SUPPLEMENT 1

Calculation of Median Age of Autism Spectrum Disorder (ASD) Identification

This article uses a survival approach to estimate the median age of ASD identification among children meeting the Autism and Developmental Disabilities Monitoring (ADDM) Network case definition for autistic disorder. This method has been used previously,[1] but other ADDM Network publications have reported the median age of identification using a different method.[2] The purpose of this supplement is to illustrate the two methods and explain the differences between the two estimates of the median age of identification.

Regarding the age of ASD identification, this article is concerned with the 2,136 children meeting ADDM Network case status for autistic disorder. Of the 2,136 children, 1,646 have a previously documented ASD diagnosis or classification. The remaining 490 have not been identified as having ASD by a community professional.

Methods for calculating the median age of identification are as follows. Method 1 used in ADDM Network prevalence reports calculates the median age of ASD identification among the children who have been identified. Applied here, this is equal to the "middle age" among the 1,646 children who have been previously identified (that is, the 823rd earliest age of ASD identification). The 490 children who were not identified as having ASD are ignored. According to this method, the median age among the 1,646 children is 51 months. In method 2, using a survival approach, the median age is calculated as the age by which half of the total population receive a diagnosis. The 490 children who have not been identified as having ASD are counted as "censored" observations. This acknowledges that these children have not been identified through age 8 years (the surveillance system does not include information past age 8), but that they might be identified in the future. Therefore, the median age among the 2,136 children (the 1,068th earliest age of ASD identification) is 62 months.

Excluding children who were not identified through age 8 results in a downward bias of the estimated age of ASD identification. This has been previously discussed in relation to the ADDM Network by Shattuck *et al.*[1] In the same way, Hertz-Picciotto and Delwiche[3] describe how the average age of ASD diagnoses (among those diagnosed) is influenced by the number of years of follow-up time.

Table S2, available online, shows that the two estimates of median age become increasingly discrepant as the proportion of children who have been identified decreases. Ignoring the un-identified children leads to an underestimate of the age of community identification for the total group of children meeting ADDM case criteria.

Sensitivity to Duration of Follow-Up

Suppose the ADDM Network followed children through age 10 (an additional 2 years), and during this time 150 of the 490 previously un-identified children were classified as having ASD by a community professional. The median age of identification using a survival approach (method 2) would remain unchanged at 62 months—half of the total group of children are identified by 62 months no matter how long the group is followed. In contrast, the median age among those who have been previously identified (method 1) would increase from 51 months to 55 months, as more children have been identified at a later age.

Similarly, if the ADDM Network followed children through age 6 years, the median age would remain at 62 months using a survival approach (method 2), but would decrease to 47 months using method 1.

One of the important features of the ADDM Network, as described in the current paper, is its inclusion of children who meet ASD criteria but have not been identified by a professional in the community. By using a survival-based analysis, we are avoiding the downward bias in estimating the age of identification and taking advantage of the ADDM Network study design.

SUPPLEMENT 2

Accelerated Failure Time Analyses

We performed multivariable log-logistic accelerated failure time analyses (using PROC LIFEREG in SAS) to determine whether certain autism spectrum disorder (ASD) diagnostic features were associated with an earlier age of ASD identification. We selected the log-logistic distribution because it does not assume a constant hazard ratio across time, and the time ratios it produces have a straightforward interpretation.[4,5] For example, a time ratio of 0.75 would suggest a 25% reduction in the age of ASD identification in one group compared to a baseline group. We observed a linear relationship ($R^2 = 0.95$) between the natural logarithm of the survival time

and the natural logarithm of the survival odds beyond that time. The survival analysis was run in three stages: univariate time ratios for each of the behavioral features; time ratios adjusted for all 12 behavioral features simultaneously; and time ratios adjusted for all behavioral features, gender, intellectual disability, the Autism and Developmental Disabilities Monitoring (ADDM) Network site, and race/ethnicity.

Results From Time Ratio Analysis

Among the study group, of the 2,136 children who meet ADDM criteria for autistic disorder, the majority (9 of the 12) of the behavioral features have time ratios significantly less than 1.0, indicating that they are associated with earlier identification (see Table S3, available online). After adjusting for all 12 features, the time ratios generally increase, but only slightly. Further adjustment for sex, race/ethnicity, ADDM Network Site, and co-occurring intellectual disability has little additional effect on the estimates.

