Sleep disturbance in school-aged children with atopic dermatitis: prevalence and severity in a cross-sectional sample

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Abstract

Rationale: Atopic dermatitis(AD) causes sleep disturbance, yet the epidemiology is not known.

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Objective: Estimate the US prevalence of sleep disturbance and its impact on psychological and neurocognitive function.

Methods: Cross-sectional survey of 180 parent-child dyads with AD, using stratified sampling based on disease severity(POEM, Patient Oriented Eczema Measure,mild(n=30)/moderate(n=75)/ severe (n=75)), age, and race (White/Black or African American/Other). Symptoms of sleep and psychologic health were assessed using PROMIS(Patient Reported Outcome Measurement Information System). To estimate prevalence of sleep disturbance, we calculated weights using post-stratification adjustment making marginal frequencies of AD severity, race, and age similar to marginal frequencies in the 2007 National Survey of Children's Health(NSCH). Unweighted regression models examined associations with sleep disturbance.

Results: In children 5–17 years with AD, we estimated sleep disturbance occurs in 66.9% [95% CI: 53.3–80.5%; 3,116,305 children]. The odds of severe sleep disturbance(worse than 95% of US children) were highest in moderate/severe vs mild AD (2.03[1.00–4.10], P=0.0495/8.68[1.82–41.49], P=0.0068). Predictors of parent-proxy reported sleep disturbance were itch intensity(adjusted β [95% CI]:1.33[0.62,2.04]) and low income(<$50k:6.64[2.05,11.23], $50to<100k:4.75[0.35,9.14]). Controlling for disease severity, itch intensity, and significant socio-demographics- parent-proxy reported sleep disturbance was associated with increased severity of sleep-related impairment, depression, fatigue, and anxiety, in addition to worse inattention and impulsivity. In fully adjusted models, children who self-reported sleep disturbance(T-score 60) had increased odds of sleep-related impairment(1.20[1.11–1.29]), depression(1.13[1.03, 1.24]), fatigue(1.28[1.06–1.54]), and anxiety(1.16[1.02–1.31]).

Conclusions: Sleep disturbance is a common symptom of AD affecting ~3 million US children and associated with neuropsychiatric impairment, including depression, anxiety, and inattention. Clinicians should screen for these symptoms in school-aged children, particularly with moderate-to-severe AD.

Introduction

Atopic dermatitis (AD), a disorder characterized by itchy skin, affects 10–20% of US children.(1) Sleep disturbance is consistently reported in 60% of children with AD and its occurrence is even higher during times of disease flare.(2, 3) Although poor sleep is one of the most distressing aspects to patients and their families,(4, 5) the number of US children with AD suffering from sleep disturbance has not been quantified.

Assessment of sleep can be performed by objective measures, such as activity monitors (actigraphy) or clinical sleep studies (polysomnography), or by patient or parent-proxy report. Patient or parent-proxy sleep assessment is considered a meaningful outcome to capture the lived experiences of sleep.(6) Our group has demonstrated the reliability and validity of the PROMIS (Patient Reported Outcome Measurement Information System) Sleep measures in school-aged children (5–17y) with AD.(7) These measures are freely

available and are the most psychometrically robust measure of patient- and parent-proxy report of sleep, allowing accurate quantification of the burden of sleep disturbance in children with AD. They can be used for epidemiologic assessment and clinically to compare to the general US population of children.

In addition to the need to quantify the national burden of sleep disturbance in AD, there is a gap in knowledge about patients at highest risk. Several studies have found disease severity as a key risk factor of sleep disturbance.(7–9) From the general sleep literature, the risk of poor sleep is higher in Black vs. White children,(10) but the risk by race in AD has not been assessed. AD and sleep disturbance are also associated with inattention and psychological symptoms (i.e. depression and anxiety).(11) In data analyzed from over 350,000 children, AD was associated with increased odds of ADD/ADHD (1.14 [95% CI, 1.03–1.26]). Moreover, in children with severe AD and fewer than 4 nights of adequate sleep per week, the odds of ADD/ADHD were up to 34.90 [15.01–82.24].(12) In a national study of adults with AD, patients with the highest level of sleep disturbance had the highest odds of anxiety and depression.(13) In children, the relationship between AD, sleep disturbance, inattention, and psychological symptoms (such as depression and anxiety) has been poorly addressed. Our overall objective was to estimate the prevalence of sleep disturbance and its impact on psychological and neurocognitive function in a sample of US children with AD. We hypothesized that children with more severe disease would experience more sleep disturbance and poorer psychological/neurocognitive function.

Methods

Selection of study cohort

We conducted a cross-sectional survey study of 180 children (5–17 years) with AD between May-July 2019 across the United States, out of 1545 screened (see Figure E1). Stratified sampling by disease severity occurred by Patient Oriented Eczema Measure (POEM)(14) (mild (0–7), n=30; moderate (8–16), n=75; and severe (17–28), n=75), and within disease severity strata: age (5–8; 9–12;13–17 years), region of the US (Midwest, NE, SE, NW, SW) and race (White/Black or African-American/other or multiracial). Other inclusion criteria were: ages 5–17 years, parent report of AD diagnosis by a healthcare provider and scratching   1 night in the past week. Exclusion criteria were defined by parent-report to questions about their child: sleep disturbance   2 nights per week due to asthma or hay fever, medication-induced itching, liver or kidney disease leading to chronic itch, active sleep apnea, restless leg syndrome, insomnia, narcolepsy, sleep disordered breathing, or urticaria. Screening questions were administered to the parent proxy, who must have slept in the same home as the child for   6 of the last 7 nights.

