup>18</sup> Malaysian study showed that sociodemographic factors were associated with a later diagnosis. One study found that Hispanic children in the US tended to receive services for ASD later than non-Hispanic White children.<sup>32</sup> Another study reported that being Black or multiracial or living in a rural area were risk factors for delayed diagnosis.<sup>30</sup>

### Parental Concerns

Regarding types of parental concerns, concerns regarding verbal communication were strongly represented for children with early parental reports, early commencement of services, and diagnosis. Children with earlier reports of behavioral concerns later had average signs of diagnosis (87.9 months), but later than children whose parents were concerned about a learning disability (69.7 months). Children exhibiting unusual movements and nonverbal communication concerns were diagnosed earlier than those who did not show these signs.<sup>32</sup>

### Diagnostic Trends Over Time

Two of the reviewed studies, one in Germany and one in the US, compared diagnostic data between younger children/more recent diagnoses and older children/less recent diagnoses to examine how ASD diagnosis may have changed over time.<sup>32,39</sup> In the German study, the average age of diagnosis for children diagnosed between 2000 and 2007 was not significantly different from that between 1998 and 2002.<sup>39</sup> In the US study, younger children with more recent diagnoses (6–11 years) had earlier parental concerns, service initiation, and ASD diagnoses than older children with less recent diagnoses (12–17 years).<sup>32</sup>

### Early Signs and Symptoms

The first signs and symptoms were described in several studies.<sup>18,23,28,35–37,42,45,46,50</sup> Speech delay was the most recognized concern between high-income (50.3%) and low/middle-income countries (53.5%), as described in Figure 4.

### Discussion

We sought to test the hypothesis that children with ASD in high-income countries would have an earlier diagnosis than children in low- and middle-income countries. Our systematic review showed that the mean age of ASD diagnosis was 55.97 months and the mean age of first concerns was 23.64 months. Although the age of diagnosis in high-income countries was earlier than that in low- and middle-income countries, there was no statistically significant difference between age of diagnosis in high-income (52.60 months) and low/middle-income countries (60.38 months). The mean age of initial concerns in high-income countries was 23.93 months and that in the low/middle-income countries was

23.27 months. There were no differences in the age of initial concerns and diagnoses between articles published before or after 2014.

The great diversity in ASD phenotype presentations, cultural differences, and differences in social status make simple, linear comparisons of the age of initial concerns and diagnosis difficult. Nevertheless, it is important to note that all the analyzed studies showed delays from initial concerns to diagnosis (mean = 37.12 months in “low- and middle-income” countries and mean = 28.67 months in “high-income” developed countries).

Despite efforts to enable earlier recognition of ASD signs, delayed ASD diagnosis remains an issue. Although ASD signs are present within the first two years of life,<sup>15</sup> a previous review indicated that the median age of diagnosis ranged from 36 months to 82 months,<sup>51</sup> consistent with the present results. A more recent meta-analysis reported that the mean age at ASD diagnosis was 60.48 months, ranging from 30.90 to 234.57 months.<sup>52</sup>

More disturbingly, when comparing studies over the years, we found no significant improvement in the diagnosis timeline. These results indicate the need for more active clinical approaches despite increased awareness of ASD and the importance of early diagnosis. There were also no differences between the mean age of delay in studies before and after 2014 ( $p=0.976$ ).

There are two major factors associated with delayed ASD diagnosis: clinical characteristics and socioeconomic factors. Concerning clinical characteristics, children with severe IDs and children who are nonverbal are more easily recognized.<sup>53</sup> Regarding socioeconomic factors, it has been suggested that later diagnosis may be related to low income, limited parent education, and being a member of a historically disenfranchised race or ethnic group.<sup>30,32,48</sup> In this regard, the Venezuelan study found an effect of socioeconomic status, whereas the German study did not.<sup>39,48</sup> An American study showed delayed diagnosis among children of Hispanic ethnicity.<sup>32</sup>

The finding that FPS were overwhelmingly parents<sup>22,23,31,32,42–44,49</sup> suggests that many health professionals who should have been alerted to signs earlier were not properly prepared to do so.

