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Sleep and exhaustion in mothers of children with atopic dermatitis

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Key points

Question: Do mothers of children with atopic dermatitis experience sleep disturbances, and to what extent are these explained by child sleep disturbances?

Findings: In this longitudinal cohort study, sleep disturbances were common among mothers of children with atopic dermatitis followed from birth through age 11, and included impaired sleep quality, subjectively insufficient sleep, and increased daytime exhaustion. Child sleep disturbances did not fully explain maternal sleep disturbances.

Meaning: Clinicians caring for children with atopic dermatitis should screen for maternal sleep disturbances and caregiver fatigue.

ABSTRACT

Importance: The wellbeing and development of children is strongly influenced by parents' physical and psychosocial health. Data from small, clinic-based studies suggest that sleep loss may be common in parents of children with atopic dermatitis (AD), but longitudinal population-based studies are lacking.

Objective: To compare sleep disturbances over time between mothers of children with and without AD, and determine whether these are associated with the child's disease severity and the child's sleep disturbances.

Setting: United Kingdom

Participants: Mother-child pairs from the Avon Longitudinal Study of Parents and Children, a population-based birth cohort in the United Kingdom.

Design: Longitudinal cohort study

Exposure: Time-varying measure of child AD activity and severity repeated at multiple time points between 2 and 11 years.

Main Outcome(s) and Measure(s): Time-varying binary measures of maternal sleep duration (< 6 hours per night vs. \geq 6 hours per night), difficulty falling asleep, early morning awakening, subjectively insufficient sleep, and daytime exhaustion, repeated at multiple time points between 2 and 11 years.

Results: 11,649 mother-child pairs were followed for a median duration of 11 years (interquartile range 7 to 11 years). 82.9% of mothers were 21 to 34 years of age, and 51.7% of children were male. Sleep duration (adjusted odds ratio [aOR] 1.09; 95% confidence interval [CI] 0.90-1.32) and early morning awakenings (aOR 1.16; 95% CI 0.93-1.46) were similar between mothers of children with and without AD. In contrast, mothers of children with AD were more likely to report difficulty falling asleep (aOR 1.36; 95% CI 1.01-1.83), subjectively insufficient sleep (aOR 1.43; 95% CI 1.24-1.66), and daytime exhaustion (aOR 1.41; 95% CI 1.12-1.78), independent of the child's comorbid asthma and/or allergic rhinitis. For all measures, worse child AD severity correlated with worse maternal sleep outcomes. The magnitude and significance of the associations was largely unchanged after adjusting for child sleep disturbances.

Conclusions and relevance: Mothers of children with AD reported difficulty falling asleep, subjectively insufficient sleep, and daytime exhaustion throughout the first 11 years of childhood. Although impaired parental sleep in AD is thought to be related to the child's nighttime awakenings, child sleep disturbances did not fully explain maternal sleep disturbances, and future research should investigate other mechanisms. In caring for children with AD, clinicians should consider maternal sleep disturbances and caregiver fatigue.

Key words: ALSPAC; sleep duration; sleep quality; atopic dermatitis; parent health

INTRODUCTION

The health, wellbeing, and development of children is strongly influenced by the physical and psychosocial health of parents.^{1,2} Parents of children with chronic illness, in particular, are susceptible to poor sleep, and impaired sleep has been associated with increased risks of cancer and cardiovascular disease,³ infectious illness,⁴ obesity⁵, and premature mortality.⁶ Previous studies have found major sleep impairments among parents of children with ventilator dependency and cystic fibrosis,^{7,8} but few studies have examined sleep patterns among parents of children with more common chronic illnesses.