Survey participants were recruited by the National Eczema Association and Op4G. Informed consent was obtained electronically. The Institutional Review Boards at Lurie Children's Hospital and Northwestern University approved the study protocol and design.

Statistical Analysis of the unweighted sample.

Summary statistics were tabulated to describe the study cohort (Table E1). Frequency and prevalence by POEM disease severity were generated for socio-demographic characteristics, clinical description, sleep habits, and questionnaire responses. Rao-Scott Chi-Square tests and t-tests were used to examine associations for categorical and continuous variables, respectively.

Applying weighted frequencies from National Survey of Children's Health (NSCH) to our study sample to estimate US prevalence of sleep disturbance and sleep-related impairment.

Weighted frequencies to more accurately estimate the US prevalence of sleep disturbance and sleep related impairment in children with AD were constructed using post-stratification factor adjustment for AD severity, race, and age based on the 2007 National Survey of Children's Health (NSCH) (the most recent study which queried about atopic dermatitis). Population estimates of AD from NSCH were generated similar to a previous study.(15) Briefly, from the NSCH, we identified a cohort of children 5–17 years who had been diagnosed by a healthcare provider with eczema or skin allergy in the past 12 months and had seen a healthcare professional for medical care at least once in the past 12 months. Weights were constructed to make the marginal frequencies of AD severity, race, and age similar to those in the 2007 NSCH. Thus, estimates based on the weighted data better represent the estimated 4.7 million children (ages 5–17 years) with AD in the United States than estimates based on the raw stratified sample.

Regression modeling on the unweighted sample to evaluate the association between disease severity, sleep disturbance, itch, psychologic symptoms and neurocognitive function

A-priori we planned to conduct unweighted logistic regression models to evaluate whether there were statistically significant differences in sleep disturbance or sleep-related impairment across disease severity groups. Crude (i.e., unadjusted) and adjusted odds ratios (OR) with 95% confidence interval (CI) are reported. Survey-weighted procedures in SAS version 9.4 (SAS Institute, Cary, NC) with Taylor series linearization were used to generate national estimates of sleep disturbance and impairment in AD.

Variables included in the regression models

AD disease severity was evaluated using parent-proxy report of the Patient Oriented Eczema Measure (POEM). The full 7-question score was used for patient disease severity characterization as described above. To isolate the effect of sleep and itch in regression models, we calculated a composite-adjusted POEM measure that removed the sleep and itch items. Itch severity was assessed using a Numerical Rating Scale (NRS) of 0–10 (10 is worst) response to the question "In the past 7 days, how bad was your child's itch on average?".

Questions were administered to parent proxy for all participants and self-reported for participants aged   8 years old. Demographic questions were completed by the parent to minimize burden on the child. The primary outcome in our study was Patient-Reported

Outcomes Measurement Information System (PROMIS) Sleep Disturbance measure.(16) The PROMIS Sleep Disturbance measure focuses on perceptions of sleep quality, sleep depth, and restoration associated with sleep, as well as difficulties and concerns with getting to sleep or staying asleep. A secondary outcome, the PROMIS Sleep-related Impairment measure, focuses on perceptions of alertness, sleepiness, and tiredness during usual waking hours, and the perceived functional impairments during wakefulness associated with sleep problems or impaired alertness. All PROMIS measures were scored using EAP-scoring, which makes use of each individual's pattern of item responses, and the IRT scores were converted to T-scores using a linear transformation ($T=10*X+50$). The presence and severity of sleep disturbance and sleep related impairment was determined based on previously established strata: for parent proxy (60–65, severe 66) and for patient-report (60–64, severe 65).(17)

The PROMIS Pediatric/Parent Proxy Profile 25 was used to assess depression, anxiety, fatigue, and peer relationships. Neurocognitive function was assessed using the MacArthur Health Behavioral Questionnaire (MacArthur HBQ) Inattention and Impulsivity subscales, with response options of 0=never/not true, 1= sometimes or somewhat true or 2=often or very true. A subscale score is computed by averaging the 6-inattention items and 9-impulsivity items.(18, 19)

Median and interquartile range (IQR) of PROMIS scores for sleep disturbance were estimated. Multivariable linear regression models were constructed to examine socio-demographic (sex, age, race, parental income, parental education attainment) and clinical (adjusted POEM, NRS of itch) associations of sleep disturbance. Model 1 examined the association of sleep disturbance as measured by PROMIS (dependent variable) and the adjusted POEM measure without sleep and itch items (independent variable). Model 2 added Numeric Rating Scale (NRS) of itch. Model 3 examined adjusted POEM, NRS of itch, and all socio-demographic characteristics that were significant in bivariable models. We separately constructed models for parent- and child-reported sleep disturbance. Crude and adjusted regression coefficients (unstandardized β) with 95% CI were estimated.