There are some noteworthy differences between the results of the time ratio analyses in Table S3, available online, and the stratified analyses in Figure 2. The time ratios in the Table S3, available online, indicate that impairments in joint attention (*DSM* 1c), emotional reciprocity (*DSM* 1d), delayed speech (*DSM* 2a), restricted interests (*DSM* 3a), and preoccupation with parts of objects (*DSM* 3d) are significantly associated with earlier identification. However, in analyses stratified by number of criteria met (Figure 2), we found little evidence indicating that children with these features were consistently identified sooner. In fact, one of the stratified comparisons suggests that children with restricted interests (*DSM* 3a) may be identified at the same time or slightly later than children who did not have this feature noted in their records.

We did not adjust for number of evaluations or the specialty of the professional who evaluated the children. These characteristics of the evaluations are likely influenced by the symptomatology of the child; for example, children may have many evaluations because they have more symptoms, or children may visit a speech pathologist because they have speech problems. Because we viewed the referral process and timeliness of evaluations as potential consequences of behavioral symptoms (and not confounders), we did not adjust for number or type of evaluations.

SUPPLEMENTAL REFERENCES

1. Shattuck PT, Durkin M, Maenner M, *et al*. Timing of identification among children with an autism spectrum disorder: findings from a population-based surveillance study. J Am Acad Child Adolesc Psychiatry.2009;48:474–483
2. Centers for Disease Control and Prevention (CDC). 2009. Prevalence of autism spectrum disorders—Autism and Developmental Disabilities Monitoring Network, United States, 2006. MMWR Surveill Summ. 2006;58:20.
3. Hertz-Picciotto I, Delwiche L. The Rise in Autism and the Role of Age at Diagnosis. Epidemiology, 2009;20:84–90
4. Kleinbaum DG, Klein M. Survival Analysis: A Self-Learning Text, 2nd ed. New York: Springer; 2005
5. Patel K, Kay R, Rowell L. Comparing proportional hazards and accelerated failure time models: an application in influenza. Pharm Stat. 2006;5:213Y224

FIGURE S1 Expanded version of Figure 1 in main article: Frequency of documented autism spectrum disorder (ASD) behavioral features by age at evaluation (years), stratified by sex, intellectual disability, race/ethnicity, history of regression, and previous community ASD identification. Note: Bar chart displays the number of case children (among 2,757) were evaluated at least once during each year of age.

