

Sleep Problems in 2- to 5-Year-Olds With Autism Spectrum Disorder and Other Developmental Delays

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abstract

BACKGROUND: Sleep problems can impact daytime behavior, quality of life, and overall health. We compared sleep habits in young children with autism spectrum disorder (ASD) and other developmental delays and disorders and in children from the general population (POP).

METHODS: We included 2- to 5-year-old children whose parent completed all items on the Children's Sleep Habits Questionnaire (CSHQ) in a multisite case-control study: 522 children with ASD; 228 children with other developmental delays and disorders with autism spectrum disorder characteristics (DD w/ASD); 534 children with other developmental delays and disorders without autism spectrum disorder characteristics (DD w/o ASD); and 703 POP. Multivariable analysis of variance compared CSHQ mean total score (TS) and subscale scores between groups. Logistic regression analysis examined group differences by using TS cutoffs of 41 and 48. Analyses were adjusted for covariates.

RESULTS: Mean CSHQ TS for children in each group: ASD (48.5); DD w/ASD (50.4); DD w/o ASD (44.4); and POP (43.3). Differences between children with ASD and both children with DD w/o ASD and POP were statistically significant. Using a TS cutoff of 48, the proportion of children with sleep problems was significantly higher in children in the ASD group versus DD w/o ASD and POP groups (adjusted odds ratios [95% confidence intervals]: 2.12 [1.57 to 2.87] and 2.37 [1.75 to 3.22], respectively).

CONCLUSIONS: Sleep problems are more than twice as common in young children with ASD and DD w/ASD. Screening for sleep problems is important in young children to facilitate provision of appropriate interventions.



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WHAT'S KNOWN ON THIS SUBJECT: Sleep problems are reported to be common in young children and even more common in children with autism spectrum disorder (ASD) and other developmental delays and disorders.

WHAT THIS STUDY ADDS: This is the largest study in which researchers have used a validated measure of sleep in children with ASD and two control groups. Sleep problems were most common in preschool-aged children with ASD or ASD features.

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Sleep problems are a public health issue in the United States,¹ impacting daytime behavior, physical health, and quality of life for children and their families.² Maladaptive daytime behaviors²⁻⁶ and medical conditions such as obesity, insulin resistance, alterations in sympathetic tone, and immune dysfunction⁷⁻⁹ are associated with poor sleep. Sleep problems are more frequently reported in children with autism spectrum disorder (ASD) and children with other developmental delays and disorders (DD) compared with children with typical development.¹⁰⁻¹⁹ Children with ASD have physiologic and developmental and/or behavioral differences that may predispose them to sleep problems.^{2,20} Sleep problems have been associated with increased repetitive, self-injurious, internalizing, and externalizing behaviors in children with ASD and result in greater stress in parents.^{6,21,22} Most studies in which sleep problems in children with ASD have been addressed have important limitations, including the use of small clinic-based samples that may oversample children with the most severe symptoms, a lack of comparison groups that impedes the ability to evaluate whether sleep problems are specific to ASD or DD in general, use of nonvalidated assessments of sleep problems, and failure to adjust for potential confounders.

Our objective in this study was to compare sleep habits, as measured by a validated instrument, the Children's Sleep Habits Questionnaire (CSHQ), in children with ASD to children with DD and children from the general population (POP), while adjusting for potential confounders in a community-based sample. We hypothesized that children with ASD would have more sleep problems than children with DD and that children with ASD and DD would have

more sleep problems than children in the POP group.

METHODS

In this study, we used data from phase 1 of the Study to Explore Early Development (SEED),²³ a multisite, community-based case-control study of children 30 to 68 months of age. Three groups of children were included in the study: children with a research classification of ASD, children with other DD, and children in the POP group. Detailed descriptions of SEED methods can be found in Schendel et al²³ and Wiggins et al.²⁴ Children with ASD and DD were recruited from early intervention and special education programs and health care providers serving children with disabilities. A "broad net" was cast to ascertain all children with ASD; therefore, the DD group includes children with mild to severe delays and disorders. The POP group was randomly selected from birth certificates among children from the same birth cohort as the ASD and DD groups. The local office of vital statistics sent postcards to families in the defined catchment areas at each site. Children were eligible to participate if they lived with a caregiver who spoke English (or English or Spanish at 2 sites) and if they were born and continued to live in the specific catchment areas at 6 sites in the United States (CA, CO, GA, MD, NC, and PA).²³ All sites obtained institutional review board approval at their site.

After enrollment, caregivers completed a telephone interview and several self-administered forms to ascertain information on child and family health and family sociodemographic characteristics. All children were screened for ASD with the Social Communication Questionnaire (SCQ)²⁵ and completed an in-person developmental assessment with the Mullen Scales of Early Learning (MSEL).²⁶ Children

who screened positive for ASD symptoms (SCQ score ≥ 11), had a previous diagnosis of ASD, or exhibited ASD symptoms during the MSEL assessment underwent an ASD evaluation that included the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R). Children classified as ASD met ADOS criteria for ASD and the following ADI-R criteria: full criteria for autism (86%), social domain and within 2 points of communication domain cutoff, communication domain and within 2 points of social domain cutoff, or social domain and at least 2 points on behavioral domain (Fig 1).²⁴

Those in the DD group did not meet study criteria for ASD but had another DD. Children with DD were classified post hoc into 2 groups: (1) other developmental delays and disorders with autism spectrum disorder characteristics (DD w/ASD) (those who received an evaluation for ASD but did not meet SEED ASD case definition) and (2) other developmental delays and disorders without autism spectrum disorder characteristics (DD w/o ASD).²⁷ Children with ASD and DD w/ASD had a much higher prevalence of elevated Child Behavior Checklist (CBCL) *t* scores for internalizing and externalizing symptoms than children in the DD w/o ASD and POP groups (see Table 1). Children from the POP group remained in the POP group even if their MSEL assessment found delays (3% had MSEL scores ≤ 70), unless they screened positive for and met criteria for ASD (Fig 1).