Regression models were also constructed to determine association of sleep disturbance with psychologic symptoms and impaired neurocognitive functioning. We examined individual domains of PROMIS (sleep-related impairment, depression, fatigue, peer relationships, and anxiety), as well as MacArthur HBQ measures of inattention and impulsivity. Models were constructed with similar stepwise variable addition of adjusted POEM, NRS of itch, and socio-demographic characteristics significant in bivariable models for each outcome.

All data processing and analyses were conducted in SPSS v26 and SAS v9.4. A two-sided P<0.05 was selected *a priori* to denote statistical significance. This study was conducted in accordance with all Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

Results

Patient characteristics

A total of 180 children and adolescents with AD and parent dyads were surveyed. POEM disease severity was associated with higher parent educational attainment, parent- and child-reported sleep disturbance and sleep-related impairment, PROMIS profile measures (depression, anxiety, physical function, and pain interference), inattention, impulsivity, itch, and CDLQI QOL burden, and inversely associated with body mass index (Table 1). In particular, increased AD severity was associated with medium effect sized, increased problems across sleep disturbance domains: difficulty falling asleep, problem with sleep, trouble sleeping, time to fall asleep, worry about being able to fall asleep, waking and trouble falling back asleep, tossing and turning, and snoring (Cramer's V 0.25, P .0001 for all)(20) (Table E2).

Prevalence of sleep disturbance and sleep-related impairment in the US population of children using weighted estimates

Across disease severity groups, a weighted 66.9% [95% CI: 53.3–80.5%] and 61.2% [46.8–75.5%] of children and adolescents with AD had parent-proxy reported sleep disturbance and sleep-related impairment (PROMIS T-score 60), respectively. Thus, an estimated 3,116,305 children ages 5–17 years with AD had sleep disturbance, and 2,849,265 had sleep-related impairment (Table 2). In bivariable logistic regression models, increasing AD disease severity was associated with increased prevalence of sleep disturbance, PROMIS T-score 60–65 (crude OR [95% CI], moderate AD: 2.71 [1.20–6.13] P=0.02 and severe AD: 7.30 [0.99–53.88], P=0.05) and severe sleep disturbance, PROMIS T-score 66 (moderate AD: 2.03 [1.00–4.10], P=0.05 and severe AD: 8.68 [1.82–41.49], P=0.007) (Figure 1). Black/African-American and White children with AD had similar levels of sleep disturbance in models adjusted for disease severity (adjusted OR [95% CI]: 1.51 [0.65–3.50], P=0.33).

AD severity was similarly associated with stepwise increases in both any sleep-related impairment, PROMIS T-score 60–65 (moderate AD: 2.86 [132–6.23], P=0.008, severe AD: 7.62 [1.23–47.12], P=0.03), and severe sleep-related impairment, PROMIS T-score 66 (moderate AD: 3.92 [1.88–8.19], P=0.0003, severe AD: 13.93 [3.16–61.34], P=0.0005). Black vs. White race was associated with increased sleep-related impairment after controlling for disease severity (2.68 [1.14–6.31], P=0.02).

Predictors of sleep disturbance in the unweighted sample

In multivariable models using stepwise variable addition, parent-proxy reported sleep disturbance T-score was associated with increased itch intensity (adjusted β [95% CI]: 1.33 [0.62, 2.04]), income (<$50k: 6.64 [2.05, 11.23], $50 to <100k: 4.75 [0.35, 9.14]), and parent with a Master's degree (4.67 [1.80, 7.54]) (Table 3A). Sleep disturbance T-score reported by children was associated with adjusted POEM (0.46 [0.08, 0.83]) and increased itch intensity (1.37 [0.58, 2.16]) (Table 3B).

Psychologic symptoms and Neurocognitive impairment in children with sleep disturbance in the unweighted sample

Children with sleep disturbance had significant decrements in psychologic and neurocognitive functioning across multiple domains. In fully-adjusted models controlling for adjusted POEM disease severity, itch intensity, and all significant socio-demographics from our stepwise models, parent-proxy reported sleep disturbance was associated with increased severity of sleep-related impairment, depression, fatigue, and anxiety, in addition to worse inattention and impulsivity (Table 4). Moreover, in similarly adjusted models, children with parent-proxy reported sleep disturbance (T-score 60) had increased odds of sleep-related impairment (1.46 [1.24–1.72]), depression (1.19 [1.08, 1.31]), fatigue (1.28 [1.14–1.45]), and anxiety (1.29 [1.13–1.46]). Child self-reported sleep disturbance was similarly associated with sleep-related impairment, depression, fatigue, and anxiety, and those with a T-score 60 had increased odds of sleep-related impairment (1.20 [1.11–1.29]), depression (1.13 [1.03, 1.24]), fatigue (1.28 [1.06–1.54]), and anxiety (1.16 [1.02–1.31]).

Discussion

This study found significant parent-proxy reported sleep disturbance occurs in a weighted 66.9% [95% CI: 53.3–80.5%] of US children with AD, ~3 million school aged children. More than half of these children had *severe* sleep disturbance, meaning their sleep is worse than 95% of children in the general population.(17) We quantified the sleep disturbance burden by disease severity groups to identify the high percentage affected, severe (91.3%) vs. moderate (79.5%) vs. mild (58.8%) patients. We previously identified that children with moderate/severe disease have ~50 minutes less sleep per night than age/sex/racially matched controls.(9) As such, it might not be surprising that most children with AD have significant sleep disturbance. Yet, it is profound and devastating to think about the impact this might have on psychologic and neurocognitive function.