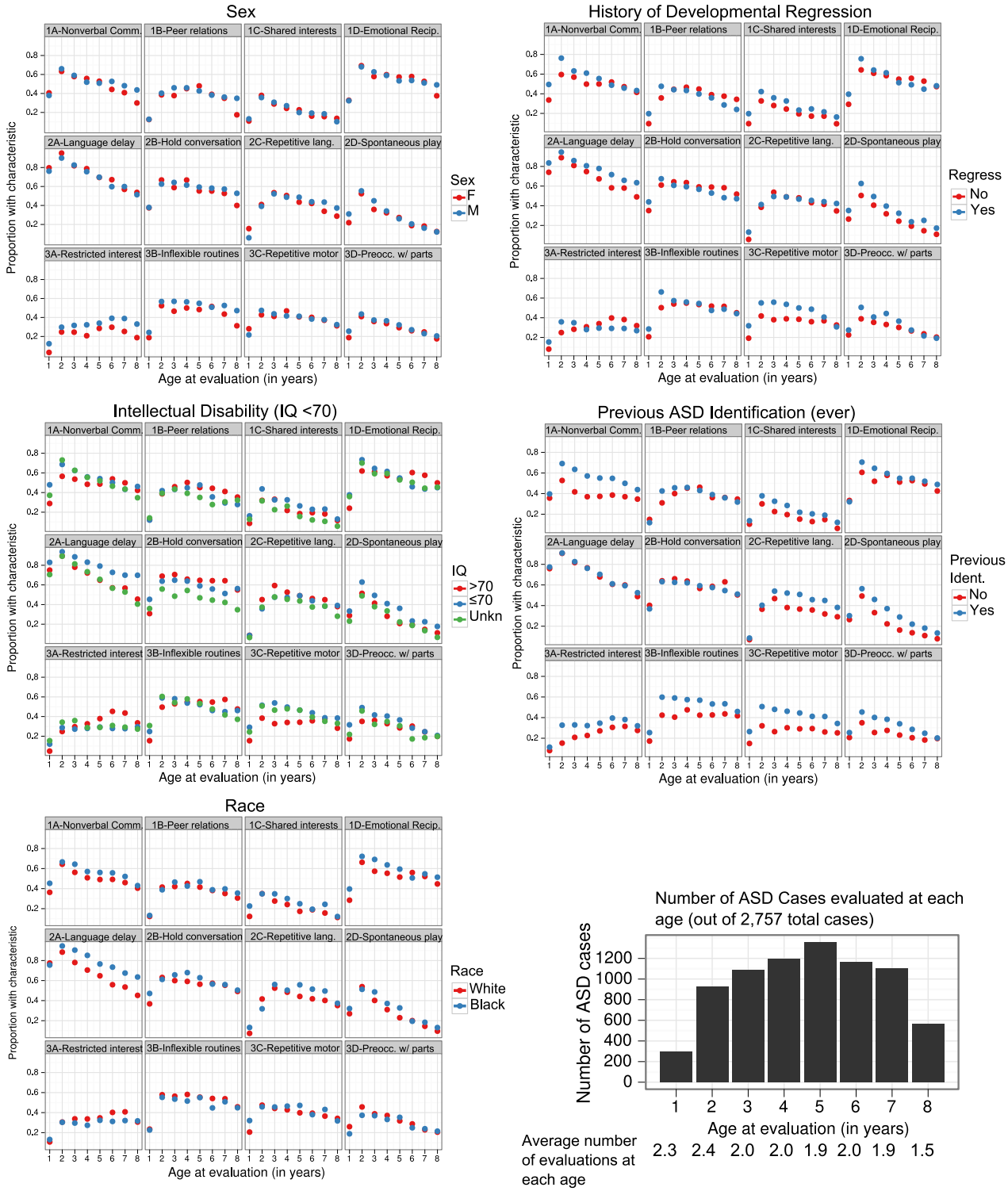

FIGURE S2 Network graph visualization of the 616 combinations of the minimum number (6) of *DSM-IV-TR* symptoms needed to meet autistic disorder criteria. Note: These 616 combinations were applied to 2,136 children meeting Autism and Developmental Disabilities Monitoring (ADDM) Network autistic disorder case status. Each point represents one of the 616 combinations of criteria, and the size of the point is scaled to the relative number of the 2,136 children fulfilling that combination. Thus, a child with all 12 *DSM-IV-TR* criteria would fulfill all 616 combinations. The graphing software visually exaggerates the differences in the sizes of the points; the ratio of the most versus least frequent combination is approximately 3.0. The links between points are weighted by the odds ratio of the two combinations occurring together. With 616 combinations, there are 189,420 interconnections between the points; for better visibility, this figure shows only the links with the strongest odds ratios (the top 10%, or 18,942 links). The network layout was rendered in Gephi (www.gephi.org) using a force-directed algorithm. In a force-directed graph, the relative position of each node (i.e., point) is determined by its relationship to other points. If two combinations are strongly associated with each other, they will tend to be positioned in close proximity to each other.