Atopic dermatitis is one of the most common chronic childhood conditions, affecting up to one in five children in developed countries.⁹ Atopic dermatitis is characteristically itchy, which is often reported to be more severe at night,^{10,11} causing nighttime awakenings secondary to itching and scratching.^{12,13} However, few studies have directly examined the relationship between parental sleep disturbances and severity of child atopic dermatitis, and have accounted for child sleep disturbances. Existing research is limited, and has focused on snapshots of small, clinic-based populations that are likely to have more severe disease than the general population.¹²⁻¹⁵ Because the severity and activity of atopic dermatitis can vary throughout childhood, longitudinal studies can provide better insight into how variations in the child's disease activity and severity over time affect parental sleep.

We aimed to determine whether mothers of children with active atopic dermatitis have impaired sleep during the first 11 years of childhood, and whether these sleep disturbances are associated with the child's disease severity and the child's sleep disturbances.

METHODS

Participants

Data for this study come from the Avon Longitudinal Study of Parents and Children (ALSPAC), a longitudinal, population-based birth cohort in the United Kingdom.^{16,17} All pregnant women residing in Avon, United Kingdom, with an expected delivery date between April 1st 1991 and December 31st 1992 were recruited. The ALSPAC study enrolled a total of 14,541 pregnancies, which resulted in 14,062 live births, of which 13,988 were alive at 1 year of age. Our study sample is limited to children who had data on atopic dermatitis from at least one survey and whose mothers had data on sleep outcomes from at least one survey, through age 11 (N=11,649 mother-child pairs; 83% of children alive at 1 year of age). The study website contains details of all the data that is available through a fully searchable data dictionary and variable search tool.¹⁸

Exposure

The primary exposure was a time-varying measure of active atopic dermatitis in the child. Mothers were asked a standardized question about flexural dermatitis at 10 time points between ages 6 months and 11 years (6, 18, 30, 42, 57, 69, 81, 103, 128, and 140 months): *“Has your child had an itchy, dry skin rash in the joints and creases of his body (e.g. behind the knees,*

elbows, under the arms) in the past year?”. This question is comparable to that used in the large International Studies of Asthma and Allergies in Childhood (ISAAC).¹⁹ Children were categorized as having *active* atopic dermatitis if their mother had reported at least two reports of flexural dermatitis, up to and including the time point being considered.²⁰⁻²² Disease severity was assessed at each time point by a question asking mothers to categorize their child’s flexural dermatitis over the past year as no problem, mild, moderate, or severe.

Maternal sleep outcomes

Five maternal sleep outcomes were measured at various time points throughout childhood (Table 1). Sleep duration was measured by a standardized categorical question repeated at five time points: *“How many hours of sleep do you get altogether now during an average night?” (1-3 hours, 4-5 hours, 6-7 hours, >7 hours)*. This variable was modeled as a dichotomous outcome, less than 6 hours per night compared to 6 or more hours per night, as the National Sleep Foundation recommends 7 to 9 hours of sleep for adults aged 26 to 64 years.²³ Difficulty falling asleep and early morning awakening were assessed at three time points by the questions *“Can you go to sleep alright?” (Never/Not very often vs. Very often/Often)* and *“Do you wake unusually early in the morning even when you haven't been woken by your child or family?” (Very often/Often vs. Never/Not very often)* respectively. Subjectively insufficient sleep was examined at four time points by a question about whether the mother felt she was getting enough sleep. Finally, daytime exhaustion was measured at seven time points by the question: *“In the past month, how often have you felt exhausted?” (Almost always vs. Sometimes/Not at all)*.

Additional covariates

Several potential confounders, mediators, and effect modifiers were identified from prior literature, and incorporated into a directed acyclic graph that was used to guide our modeling strategy (Supplemental eFigure1). These included child and mother demographic characteristics (child gender, child age, mother race/ethnicity, maternal age at delivery), indicators of socio-economic status, household smoking exposure, presence of comorbid atopic diseases in the child (asthma or allergic rhinitis), maternal sleep problems during pregnancy, maternal history of any atopic condition (atopic dermatitis, asthma, or allergic rhinitis), and child sleep disturbances. Socio-economic status was measured using prenatal questionnaires collected from parents at study enrollment, including the mother's highest education qualification, social class based on occupation (highest of either parent), household crowding index (number of people living in the household divided by the number of rooms in the house), and a financial difficulties score, assessing the mother's self-reported difficulty to afford food, clothing, heating, rent/mortgage, and items necessary to care for her baby. Maternal sleep problems during pregnancy were assessed by prenatal questionnaire, based on questions about difficulty falling asleep at 18 and 32 weeks of gestation.