All children included in this analysis were born between September 1, 2003, and August 31, 2006, completed a developmental evaluation, and had a caregiver-completed interview and CSHQ.²⁸ The CSHQ is a 33-item parent-completed questionnaire with 8 subscales: Bedtime Resistance, Sleep Onset Delay, Sleep Duration, Sleep Anxiety, Night Waking, Parasomnias, Sleep

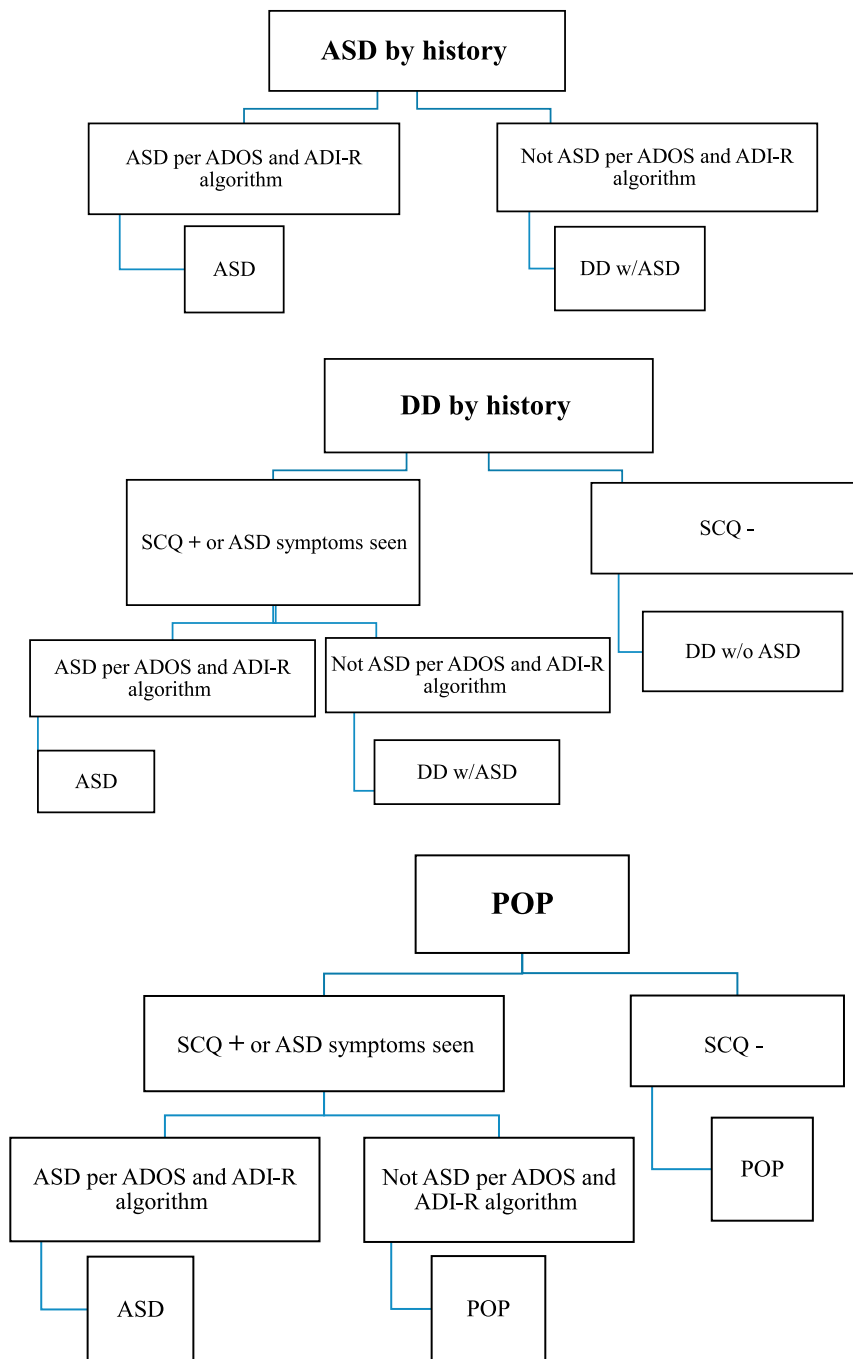


FIGURE 1
SEED research classifications. For the ADOS and ADI-R algorithm, a child was classified as having ASD if the child met ADOS criteria and 1 of 3 ADI-R relaxed criteria: (1) met the social domain cutoff and was within 2 points of the communication domain cutoff, (2) met the communication domain cutoff and was within 2 points of the social domain cutoff, or (3) met the social domain cutoff and had at least 2 points on the behavioral domain. SCQ +, SCQ score ≥ 11 ; SCQ -, SCQ score < 11 .