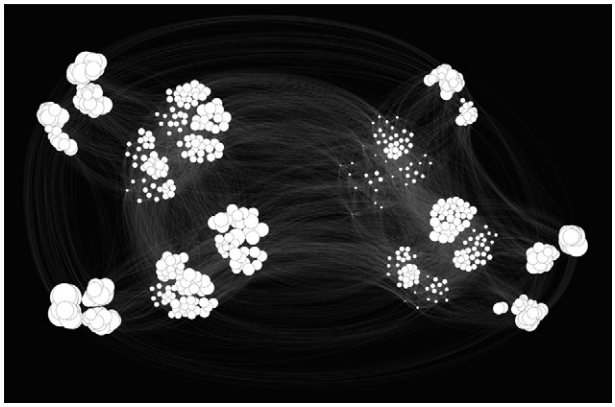

FIGURE S3 The graphs in this panel are the same as the graph shown in Figure S2, available online (without edges). Note: Each of the graphs highlights which of the 616 combinations contain a particular *DSM-IV-TR* criterion for autism spectrum disorder (ASD). Within each facet, the colored points contain the selected feature, and the white points do not. For example, in the upper-left panel, the green dots are combinations that include *DSM* 1a (impairments in nonverbal communication), whereas the white dots do not include *DSM* 1a. In general, more frequently documented *DSM-IV-TR* criteria are distributed more homogeneously throughout the graph, whereas the combinations containing less frequently documented criteria tend to "stick together." The segregation of certain features (3A, 1C, 3D) is striking because the layout of the graph does not explicitly contain information about the individual criteria; which suggests that the combinations containing certain features are more likely to co-occur. On the other hand, the requirements of the diagnostic criteria (six items; minimum of two in social; one in communication; one in repetitive/restricted behavior and interests) can exert influence over how we perceive symptoms "clustering" together among children with ASD.