Although this does not imply causality, we noted that depression, as well as anxiety, assessed by parent-proxy report on PROMIS measures, were significantly associated with poor sleep (β=0.67 [0.46, 0.88], p<0.01 and 0.79 [0.57, 1.01], p<0.01, respectively), even when controlling for disease severity, itch and sociodemographic variables. Parent and child responses were fairly concordant in the present study. This suggests that poor sleep is associated with mental health comorbidities in AD, an association also found in adult AD cohorts.(13, 21) Although peer relationships can worsen with AD,(22) we did not find it associated with sleep disturbance. Inattention and impulsivity were also significantly associated in fully adjusted models with sleep disturbance, the small unstandardized β reflecting the narrow range of numbers used for these scores (β=0.03 [0.02, 0.04], p<0.01 and 0.02 [0.01, 0.04], p<0.01, respectively). The most commonly noted symptoms of inattention in our cohort were: losing things, jumping from one activity to another, not seeming to listen, and difficulty following directions or instructions (Table E3).

Although we did not study sleep longitudinally, one previous cohort study from the United Kingdom among almost 5000 children with AD affirms that sleep disturbance in AD is experienced throughout childhood in children with active AD(23) as well as in their parents.(24) This suggests that psychologic and neurocognitive effects are ongoing.(22,

25) Although causation cannot be proven, longitudinal studies investigating the impact of childhood sleep disturbance in general populations have suggested an increased risk of anxiety, inattention and impulsivity.(26, 27) In fact, more long-term childhood sleep deficits are associated with more deficits in both cortical gray matter and white matter, including in the prefrontal cortex.(28) Specific brain activation pathways are shared in studies associating sleep disturbance and ADHD,(29) and in AD brain imaging studies, the prefrontal cortex is also an area of interest.(30) Systemic inflammation, such as elevated IL-6 levels in sleep disturbance, might also be part of the association between AD, neurocognitive and psychologic impairment.(31) Further work in this area is needed.

Stepwise linear regression modeling in this study also provides putative evidence of associations driving sleep disturbance in this age group. Itch was associated with sleep disturbance in fully adjusted models, in both parent-proxy and child report. Interestingly, in the model using parent-proxy reported sleep disturbance, lower income and having a Master's degree each were associated with a greater likelihood of experiencing sleep disturbance. In child self-report, there was no significant contribution of sociodemographic variables. In this study, race was not significantly associated with an increased risk of sleep disturbance in fully adjusted models. This also points out that parent versus child-report, while fairly concordant, still captures different perspectives about the child's sleep. Children can self-report starting at ~5 years old using PROMIS assessments, but might under-report symptoms.(7) If possible, clinicians should capture data from both parent/children, and rely more heavily on self-report in older children, while pursuing flagged values from either source. Clinical algorithms are acceptable which include either parent or child report.(7) Figure 2 is our purported algorithm for clinical use to screen and monitor sleep disturbance in school aged children with AD.

Limitations

This study has some limitations. First, disease severity and assessments were all based on parent-proxy or patient report; objective data was not available. Indeed, we have previously demonstrated that objective sleep disturbance (actigraphy) and PROMIS sleep assessment are distinct domains.(7) Our study is limited to cross-sectional data, so the longitudinal impact of AD on sleep was indeterminable. Additionally, our population-based estimates have inherent limitations as they were not sampled directly, and limited based on extrapolation of older data from 2007 NSCH. This data source did not include PROMIS questions about sleep and was chosen only for an estimate of population-based AD prevalence in the US. It was not used to generate a comparator group. Our cohort excluded patients with poorly controlled asthma, poorly controlled allergic rhinitis and other sleep disturbing conditions, which might be underestimating the prevalence and severity of sleep disturbance in AD. Given that the study questionnaire focused on AD and quality of life, respondents were not be blinded to the intent of the study. Although we utilized a stratified sampling approach to ensure adequate distribution of samples across all strata and allow for estimation of the sleep disturbance within each strata, it is a limitation that our estimates are based off a relatively small sample. Finally, minority populations frequently have worse AD severity, we used a targeted stratification plan wherein race was evenly represented across

disease severity group. Although this is a strength of the study, it does unfortunately limit the ability to assess race-severity associations in these data.

Conclusions

As suggested in practice guidelines(32, 33) and from our findings, all children with AD should be screened for sleep disturbance, particularly those with worse itch and moderate/severe disease severity. One large cross-sectional study in adults gives hope that controlled disease can improve sleep, depression and anxiety.(34) Although some degree of impairment is still present compared to control patients, significant improvement is possible. In addition to sleep disturbance, psychologic and neurocognitive effects of AD are important to screen for in the clinic setting. Those with moderate or severe disease are at greatest risk of sleep disturbance, and have the largest treatment burden. Parents, patients and providers should align on a personalized medication and treatment regimen to avoid these severe consequences of AD.