The most frequently reported first concerns were “delayed or absent speech” and “delays in social skills.” In addition, some symptoms that are not only associated with ASD can be indicators for a more accurate evaluation, such as motor delays, general medical conditions, eating problems, excessive crying, delayed toilet training, and sleeping disorders. These signs and symptoms are included in the Modified Checklist for Autism in Toddlers (M-Chat), an easy and free screening tool that can be used in pediatric settings.<sup>54</sup> However, this tool should be used with caution as it has low sensitivity, and monitoring for signs of ASD in screen-negative children should be continued.<sup>55</sup>

Some of the ASD criteria of DSM-5<sup>1</sup> were not reported as first concerns, such as sensory disorders, inflexible adherence to routines, and highly restricted and fixated interests. Although repetitive/restricted behavior was mentioned, it was not as significant as the other reported concerns. These results highlight the importance of screening tools not only based on the ASD diagnostic criteria but also common first symptoms reported. Screening is a powerful strategy for improving early diagnosis and, consequently, early intervention enrollment. Early intervention is based on the concept of neuroplasticity, that is, the ability of the brain to reorganize in response to experience via changes in neural circuitry.<sup>56</sup>

In a prospective cohort study, Pierce<sup>57</sup> evaluated the stability of ASD diagnosis made between 12 and 36 months old and then compared the results with those of other developmental problems and those of typical development; the overall diagnostic stability of ASD among young children diagnosed with ASD was 0.84, which was higher than that of any of the compared diagnostic groups (eg ASD features without a diagnosis, developmental delays, language delays). Moreover, the results suggested that an ASD diagnosis can be reliable in children as young as 14 months old.<sup>58</sup>

Although no long-term studies have compared the outcomes of screened versus non-screened children, arguments for screening thus far have been based on the negligible cost of screening relative to the life-long economic costs of ASD.

Furthermore, in low- and middle-income countries, most children identified by screening had not been previously identified as having ASD by parents or physicians.<sup>58</sup> At this stage, there is no debate about whether or not to screen for ASD; however, researchers and clinicians should discuss the best approach and how to move from screening to timely diagnosis. In 2016, the US Preventive Service Task Force (USPSTF) concluded that

the current evidence is insufficient to assess the balance of benefits and harms of screening for ASD in young children for whom no concerns of ASD have been raised by their parents or a clinician.

The USPSTF classified this recommendation as grade I, indicating that more research is required in this field.<sup>29</sup> The absence of universal ASD screening places the responsibility for early diagnosis on health professionals, teachers, and parents, who in many cases are not well-prepared to recognize the signs of ASD in infants or toddlers. Thus, universal screening programs should expand the opportunity for toddlers to receive early intervention, and thus have a better prognosis. The aforementioned USPSTF statement should not be understood as a contraindication for screening, but rather as a statement of the urgent need for long-term studies of screening outcomes.

The ASD prevalence rates reported in low- and middle-income countries<sup>7–9,11,12,48</sup> are likely gross underestimates. A recent review of the global prevalence of ASD showed that 86.5% of cases identified in epidemiological studies were in North America, Europe, and Japan, where only 10% of the world's children live.<sup>59</sup> This discrepancy might be due to the following: difficulties associated with conducting research in developing countries; a lack of ASD awareness among parents, teachers, and health professionals; attribution of behavioral problems to poor parenting skills;<sup>59</sup> and limited healthcare access.<sup>13</sup>

Our study has some notable limitations. First, only 30 studies were eligible for inclusion that were quite varied in design, with their inherent limitations. This limited study inclusion might have occurred, at least in part, because our aim was limited to specifically evaluating the delay of ASD diagnosis. Unfortunately, most of the studies retrieved on the diagnosis did not evaluate the first signs recognized by the parents. However, the limited data available were found to be concordant with the data obtained in other settings. Second, the analysis sample may have been biased as some of the studies were performed at referral centers.<sup>20,26,28,32,34,38,41–44,48,49</sup> As referral centers are expected to be better prepared to recognize signs of ASD than non-referral local centers, it is reasonable to conclude that the current situation of ASD delayed diagnosis might be worse than that portrayed in this review. Another limitation is that most of the studies included did not distinguish participants by ASD severity.<sup>22,31,41,43,44,48,49</sup> This shortcoming makes it difficult to compare the age of reported concerns and age of diagnosis, given that more severe patients are more easily recognized.

## Conclusion

To the best of our knowledge, this is the first systematic review comparing ASD diagnosis and treatment delays in low-, middle-, and high-income countries. Additionally, we have provided an account of the most frequent first concerns of FPS, which is extremely important for early recognition and screening for ASD. On average, there was a 32.33-month delay between initial concerns of the FPS and ASD diagnosis in the reviewed studies. This delay has been stable for many years. In most of the cases, the FPS were parents rather than healthcare professionals. This review highlights the urgent need for standardized tools for early ASD diagnosis, which is challenging because of the high phenotypic variability among people with autism. There is a need for more studies on ASD diagnosis, especially in low- and middle-income countries. Elucidation of the epidemiology and clinical course of ASD is critical for the developing public health programs and medical education strategies for the effective recognition and treatment of ASD effectively.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare that they have no competing interests.

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