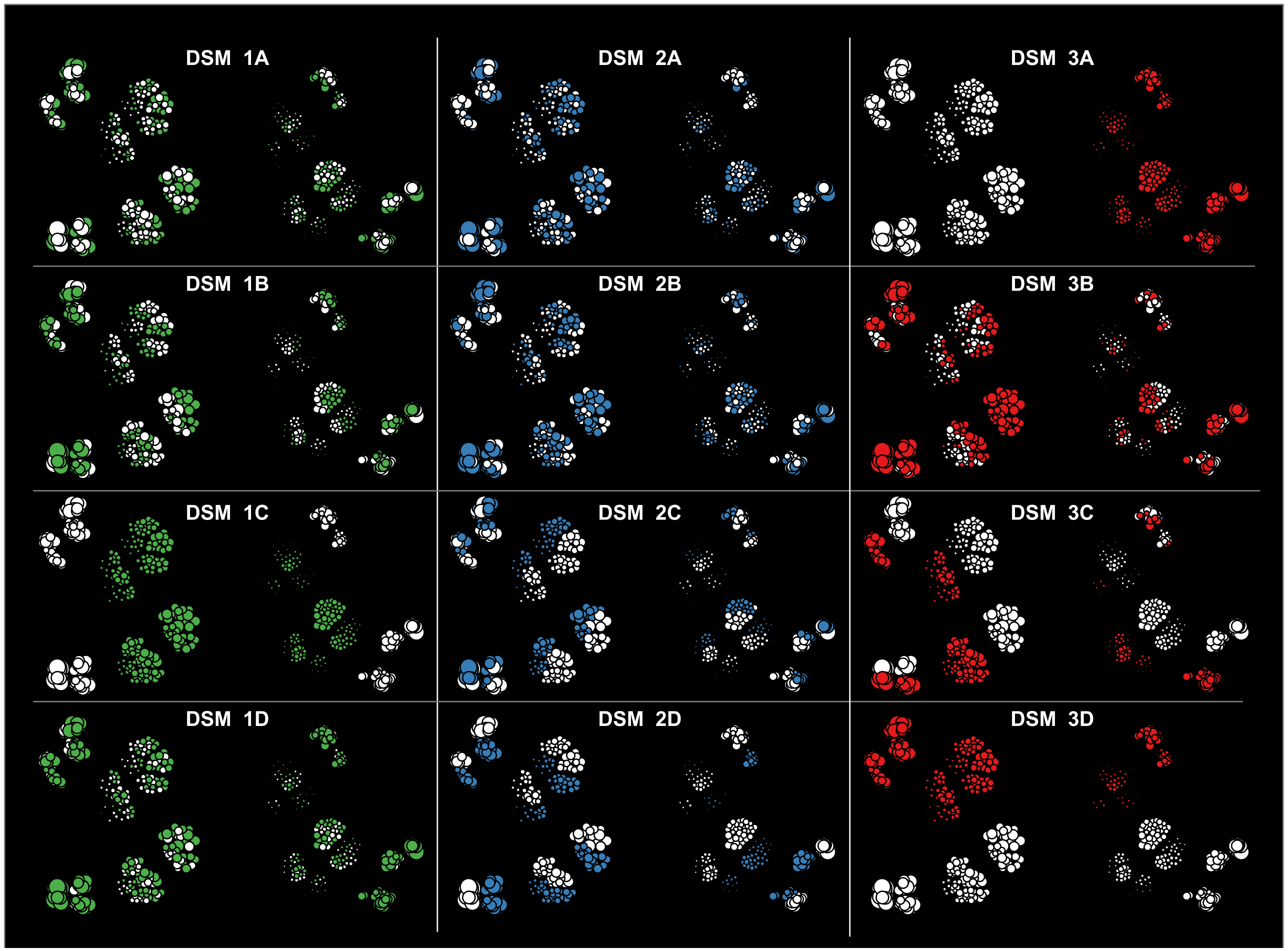

TABLE S1 Diagnostic Criteria for Autistic Disorder, Pervasive Developmental Disorder–Not Otherwise Specified (PDD-NOS), and Asperger's Disorder (Adapted From *DSM-IV-TR*)

Domain of impairment (no. of items) brief description of criteria	Minimum No. of Criteria Needed in Each Domain for Diagnosis		
	Autistic Disorder	Pervasive Developmental Disorder–Not Otherwise Specified	Asperger's Disorder
1. Social interaction (4) 1a: Nonverbal social communication 1b: Peer relations 1c: Joint attention 1d: Emotional reciprocity	2	1	2
2. Communication (4) 2a: Delay of spoken language 2b: If verbal, ability to hold a conversation 2c: Stereotyped/repetitive language 2d: Lack of spontaneous pretend play	1		No cognitive or language delays
3. Repetitive/restricted behaviors and interests (4) 3a: Restricted interests 3b: Inflexible routines/rituals 3c: Stereotyped motor behavior 3d: Preoccupation with parts of objects	1	1 in either domain	1
Minimum Total Required No. of Criteria	6	2	3
Onset of delays before age 3 years	Yes		

TABLE S2 Proportion of Children With a Community Identification and Median Age of Identification Among Children Meeting the Autism and Developmental Disabilities Monitoring (ADDM) Network Autistic Disorder Case Definition (Stratified by Number of Behavioral Diagnostic Criteria Met)

No. of *DSM* Criteria	% With Community Identification	Median Age (y) of Community Identification Among Those With Community Identification by Age 8 (Total n = 1,646)	Overall Median Age (y) of Community Identification (Total n = 2,136)
6	47.7	5.7	Not reached
7	57.4	5.2	8.2
8	61.6	5.2	7.4
9	74.0	4.4	5.4
10	83.0	4.4	5.2
11	89.2	4.0	3.6
12	93.4	3.6	3.8

TABLE S3 Association Between Observation Diagnostic Features and Age of Autistic Disorder Identification for Children Meeting the Autism and Developmental Disabilities Monitoring (ADDM) Network Criteria for Autistic Disorder (n = 2,136)