The large prevalence of AD and the high frequency of sleep disturbance make this topic an important, yet long understudied problem.(2, 35) A publication from the sleep medicine literature further underscores the recognition from other fields that AD has the potential to induce devastating neurocognitive effects from prolonged sleep disturbance.(3) Our ongoing work focuses on uncovering the mechanism of sleep disturbance in AD to develop more targeted treatment approaches. In the meantime, we refer clinicians to our previously published algorithm to screen, assess and treat sleep disturbance in children with AD.(7)

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations used:

AD	atopic dermatitis
PROMIS	Patient Reported Outcome Measurement Information System
POEM	Patient Oriented Eczema Measure
NSCH	National Survey of Children's Health
OR	odds ratios
CI	confidence interval
NRS	Numerical Rating Scale

MacArthur HBQ	MacArthur Health Behavioral Questionnaire
IQR	interquartile range
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
SDi	Sleep Disturbance
ADHD	Attention Deficit Hyperactive Disorder
BMI	Body Mass Index
PIQ-C	PROMIS Pediatric Itch Questionnaire-Child

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What is already known about this topic?

Sleep disturbance is common in atopic dermatitis(AD). Patient Reported Outcome Measurement Information System(PROMIS) sleep disturbance is a meaningful outcome to capture the lived experiences of sleep, which our group has validated in pediatric AD.

What does this article add to our knowledge?

~3 million US children experience AD-induced sleep disturbance. This equates to 67% of all children with AD, and 91% with severe disease. Sleep disturbance in AD is associated with neuropsychiatric impairment- depression, anxiety, and inattention.

How does this study impact current management guidelines?

Clinicians should screen for sleep disturbance and neuropsychiatric symptoms in school-aged children, particularly with moderate-to-severe AD.
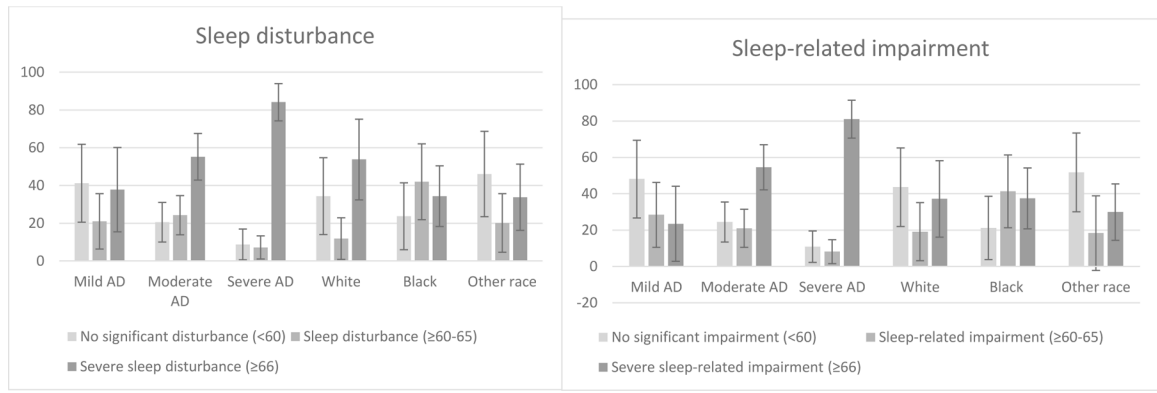
Figure 1:
Weighted proportion of children with sleep disturbance and sleep-related impairment, by atopic dermatitis severity and race. Error bars reflect 95% confidence interval.

Figure 2.

Clinical screening algorithm for sleep disturbance in school aged children with AD.

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SDi= Sleep Distrubance, PROMIS= Patient Reported Outcome Measurement Information System

Table 1.