Disordered Breathing, and Daytime Sleepiness.²⁸ Parents were instructed to answer questions regarding their child's sleep during a typical recent week. Each question had 3 possible

answers: 1 = rarely (0–1 times per week), 2 = sometimes (2–4 times per week), and 3 = usually (5–7 times per week). Higher scores indicate more sleep concerns. A total score (TS) was

obtained by summing the subscale scores. The CSHQ was validated in children 4 to 10 years of age and has adequate internal consistency, acceptable test-retest reliability, and acceptable validity by differentiating children seen in a sleep clinic from a community sample that excluded children with psychiatric conditions such as attention-deficit/hyperactivity disorder (ADHD) and depression.²⁸ Although it has not been validated in children < 4 years of age or in children with ASD, the CSHQ has been used in both groups.^{4,16,29,30} A TS of 41 differentiated a clinical sample of children with sleep problems from a community-based sample.³¹ On the basis of a previous analysis of data from the Autism Treatment Network (T.K., unpublished data), we were concerned that the TS cutoff of 41 would overidentify sleep problems in our young sample. We also used a TS cutoff of 48 that was the cutoff score for the highest quartile in the POP group. This provided a more conservative cutoff score for the CSHQ on the basis of literature in which it has been estimated that $\sim 25\%$ of young children have sleep problems.^{15,17} Additionally, melatonin use in the previous month was collected for 84% of children.

We evaluated the difference in TS both as a continuous and a dichotomous variable, using the cutoff scores 41 and 48. We adjusted for the following variables: maternal education and race or ethnicity, family income, and child sex, age at enrollment, cognitive scores on the MSEL, and genetic and/or neurologic diagnoses (Down syndrome, fragile X syndrome, Rett syndrome, tuberous sclerosis, cerebral palsy, and neurofibromatosis). Data on these covariates were obtained from the caregiver interview and the MSEL. Least squares means were used to determine average TS and subscale scores for each group. To compare TS and subscale scores on the CSHQ as

TABLE 1 Characteristics of Children With a 100% Complete CSHQ (*n* = 1987)

	ASD Cases (<i>n</i> = 522)	DD w/ASD (<i>n</i> = 228)	DD w/o ASD (<i>n</i> = 534)	POP (<i>n</i> = 703)
Child sex, <i>n</i> (%)				
Male	436 (83.5)	175 (76.8)	340 (63.7)	383 (54.5)
Maternal race or ethnicity, <i>n</i> (%)				
Non-Hispanic white	290 (55.6)	111 (48.7)	352 (65.9)	509 (72.4)
African American	100 (19.2)	65 (28.5)	67 (12.5)	74 (10.5)
Other	124 (23.8)	52 (22.8)	107 (20)	111 (15.8)
Maternal education, <i>n</i> (%)				
Some college or less	246 (47.1)	143 (62.7)	187 (35)	218 (31)
Bachelor's	156 (29.9)	55 (24.1)	184 (34.5)	270 (38.4)
Graduate school	114 (21.8)	30 (13.2)	159 (29.8)	210 (29.9)
Family income, <i>n</i> (%)				
First quartile	115 (22)	85 (37.3)	69 (12.9)	85 (12.1)
Second quartile	135 (25.9)	62 (27.2)	138 (25.8)	150 (21.3)
Third quartile	124 (23.8)	35 (15.4)	162 (30.3)	188 (26.7)
Fourth quartile	130 (24.9)	31 (13.6)	143 (26.8)	261 (37.1)
Child genetic and/or neurologic diagnosis ^a , <i>n</i> (%)				
Yes	20 (3.8)	9 (3.9)	35 (6.6)	4 (0.6)
Child cognitive (MSEL) composite standard score, <i>n</i> (%)				
≤70	317 (60.7)	73 (32)	94 (17.6)	21 (3)
Child CBCL, <i>n</i> (%)				
Externalizing <i>t</i> score ≥65	181 (35.2)	62 (27.2)	30 (5.7)	23 (3.4)
Internalizing <i>t</i> score ≥65	241 (46.9)	74 (32.5)	40 (7.6)	36 (5.3)
Child melatonin use, <i>n</i> (%)				
Yes	32 (6.1)	13 (5.7)	2 (0.4)	6 (0.9)
Child age in mo, mean (SD)	55.6 (6.9)	56.4 (7.5)	55.9 (7.4)	55.5 (7.7)
Child cognitive (MSEL) composite standard score, mean (SD)	67.3 (19.9)	79.6 (19.1)	90.8 (20.6)	103.2 (14.6)

^a Down syndrome, fragile X syndrome, Rett syndrome, tuberous sclerosis, cerebral palsy, and neurofibromatosis.

a continuous outcome between groups (ASD, DD w/ASD, DD w/o ASD, and POP), multivariate analysis of variance was used. Multivariable logistic regression adjusting for the same variables noted above was used to examine group differences in sleep problems using both TS cutoffs. In all analyses, the ASD group was compared with each of the 3 control groups. We did not adjust for melatonin use because we found that melatonin use was associated with higher CSHQ TS (a marker of severity of sleep problems).

We primarily report results of the complete case analyses (CSHQ 100% complete, *n* = 1987). Additionally, we performed a sensitivity analysis imputing missing CSHQ data for children whose parents responded to >90% of the CSHQ questions (*n* = 2339). We created 10 imputed data sets using the fully conditional specification technique.³² The

imputation model included all covariates used in the complete case analyses. Findings in which multiple imputation was used are presented in Supplemental Tables 5 through 8.