	Univariate Time Ratio (95% CI)		Adjusted for Other *DSM* Criteria Time Ratio (95% CI)		Adjusted for ADDM Site Gender, Race, Intellectual Disability Time Ratio (95% CI)	
ASD diagnostic criterion						
1a (nonverbal communication)	0.61	(0.55, 0.67)	0.73	(0.66, 0.81)	0.74	(0.68, 0.82)
1b (peer relations)	0.93	(0.87, 1.01)	0.95	(0.98, 1.12)	1.01	(0.95, 1.07)
1c (sharing enjoyment/interests)	0.75	(0.71, 0.79)	0.86	(0.82, 0.90	0.84	(0.80, 0.89)
1d (emotional reciprocity)	0.66	(0.56, 0.77)	0.76	(0.66, 0.87)	0.76	(0.67, 0.87)
2a (spoken language)	0.77	(0.68, 0.87)	0.84	(0.76, 0.95)	0.81	(0.72, 0.90)
2b (hold a conversation)	1.10	(1.00, 1.21)	1.14	(1.05, 1.25)	1.09	(1.00, 1.18)
2c (stereotyped language)	0.97	(0.90, 1.04)	1.02	(0.95, 1.09)	1.00	(0.94, 1.06)
2d (spontaneuous play)	0.69	(0.66, 0.73)	0.81	(0.76, 0.86)	0.81	(0.77, 0.86)
3a (restricted interests)	0.87	(0.82, 0.92)	0.94	(0.88, 0.99)	0.94	(0.89, 0.99)
3b (inflexible routines/rituals)	0.66	(0.60, 0.72)	0.74	(0.68, 0.81)	0.74	(0.68, 0.80)
3c (stereotyped motor)	0.66	(0.62, 0.70)	0.77	(0.72, 0.82)	0.80	(0.76, 0.85)
3d (preoccupation with parts)	0.73	(0.69, 0.78)	0.87	(0.82, 0.92)	0.87	(0.83, 0.92)
Race/ethnicity						
Non-Hispanic white	1.00	Reference	—		1.00	Reference
Non-Hispanic black	1.04	(0.97, 1.11)	—		1.10	(1.04, 1.18)
Hispanic, unknown, and other	1.08	(1.00, 1.15)	—		1.09	(1.03, 1.16)
Known to have IQ <70	0.88	(0.83, 0.93)	—		0.92	(0.87, 0.97)
IQ > 70 and IQ not reported	1.00	Reference	—		1.00	Reference
Male sex	0.95	(0.88, 1.02)	—		0.99	(0.93, 1.05)
ADDM site						
Alabama	1.14	(1.01, 1.29)	—		1.06	(0.95, 1.17)
Arizona	1.20	(1.10, 1.31)	—		1.15	(1.06, 1.25)
Colorado	1.17	(0.97, 1.43)	—		1.21	(1.02, 1.43)
Florida	0.70	(0.61, 0.80)	—		0.68	(0.60, 0.78)
Georgia	1.00	Reference	—		1.00	Reference
Maryland	0.81	(0.72, 0.92)	—		0.69	(0.62, 0.77)
Missouri	0.85	(0.77, 0.94)	—		0.84	(0.76, 0.92)
North Carolina	0.95	(0.85, 1.06)	—		0.98	(0.89, 1.07)
Pennsylvania	0.88	(0.78, 1.00)	—		0.89	(0.79, 0.98)
South Carolina	0.97	(0.86, 1.09)	—		0.99	(0.89, 1.09)
Wisconsin	0.89	(0.80, 0.99)	—		0.89	(0.81, 0.98)

Note: Time ratios < 1.0 denote earlier identification when feature is noted in the records. ASD = autism spectrum disorder.

TABLE S4 Proportion of the Autism and Developmental Disabilities Monitoring (ADDM) Network Autism Spectrum Disorder (ASD) Case Children With Abstracted Evaluations at Each Year of Age, Stratified by IQ Level (IQ > 70, IQ ≤ 70, IQ Unknown)

Age (y) at Evaluation	Total No. Evaluated	IQ > 70 n (% of All With IQ > 70)	IQ ≤ 70 n (% of All With IQ ≤ 70)	IQ Unknown n (% of All With Unknown IQ)
1	299	104 (8.3)	117 (15.0)	78 (10.7)
2	925	331 (26.6)	334 (42.7)	260 (35.5)
3	1092	455 (36.6)	375 (48.0)	262 (35.8)
4	1199	506 (40.7)	415 (53.1)	278 (38.0)
5	1359	594 (47.8)	451 (57.7)	314 (42.9)
6	1162	605 (48.7)	301 (38.5)	256 (35.0)
7	1104	599 (48.2)	289 (37.0)	216 (29.5)
8	567	277 (22.3)	169 (21.6)	121 (16.5)
Total no. of ADDM ASD cases in each IQ category	2,757	1,243	782	732

Note: The percentage shown in each column is the proportion of children who had an evaluation at a given year of age. For example, 104 of 1,243 children (8.3%) with known IQ > 70 had evaluations when they were 1 year (12–23 months) of age.