Patient Characteristics

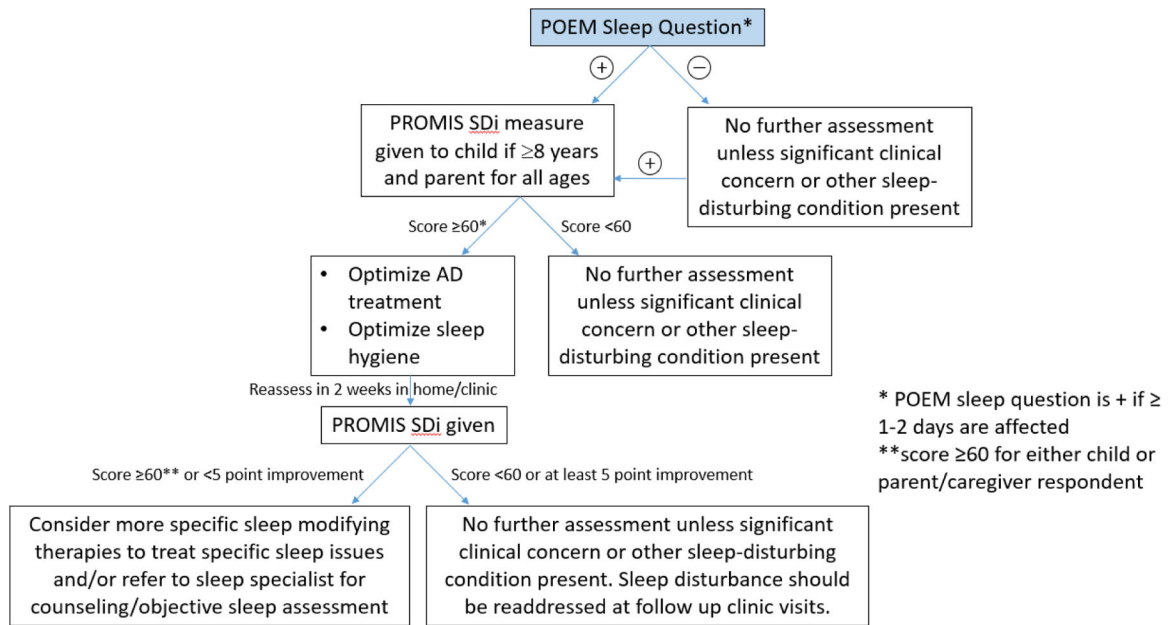| Variable	Disease severity by Patient Oriented Eczema Measure (POEM)			
	Mild (n=30)	Moderate (n=75)	Severe (n=75)	P-value
Male, n (%)	18 (60.0)	40 (53.3)	42 (56.0)	0.82
Age, mean (SD)	11.1 (3.7)	10.6 (3.6)	11.0 (3.6)	0.78
Race, n (%)				1.00
Black	10 (33.3)	24 (32.0)	24 (32.0)	
White	11 (36.7)	27 (36.0)	27 (36.0)	
Other	9 (30.0)	24 (32.0)	24 (32.0)	
Hispanic/Latino, n (%)	2 (6.7)	11 (14.7)	10 (13.3)	0.58
Parent POEM, mean (SD)	5.1 (1.9)	11.6 (2.3)	21.0 (3.2)	**<0.01**
Child POEM, mean (SD) (n=133)	4.2 (2.6)	11.5 (5.1)	18.5 (7.0)	**<0.01**
Region, n (%)				0.77
Northeast	4 (13.3)	11 (14.7)	13 (17.3)	
South	12 (40.0)	32 (42.7)	26 (34.7)	
Midwest	6 (20.0)	14 (18.7)	10 (13.3)	
West	8 (26.7)	18 (24.0)	26 (34.7)	
Rural/Urban, n (%)				0.34
Urban	13 (43.3)	32 (42.7)	27 (36.0)	
Suburban	13 (43.3)	34 (45.3)	44 (58.7)	
Rural	4 (13.3)	9 (12.0)	4 (5.3)	
Asthma, n (%)	7 (23.3)	13 (17.3)	11 (14.7)	0.57
Allergic Rhinitis, n (%)	12 (40.0)	25 (33.3)	15 (20.0)	0.07
Food Allergy, n (%)	7 (23.3)	21 (28.0)	28 (37.3)	0.28
ADHD, n (%)	2 (6.7)	16 (21.3)	12 (16.0)	0.19
Parental Education, n (%)				**<0.01**
Associate's Degree or below	22 (73.3)	38 (50.7)	21 (28.0)	
Bachelor's Degree	6 (20.0)	21 (28.0)	23 (30.7)	
Master's Degree or higher	2 (6.7)	15 (20.0)	31 (41.3)	
Household Income, n (%)				0.97
Under $50,000	13 (43.3)	37 (49.3)	34 (45.3)	
$50,000 to <$100,000	12 (40.0)	25 (33.3)	29 (38.7)	
>$100,000	3 (10.0)	10 (13.3)	8 (10.7)	
Parental Age, mean (SD)	41.4 (5.8)	39.6 (6.5)	41.2 (6.1)	0.20
BMI, mean (SD)	21.0 (5.8)	18.5 (4.4)	18.8 (4.0)	**0.03**
Parent-Proxy Reported Sleep Timing/Habits				
Bed time, weekdays, mean hh:mm (SD)	21:14 (1:00)	21:30 (0:59)	21:29 (1:09)	0.45
Bed time, weekends, mean hh:mm (SD)	22:23 (1:30)	22:32 (1:39)	22:19 (1:40)	0.69