RESULTS

Of the 2600 eligible children who completed a clinical evaluation and obtained a final classification, 2339 had <10% missing items. However, 15% still had missing data on some items; therefore, our complete case analysis (100% CSHQ complete) included 1987 children (Fig 2). The characteristics of these children are presented in Table 1. Children in the ASD group were more likely to be boys, have lower MSEL scores, and were less likely to come from families with higher income and have mothers that were non-Hispanic white and graduated from a 4-year college, compared with DD and POP groups. Children in the ASD group also had

associated neurologic and/or genetic conditions more often than POP but less than the DD group. Among those with 100% completion of the CSHQ, a total of 1674 children had data on melatonin use. Children with ASD were more likely to use melatonin in the previous month, and those children using melatonin had a higher mean CSHQ TS than children who did not use melatonin (Table 2).

CSHQ total and subscale scores for children with ASD were significantly higher than scores for children in the DD w/o ASD and POP groups. However, total and subscale scores were not significantly different between children with ASD and DD w/ASD (Table 3). Using the more conservative TS cutoff of 48, the odds of sleep problems were significantly higher in children with ASD compared with POP (adjusted odds ratio [aOR] = 2.37, 95% confidence

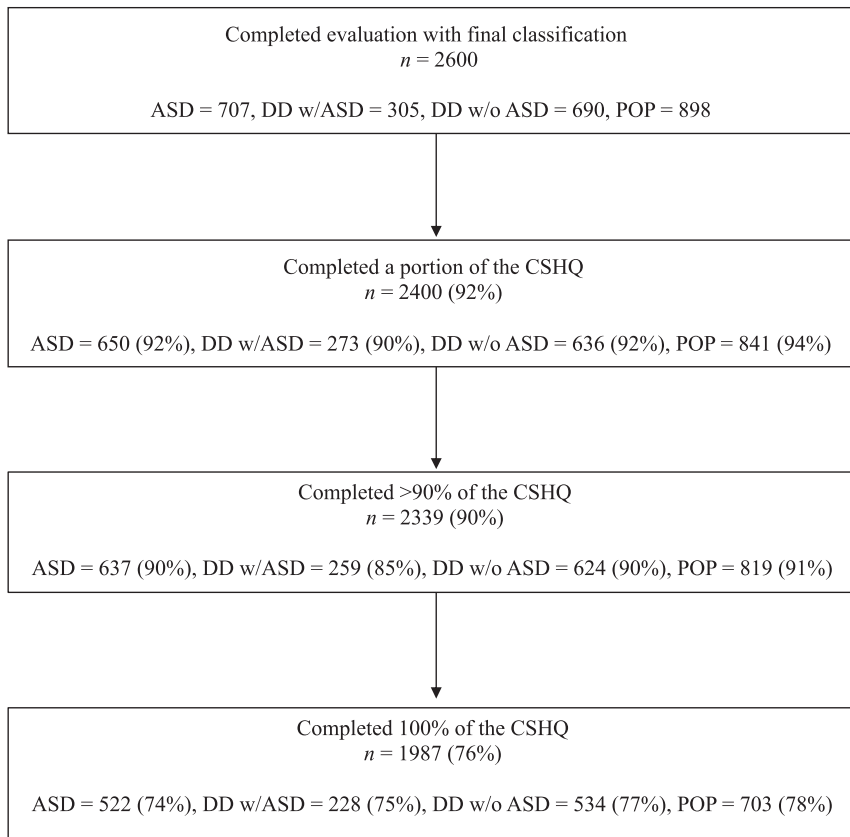


FIGURE 2
SEED subject disposition.

interval [CI] = 1.75 to 3.22) and in children with ASD compared with DD w/o ASD (aOR = 2.12, 95% CI = 1.57 to 2.87). The results were attenuated but similar when the cutoff of 41 was used (aOR of 1.45 and 1.75, respectively). There were no differences between the ASD and DD w/ASD group at either TS cutoff (Table 4).

In general, the above results were similar when missing CSHQ items were replaced by using multiple imputation (See Supplemental Tables 5 through 8).

DISCUSSION

Using the more conservative CSHQ TS cutoff of 48 to define sleep problems, we found that children with ASD and DD w/ASD symptoms have more than twice the odds of sleep problems than POP and children with DD w/o ASD. The reported prevalence of sleep problems in children with ASD and DD has varied between 40% and 83% in previous studies compared with ~9% to 50% in children with typical development.^{10-19,33,34} We found that 47% of parents reported sleep problems in their child with ASD

compared with 57% in children with DD w/ASD, 29% in children with DD w/o ASD, and 25% in POP. When the less conservative cutoff TS of 41 was used, 78% of children with ASD had sleep problems compared with 83% in children with DD w/ASD, 67% in children with DD w/o ASD, and 61% in POP. Using a TS of 48, our findings were consistent with a smaller study of 2- to 5-year-old children in which researchers found sleep problems in 53% of children with ASD, 46% in children with DD, and 32% in children with typical development.¹²

The higher reported occurrence of sleep problems in children with ASD and DD w/ASD, versus children with DD w/o ASD and POP, may be due to multiple contributing factors, including physiologic differences (eg, arousal regulation and melatonin metabolism), sleep disorders (eg, periodic limb movement disorder, obstructive sleep apnea), developmental comorbidities (eg, ADHD), medical comorbidities causing sleep disruption (eg, constipation, obesity, gastroesophageal reflux disease),³⁵⁻³⁸ communication impairments, and behavioral disturbances (eg, difficulty with transitions or obsessions that may interfere with initiating sleep). Children with ASD are more likely to have anxiety, which may predispose them to sleep problems.³⁹⁻⁴¹ The phenotypic overlay between children with ASD and children with DD w/ASD may explain the similarities in sleep disturbance among these 2 groups. Children with ASD and DD w/ASD have higher rates of obsessive compulsive symptoms, self-injurious behavior, ADHD symptoms, and

TABLE 2 Mean CSHQ TS (100% Complete) by Final Classification and by Use of Melatonin

	Melatonin Use			No Melatonin Use		
	n	Mean (SD)	Range	n	Mean (SD)	Range
ASD average TS	32	57.7 (11.2)	(37.0-85.0)	414	47.9 (9.2)	(33.0-76.0)
DD w/ASD average TS	13	55.6 (8.5)	(41.0-69.0)	183	50.2 (9.9)	(33.0-76.0)
DD w/o ASD average TS	2	43.0 (8.5)	(37.0-49.0)	440	44.4 (7.3)	(33.0-70.0)
POP average TS	6	45.8 (6.1)	(39.0-57.0)	584	43.3 (6.6)	(33.0-66.0)

TABLE 3 Average Difference in the Mean CSHQ TS and Subscale Scores by Final Classification for Children Whose Caregiver Completed 100% of the CSHQ

	Mean (SD)				Adjusted Mean Difference (95% CI)		
	ASD (n = 522)	DD w/ASD (n = 228)	DD w/o ASD (n = 534)	POP (n = 703)	ASD Versus DD w/ASD	ASD Versus DD w/o ASD	ASD Versus POP
CSHQ TS	48.5 (9.7)	50.4 (9.8)	44.4 (7.3)	43.3 (6.7)	-1.1 (-2.9 to 0.7)	3.5 (2.0 to 4.9)**	4.4 (2.9 to 5.8)**
Bedtime resistance	9.6 (3.5)	10.1 (3.4)	8.5 (2.9)	8.1 (2.8)	-0.4 (-1.1 to 0.3)	0.7 (0.1 to 1.2)*	0.9 (0.3 to 1.5)**
Sleep onset delay	1.7 (0.8)	1.7 (0.8)	1.4 (0.6)	1.4 (0.6)	0.0 (-0.1 to 0.2)	0.2 (0.1 to 0.4)**	0.3 (0.1 to 0.4)**
Sleep duration	4.2 (1.7)	4.3 (1.6)	3.7 (1.2)	3.6 (1.0)	-0.1 (-0.4 to 0.2)	0.4 (0.1 to 0.6)**	0.5 (0.2 to 0.7)**
Sleep anxiety	6.3 (2.1)	6.5 (2.3)	5.7 (1.9)	5.5 (1.8)	0.0 (-0.5 to 0.4)	0.6 (0.2 to 1.0)**	0.8 (0.4 to 1.1)**
Night waking	4.5 (1.7)	4.7 (1.7)	4.1 (1.4)	3.9 (1.3)	-0.1 (-0.5 to 0.2)	0.3 (0.1 to 0.6)*	0.5 (0.2 to 0.8)**
Parasomnias	9.5 (2.1)	9.5 (2.3)	8.8 (1.7)	8.6 (1.6)	0.2 (-0.3 to 0.6)	0.8 (0.5 to 1.1)**	1.0 (0.6 to 1.3)**
Sleep disordered breathing	3.6 (1.0)	3.6 (1.0)	3.4 (0.9)	3.3 (0.7)	0.0 (-0.2 to 0.2)	0.1 (0.0 to 0.3)*	0.2 (0.1 to 0.4)*
Daytime sleepiness	12.5 (3.4)	13.4 (3.5)	11.8 (2.8)	11.8 (2.8)	-0.6 (-1.3 to 0.1)	0.6 (0.1 to 1.2)*	0.6 (0.1 to 1.2)*

Adjusted for child sex, genetic condition, MSEL score, and age at enrollment and maternal race or ethnicity, education, and income.

* $P < .024$;

** $P < .001$.

developmental and communication impairments than children with DD w/o ASD.²⁷ The role of possible interactions between co-occurring conditions and sleep problems should therefore be considered in future research studies.

Melatonin use was more common in children with ASD and DD w/ASD than in children with DD w/o ASD and children from the POP group. Melatonin has a role in regulating the circadian sleep cycle⁴² and has been reported to be low in individuals with ASD.⁴³⁻⁴⁶ It has been used to treat sleep problems in children with ASD.^{47,48} Consistent with other studies, we found that children taking melatonin had a higher CSHQ TS.⁴⁹ This is not surprising because children with greater sleep problems are more likely to take melatonin. Because a higher proportion of children with ASD and DD w/ASD versus children with DD w/o ASD and POP were taking melatonin, we may have underestimated sleep problems

in children with ASD and DD w/ASD because we do not know what CSHQ scores would have been in the absence of melatonin. Additionally, the CSHQ is not used to measure severity of sleep disturbance; therefore, if a child's sleep onset latency improved from 2 hours to 30 minutes with melatonin, the child would still take more than 20 minutes to fall asleep, and the CSHQ score would not change.