Variable	Disease severity by Patient Oriented Eczema Measure (POEM)			
	Mild (n=30)	Moderate (n=75)	Severe (n=75)	P-value
Wake time, weekdays, mean hh:mm (SD)	07:05 (1:26)	07:24 (1:16)	07:15 (1:40)	0.60
Wake time, weekends, mean hh:mm (SD)	8:51 (1:48)	8:44 (1:40)	8:50 (1:46)	0.93
Sleep Onset Latency, weekdays, n (%)				0.32
30 minutes	20 (66.7)	43 (57.3)	38 (50.7)	
>30 minutes	10 (33.3)	32 (42.7)	37 (49.3)	
Sleep Onset Latency, weekends, n (%)				0.63
30 minutes	21 (70.0)	47 (62.7)	45 (60.0)	
>30 minutes	9 (30.0)	28 (37.3)	30 (40.0)	
Naps on weekdays, n (%)	9 (30.0)	20 (26.7)	27 (36.0)	0.46
Naps on weekends, n (%)	5 (16.7)	16 (21.3)	16 (21.3)	0.85
Parent-Proxy Reported Sleep, mean (SD)				
Sleep Disturbance	55.7 (7.5)	59.8 (10.8)	67.1 (9.5)	**<0.01**
Sleep-Related Impairment	52.6 (11.8)	57.4 (7.8)	62.1 (12.6)	**0.03**
Child Reported Sleep, mean (SD) (n=133)				
Sleep Disturbance	60.5 (7.8)	65.0 (7.8)	70.3 (7.2)	**<0.01**
Sleep-Related Impairment	56.9 (9.9)	63.9 (8.8)	67.7 (10.8)	**<0.01**
Parent-Proxy Reported PROMIS Profile, mean (SD)				
Depression/Sadness	49.8 (9.3)	55.4 (10.8)	62.3 (13.1)	**<0.01**
Peer Relationships	40.9 (11.1)	43.0 (9.7)	43.2 (9.1)	0.51
Anxiety	48.9 (10.9)	55.5 (11.1)	62.0 (14.1)	**<0.01**
Physical Function/Mobility	50.3 (8.3)	45.4 (9.8)	40.1 (9.9)	**<0.01**
Pain Interference	52.6 (9.0)	57.4 (7.7)	60.7 (7.9)	**<0.01**
Child Reported PROMIS Profile, mean (SD) (n=133)				
Depression/Sadness	49.3 (9.4)	54.4 (10.7)	57.7 (11.4)	**0.01**
Peer Relationships	44.4 (10.7)	46.5 (10.9)	43.4 (10.1)	0.27
Anxiety	46.8 (10.3)	52.1 (11.7)	56.1 (12.5)	**0.01**
Physical Function/Mobility	51.2 (9.1)	47.7 (10.3)	41.6 (9.9)	**<0.01**
Pain Interference	46.9 (9.7)	54.0 (9.6)	59.3 (8.4)	**<0.01**
CDLQI, mean (SD)	6.2 (6.5)	11.7 (7.1)	16.8 (6.6)	**<0.01**
Parent-Reported PIQ-C, mean (SD)	43.4 (7.6)	50.5 (7.2)	57.3 (7.1)	**<0.01**
Child-Reported PIQ-C, mean (SD) (n=133)	40.7 (8.6)	48.5 (9.1)	53.9 (7.9)	**<0.01**
Inattention, MacArthur Score, mean (SD)	0.6 (0.6)	0.9 (0.6)	1.1 (0.5)	**<0.01**
Impulsivity, MacArthur Score, mean (SD)	0.5 (0.6)	0.8 (0.6)	1.0 (0.6)	**<0.01**
Parent-Reported Itch NRS, mean (SD)	3.8 (2.2)	5.4 (1.9)	7.6 (1.3)	**<0.01**
Child-Reported Itch NRS, mean (SD) (n=133)	3.4 (2.5)	5.2 (2.4)	7.1 (2.2)	**<0.01**

*POEM=Patient Oriented Eczema Measure; ADHD=Attention Deficit Hyperactive Disorder; BMI=Body Mass Index; PROMIS= Patient-Reported Outcomes Measurement Information System; CDLQI=Children's Dermatology Life Quality Index; PIQ-C=PROMIS Pediatric Itch Questionnaire-Child; NRS=Numeric Rating Scale; hh:mm= hours: minutes

Table 2.

Estimated national prevalence of sleep disturbance and sleep-related impairment, by AD severity and race.

	No sleep disturbance	Sleep disturbance	Severe sleep disturbance	No sleep-related impairment	Sleep-related impairment	Severe sleep-related impairment
POEM severity of AD						
Mild	1,246,572 (40.3%)	636,118 (21.0%)	1,143,962 (37.8%)	1,456,317 (48.1%)	860,844 (28.4%)	709,490 (23.4%)
Moderate	262,342 (20.6%)	309,683 (24.3%)	704,275 (55.2%)	312,222 (24.5%)	267,908 (21.0%)	696,170 (54.5%)
Severe	30,920 (8.8%)	25,359 (7.2%)	296,909 (84.1%)	3,8335 (10.9%)	28,747 (8.1%)	286,106 (81.0%)
Race						
White	970,961 (34.3%)	336,321 (11.9%)	1,520,678 (53.8%)	1,234,209 (43.6%)	54,1172 (19.1%)	1,052,580 (37.2%)
Black	289,252 (23.7%)	512,547 (42.0%)	419,385 (34.3%)	25,8677 (21.2%)	50,4947 (41.3%)	457,560 (37.5%)
Other	279,621 (46.1%)	122,292 (20.1%)	205,083 (33.8%)	313,989 (51.7%)	111,380 (18.3%)	181,626 (29.9%)
Total *	1,539,834 (33.1%)	971,160 (20.9%)	2,145,145 (46.1%)	1,806,874 (38.8%)	1,157,499 (24.9%)	1,691,766 (36.3%)

*
Reflects total number and percentage of US population with atopic dermatitis that experience sleep disturbance or sleep-related impairment respectively.