We also noted differences in mean subscale scores between groups. Compared with DD w/o ASD and POP groups, children with ASD had higher mean scores in all the subscales. However, as with TS, no differences were found between the ASD and DD w/ASD groups. With this finding and the overlap in core and co-occurring conditions between the ASD and DD w/ASD groups, it is suggested that some of the aspects of sleep problems may be related to core ASD symptoms and/or co-occurring conditions (eg, ADHD, obsessive-compulsive

disorder). For example, ADHD and insistence on sameness may be related to bedtime resistance and sleep anxiety subscale scores.

The identification of sleep problems in children with ASD symptoms is particularly important because of the impact of poor sleep on the child's daytime behavior and on the quality of life of family members. Over the past 20 years, there has been significant advances in the treatment of sleep issues in children with ASD. Sleep education interventions have been found to be helpful in all groups but may require modifications and creativity in children with ASD and DD.^{50,51} In addition, melatonin has been found to be efficacious in the treatment of sleep onset delay in children with DD and ASD.^{47,48} Because sleep is multidimensional and children with ASD have multiple co-occurring conditions, there may be a need to use multiple interventions simultaneously in children with ASD.

TABLE 4 Odds of a CSHQ TS Above the Specified Threshold for Children With ASD Classification Compared With the Other Group Final Classification (With CSHQ 100% Complete)

	Frequency, %				aOR (95% CI)		
	ASD (n = 522)	DD w/ASD (n = 228)	DD w/o ASD (n = 534)	POP (n = 703)	ASD Versus DD w/ASD	ASD Versus DD w/o ASD	ASD Versus POP
TS >41	78.0	82.9	66.5	60.7	0.86 (0.56 to 1.33)	1.45 (1.05 to 2.00)*	1.75 (1.27 to 2.42)**
TS >48	46.9	57.0	28.5	25.0	0.79 (0.56 to 1.13)	2.12 (1.57 to 2.87)**	2.37 (1.75 to 3.22)**

Adjusted for child sex, genetic and/or neurologic condition, MSEL score, and age at enrollment and maternal race or ethnicity, education, and income.

* $P = .023$;

** $P < .001$.

Strengths

This study has many strengths. We used data from SEED, which is the largest community-based, geographically diverse epidemiologic study of ASD risk factors and child health. We used a validated measure of sleep in a well-characterized sample of preschool-aged children with ASD. Final ASD classification was based on the use of standardized instruments administered in person by research-reliable clinicians. SEED also included 2 comparison groups: children with DDs and POP. The POP group appeared to represent the general population well from a developmental and behavioral standpoint, with a mean MSEL score of 102.3 and <4% to 6% with elevated CBCL internalizing and externalizing problems *t* scores. The large sample size also allowed adjustment for multiple covariates. Our results align with other studies and can be used to confirm that sleep problems are common among preschool-aged children, particularly those with ASD features.

Limitations

This study has limitations. The CSHQ is a parent-completed questionnaire. There was no objective measure of sleep and no clinical assessment of sleep problems. The CSHQ was originally designed to compare groups and not to make a sleep disorder diagnosis. Therefore, determining the exact prevalence of sleep problems on the basis of CSHQ results may be problematic. However, Souders et al¹⁶ found that the CSHQ was consistent with actigraphy in measuring sleep issues in children ages 4 to 10 years with and without ASD. The CSHQ, like other sleep questionnaires, is used to address frequency and not severity of sleep problems⁵²; hence, in this study, we cannot compare the severity of sleep problems between the study groups. In addition, more children with ASD and DD w/ASD were being treated

with melatonin; therefore, their scores may be an underestimate of the true differences. We are also missing data on melatonin use in 16% of the subjects.

Although the CSHQ has been widely used with children,²⁸ it has not been validated in children <4 years or in children with ASD. The CSHQ also includes some items such as bed-wetting, which are not as relevant in younger children or children with developmental delays. It is possible that the CSHQ cutoff score of 41 may overidentify sleep problems in our younger age group; therefore, we used a much higher cutoff score of 48 on the basis of the score defining the top 25th percentile in POP. This higher cutoff score has not been confirmed by others, and it is possible that this may have resulted in an underestimation of sleep problems in POP.

Approximately 10% of parents did not complete >90% of CSHQ questions, and another 15% did not complete all questions. This could introduce a response bias. However, the results were similar between the 100% complete sample and those obtained after multiple imputation. Finally, parents of children recruited from the general population in this study tended to be more frequently white or non-Hispanic and more highly educated than parents of children in this study with ASD or DD. Despite adjusting for race, maternal education, and family income, it is possible that selection bias should still be considered when interpreting the results of these analyses.

CONCLUSIONS

The results of this study are consistent with the hypothesis that sleep problems are common in all children 2 to 5 years of age, with an even higher prevalence in children with ASD and DD w/ASD. After adjusting for other variables, children with ASD and those with DD w/ASD

had significantly higher mean TS on the CSHQ than children in the DD w/o ASD and POP groups. Because of the prevalence of sleep problems in young children with ASD features and the impact of poor sleep on daytime behavior and overall health for the child and family, further study is needed to address the etiology and management of sleep problems in children with ASD.

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ABBREVIATIONS

ADHD:	attention-deficit/hyperactivity disorder
ADI-R:	Autism Diagnostic Interview-Revised
ADOS:	Autism Diagnostic Observation Schedule
aOR:	adjusted odds ratio
ASD:	autism spectrum disorder
CBCL:	Child Behavior Checklist
CI:	confidence interval
CSHQ:	Children's Sleep Habits Questionnaire
DD:	other developmental delays and disorders
DD w/ASD:	other developmental delays and disorders with autism spectrum disorder characteristics
DD w/o ASD:	other developmental delays and disorders without autism spectrum disorder characteristics
MSEL:	Mullen Scales of Early Learning
POP:	children from the general population
SCQ:	Social Communication Questionnaire
SEED:	Study to Explore Early Development
TS:	total score

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REFERENCES

1. Perry GS, Patil SP, Presley-Cantrell LR. Raising awareness of sleep as a healthy behavior. *Prev Chronic Dis*. 2013;10:E133
2. Reynolds AM, Malow BA. Sleep and autism spectrum disorders. *Pediatr Clin North Am*. 2011;58(3):685–698
3. Didden R, Sigafoos J. A review of the nature and treatment of sleep disorders in individuals with developmental disabilities. *Res Dev Disabil*. 2001;22(4):255–272
4. Honomichl RD, Goodlin-Jones BL, Burnham M, Gaylor E, Anders TF. Sleep patterns of children with pervasive developmental disorders. *J Autism Dev Disord*. 2002;32(6):553–561
5. Mazurek MO, Sohl K. Sleep and behavioral problems in children with autism spectrum disorder. *J Autism Dev Disord*. 2016;46(6):1906–1915
6. Quine L. Sleep problems in children with mental handicap. *J Ment Defic Res*. 1991;35(pt 4):269–290
7. Careaga M, Rogers S, Hansen RL, Amaral DG, Van de Water J, Ashwood P. Immune endophenotypes in children with autism spectrum disorder. *Biol Psychiatry*. 2017;81(5):434–441
8. Hill AP, Zuckerman KE, Fombonne E. Obesity and autism. *Pediatrics*. 2015; 136(6):1051–1061
9. Quist JS, Sjödin A, Chaput JP, Hjorth MF. Sleep and cardiometabolic risk in children and adolescents. *Sleep Med Rev*. 2016;29:76–100
10. Couturier JL, Speechley KN, Steele M, Norman R, Stringer B, Nicolson R. Parental perception of sleep problems in children of normal intelligence with pervasive developmental disorders: prevalence, severity, and pattern. *J Am Acad Child Adolesc Psychiatry*. 2005; 44(8):815–822
11. Gerber L. Sleep deprivation in children: a growing public health concern. *Nurs Manage*. 2014;45(8):22–28; quiz 29
12. Krakowiak P, Goodlin-Jones B, Hertz-Picciotto I, Croen LA, Hansen RL. Sleep problems in children with autism spectrum disorders, developmental delays, and typical development: a population-based study. *J Sleep Res*. 2008;17(2):197–206
13. Richdale AL, Schreck KA. Sleep problems in autism spectrum disorders: prevalence, nature, & possible biopsychosocial aetiologies. *Sleep Med Rev*. 2009;13(6):403–411
14. Sadeh A, Mindell JA, Luedtke K, Wiegand B. Sleep and sleep ecology in the first 3 years: a web-based study. *J Sleep Res*. 2009;18(1):60–73
15. Singareddy R, Moole S, Calhoun S, et al. Medical complaints are more common in young school-aged children with parent reported insomnia symptoms. *J Clin Sleep Med*. 2009;5(6):549–553
16. Souders MC, Mason TB, Valladares O, et al. Sleep behaviors and sleep quality in children with autism spectrum disorders. *Sleep*. 2009;32(12):1566–1578
17. Teng A, Bartle A, Sadeh A, Mindell J. Infant and toddler sleep in Australia and New Zealand. *J Paediatr Child Health*. 2012;48(3):268–273
18. Devnani PA, Hegde AU. Autism and sleep disorders. *J Pediatr Neurosci*. 2015; 10(4):304–307
19. Richdale AL. Sleep problems in autism: prevalence, cause, and intervention. *Dev Med Child Neurol*. 1999;41(1):60–66
20. Mazurek MO, Petroski GF. Sleep problems in children with autism spectrum disorder: examining the contributions of sensory over-responsivity and anxiety. *Sleep Med*. 2015;16(2):270–279
21. Goldman SE, Surdyka K, Cuevas R, Adkins K, Wang L, Malow BA. Defining the sleep phenotype in children with autism. *Dev Neuropsychol*. 2009;34(5): 560–573
22. Soke GN, Rosenberg SA, Hamman RF, et al. Factors associated with self-injurious behaviors in children with autism spectrum disorder: findings from two large national samples. *J Autism Dev Disord*. 2017;47(2): 285–296
23. Schendel DE, Diguiseppi C, Croen LA, et al. The Study to Explore Early Development (SEED): a multisite epidemiologic study of autism by the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) network. *J Autism Dev Disord*. 2012;42(10):2121–2140