Table 3:

Stepwise linear regression model evaluating the associations between atopic dermatitis disease severity, itch and significant sociodemographic factors and the outcome of sleep disturbance

Table 3A. Parent-proxy reported sleep disturbance (n=180)			Table 3B. Child self-reported sleep disturbance (n=133)	
	Multivariable model		**Multivariable model**	
Characteristic	**Adjusted β [95% CI]**	**P-value**	**Adjusted β [95% CI]**	**P-value**
Model 1				
POEM without itch/sleep	0.77 [0.53, 1.01]	**<.0001**	0.95 [0.66, 1.24]	**<.0001**
Model 2				
POEM without itch/sleep	0.38 [0.11, 0.66]	**0.007**	0.47 [0.12, 0.83]	**0.009**
Numeric Rating Scale Itch	1.32 [0.61, 2.03]	**0.0003**	1.37 [0.57, 2.16]	**0.0009**
Model 3				
POEM without itch/sleep	0.24 [−0.07, 0.54]	0.13	0.46 [0.08, 0.83]	**0.02**
Numeric Rating Scale Itch	1.33 [0.62, 2.04]	**0.0003**	1.37 [0.58, 2.16]	**0.0008**
Parental income				
Under $50,000	6.64 [2.05, 11.23]	**0.005**		
$50,000 to <$100,000	4.75 [0.35, 9.14]	**0.03**		
>$100,000	1.00 [ref]	-		
Parental Education				
Associate's Degree	1.00 [ref]	-	1.00 [ref]	-
Bachelor's Degree	1.58 [−0.85, 4.02]	0.20	−0.12 [−3.42, 3.18]	0.94
Master's Degree	4.67 [1.80, 7.54]	**0.002**	1.04 [−2.07, 4.16]	0.51

Bold-face indicates statistical significance. Model 3 controls for sociodemographic factors significantly associated with sleep disturbance in bivariable models.

Table 4.

Association of sleep disturbance[*] with psychologic symptoms and neurocognitive function.

	Crude β [95% CI]	P-value	POEM adjust Adj β [95% CI][**]	P-value	POEM+NRS itch Adj β [95% CI][**]	P-value	Fully-adjusted Adj β [95% CI][***]	P-value
Parent proxy response 5–17 years (n=180)								
PROMIS pediatric profile								
Sleep-related impairment	1.08 [0.96, 1.19]	**<.0001**	1.00 [0.85, 1.14]	**<.0001**	1.00 [0.84, 1.15]	**<.0001**	1.01 [0.86, 1.17]	**<.0001**
Depression	0.89 [0.71, 1.08]	**<.0001**	0.74 [0.53, 0.95]	**<.0001**	0.72 [0.51, 0.93]	**<.0001**	0.67 [0.46, 0.88]	**<.0001**
Fatigue	0.96 [0.79, 1.12]	**<.0001**	0.88 [0.69, 1.07]	**<.0001**	0.87 [0.69, 1.06]	**<.0001**	0.76 [0.56, 0.97]	**<.0001**
Peer relationships	−0.06 [−0.28, 0.15]	0.55	−0.08 [−0.36, 0.20]	0.57	−0.08 [−0.38, 0.22]	0.61	−0.10 [−0.43, 0.23]	0.54
Anxiety	0.93 [0.73, 1.14]	**<.0001**	0.79 [0.55, 1.03]	**<.0001**	0.81 [0.58, 1.05]	**<.0001**	0.79 [0.57, 1.01]	**<.0001**
MacArthur HBQ ADHD symptoms								
Inattention	0.03 [0.02, 0.05]	**<.0001**	0.03 [0.02, 0.04]	**<.0001**	0.03 [0.02, 0.04]	**<.0001**	0.03 [0.02, 0.04]	**<.0001**
Impulsivity	0.03 [0.02, 0.04]	**<.0001**	0.02 [0.01, 0.04]	**<.0001**	0.03 [0.02, 0.04]	**<.0001**	0.02 [0.01, 0.04]	**<.0001**
Child self-report 8–17 years (n=133)								
PROMIS pediatric profile								
Sleep-related impairment	0.93 [0.82, 1.05]	**<.0001**	0.81 [0.66, 0.95]	**<.0001**	0.79 [0.62, 0.96]	**<.0001**	0.87 [0.71, 1.03]	**<.0001**
Depression	0.67 [0.48, 0.86]	**<.0001**	0.60 [0.39, 0.81]	**<.0001**	0.66 [0.47, 0.84]	**<.0001**	0.66 [0.46, 0.86]	**<.0001**
Fatigue	0.83 [0.71, 0.96]	**<.0001**	0.69 [0.52, 0.86]	**<.0001**	0.67 [0.49, 0.86]	**<.0001**	0.69 [0.51, 0.87]	**<.0001**
Peer relationships	−0.13 [−0.37, 0.10]	0.27	−0.11 [−0.41, 0.20]	0.48	−0.13 [−0.45, 0.20]	0.44	−0.13 [−0.48, 0.22]	0.46
Anxiety	0.69 [0.51, 0.87]	**<.0001**	0.61 [0.40, 0.82]	**<.0001**	0.68 [0.49, 0.87]	**<.0001**	0.69 [0.49, 0.88]	**<.0001**

[*] PROMIS T-score parent-proxy sleep disturbance or child self-report sleep disturbance, respectively

[**] Adjusted for POEM composite severity score without sleep or itch items

[***] Adjusted for POEM composite without sleep or itch items, itch NRS, and significant socio-demographics from Table 2