24. Wiggins LD, Reynolds A, Rice CE, et al. Using standardized diagnostic instruments to classify children with autism in the Study to Explore Early Development. *J Autism Dev Disord.* 2015;45(5):1271–1280
25. Rutter M, Bailey A, Lord C. *SCQ: Social Communication Questionnaire.* Los Angeles, CA: Western Psychological Services; 2003
26. Mullen E. *Mullen Scales of Early Learning.* San Antonio, TX: Pearson; 1995
27. Wiggins LD, Levy SE, Daniels J, et al. Autism spectrum disorder symptoms among children enrolled in the Study to Explore Early Development (SEED). *J Autism Dev Disord.* 2015;45(10):3183–3194
28. Owens JA, Spirito A, McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children. *Sleep.* 2000;23(8):1043–1051
29. Goodlin-Jones BL, Sitnick SL, Tang K, Liu J, Anders TF. The Children's Sleep Habits Questionnaire in toddlers and preschool children. *J Dev Behav Pediatr.* 2008;29(2):82–88
30. Hodge D, Parnell AMN, Hoffman CD, Sweeney DP. Methods for assessing sleep in children with autism spectrum disorders: a review. *Res Autism Spectr Disord.* 2012;6(4):1337–1344
31. Owens JA, Maxim R, Nobile C, McGuinn M, Msall M. Parental and self-report of sleep in children with attention-deficit/hyperactivity disorder. *Arch Pediatr Adolesc Med.* 2000;154(6):549–555
32. Lee KJ, Carlin JB. Multiple imputation for missing data: fully conditional specification versus multivariate normal imputation. *Am J Epidemiol.* 2010;171(5):624–632
33. Schreck KA, Mulick JA. Parental report of sleep problems in children with autism. *J Autism Dev Disord.* 2000;30(2):127–135
34. Wiggs L, Stores G. Sleep patterns and sleep disorders in children with autistic spectrum disorders: insights using parent report and actigraphy. *Dev Med Child Neurol.* 2004;46(6):372–380
35. Fujiwara Y, Arakawa T, Fass R. Gastroesophageal reflux disease and sleep. *Gastroenterol Clin North Am.* 2013;42(1):57–70
36. Jones RA, Downing K, Rinehart NJ, et al. Physical activity, sedentary behavior and their correlates in children with autism spectrum disorder: a systematic review. *PLoS One.* 2017;12(2):e0172482
37. American Academy of Sleep Medicine. *International Classification of Sleep Disorders.* 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014
38. Zheng Z, Zhang L, Li S, et al. Association among obesity, overweight and autism spectrum disorder: a systematic review and meta-analysis. *Sci Rep.* 2017;7(1):11697
39. Pollock JI. Night-waking at five years of age: predictors and prognosis. *J Child Psychol Psychiatry.* 1994;35(4):699–708
40. Weissbluth M. Sleep duration, temperament, and Conners' ratings of three-year-old children. *J Dev Behav Pediatr.* 1984;5(3):120–123
41. Clarkson S, Williams S, Silva PA. Sleep in middle childhood—a longitudinal study of sleep problems in a large sample of Dunedin children aged 5-9 years. *Aust Paediatr J.* 1986;22(1):31–35
42. Veatch OJ, Goldman SE, Adkins KW, Malow BA. Melatonin in children with autism spectrum disorders: how does the evidence fit together? *J Nat Sci.* 2015;1(7):e125
43. Kulman G, Lissoni P, Rovelli F, Roselli MG, Brivio F, Sequeri P. Evidence of pineal endocrine hypofunction in autistic children. *Neuroendocrinol Lett.* 2000;21(1):31–34
44. Melke J, Goubran Botros H, Chaste P, et al. Abnormal melatonin synthesis in autism spectrum disorders. *Mol Psychiatry.* 2008;13(1):90–98
45. Nir I, Meir D, Zilber N, Knobler H, Hadjez J, Lerner Y. Brief report: circadian melatonin, thyroid-stimulating hormone, prolactin, and cortisol levels in serum of young adults with autism. *J Autism Dev Disord.* 1995;25(6):641–654
46. Tordjman S, Anderson GM, Pichard N, Charbuy H, Touitou Y. Nocturnal excretion of 6-sulphatoxymelatonin in children and adolescents with autistic disorder. *Biol Psychiatry.* 2005;57(2):134–138
47. Braam W, Smits MG, Didden R, Korzilius H, Van Geijlswijk IM, Curfs LM. Exogenous melatonin for sleep problems in individuals with intellectual disability: a meta-analysis. *Dev Med Child Neurol.* 2009;51(5):340–349
48. Malow B, Adkins KW, McGrew SG, et al. Melatonin for sleep in children with autism: a controlled trial examining dose, tolerability, and outcomes. *J Autism Dev Disord.* 2012;42(8):1729–1737; author reply 1738
49. Malow BA, Katz T, Reynolds AM, et al. Sleep difficulties and medications in children with autism spectrum disorders: a registry study. *Pediatrics.* 2016;137(suppl 2):S98–S104
50. Jan JE, Owens JA, Weiss MD, et al. Sleep hygiene for children with neurodevelopmental disabilities. *Pediatrics.* 2008;122(6):1343–1350
51. Malow BA, Adkins KW, Reynolds A, et al. Parent-based sleep education for children with autism spectrum disorders. *J Autism Dev Disord.* 2014;44(1):216–228
52. Spruyt K, Gozal D. Pediatric sleep questionnaires as diagnostic or epidemiological tools: a review of currently available instruments. *Sleep Med Rev.* 2011;15(1):19–32

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