Time-varying covariates included child comorbid atopic disease, household smoking exposure, and child sleep disturbances. A child was determined to have comorbid atopic disease at each time point examined if his or her mother reported asthma and/or allergic rhinitis symptoms at that time point, similar to the questions used in the large ISAAC studies.²⁴ Models also included a measure of household smoking exposure, assessed by maternal questionnaire about the number

of smokers living in the household at multiple time points throughout childhood. Finally, child sleep disturbances were measured by a standardized question about the frequency of nighttime awakenings (dichotomized at ≥ 1 awakening per night) at 6 time points in early childhood (30, 42, 57, 69, 81, and 115 months). Child nighttime awakenings have been shown to be a valid measure of atopic dermatitis-associated child sleep disturbances throughout childhood.²⁵

Missing data

As has been described in detail elsewhere, there is both intermittent missing data and attrition (i.e. loss to follow-up) in the ALSPAC cohort.¹⁶ Multiple imputation was used to impute missing exposure, outcome, and covariate data. Iterative chained equations were used, as most variables in our models did not follow a normal distribution. Fifty imputed datasets were generated and used to repeat primary analyses.

Analyses

Cross-sectional logistic regression analyses were performed to compare maternal sleep outcomes between mothers of children with and without atopic dermatitis at each time point. Longitudinal analyses with repeated measures of the exposure, outcome, and time-varying covariates were then performed using mixed effects models with random slopes and intercepts for each individual, to estimate the subject-specific odds ratios for each of the maternal sleep outcomes. The minimally sufficient adjustment set was determined using our directed acyclic graph (Supplemental eFigure1), and these predictors were included in multivariable models. Multivariable model 1 represents the fully adjusted model to determine the total effect of child

atopic dermatitis on maternal sleep, and model 2 additionally adjusted for child sleep disturbances at each time point to estimate the direct effect of child atopic dermatitis on maternal sleep, independent of child sleep disturbances. Interactions between child atopic dermatitis and child comorbid atopic disease (asthma or allergic rhinitis), child age, child gender, and maternal education were tested. All statistical analyses were performed using STATA version 14.2 (StataCorp, College Station, Texas).

Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. The study was considered exempt from UCSF IRB review because all data obtained by investigators were fully de-identified.

RESULTS

The study sample was composed of 11,649 mother-child pairs, followed for a median duration of 11 years (interquartile range 7 to 11 years). Mothers of children with atopic dermatitis were more likely have a personal history of atopy, and have a higher education qualification and social class (Table 2). The annual period prevalence of child atopic dermatitis ranged from 16% to 21%, and 22% to 39% of children with atopic dermatitis reported moderate to severe disease at any given time point.

The proportion of all mothers who reported each of the five sleep outcomes was fairly consistent across ages: 5-12% reported sleeping less than 6 hours per night, 18-20% reported early morning

awakenings, 12-13% reported difficulty falling asleep, 38-43% reported subjectively insufficient sleep, and 6-10% reported daytime exhaustion during the first 11 years of their child's life.

In unadjusted cross-sectional analyses comparing mothers of children with and without atopic dermatitis at individual time points, results were generally consistent across all child ages (Supplemental eTable1). In longitudinal analyses, sleep duration and early morning awakening were similar for mothers of children with active atopic dermatitis compared to mothers of children who never reported atopic dermatitis (Table 3). In contrast, mothers of children with active atopic dermatitis were more likely to report difficulty falling asleep (adjusted odds ratio [aOR] 1.36; 95% confidence interval [CI] 1.01 - 1.83), subjectively insufficient sleep (aOR 1.43; 95% CI 1.24 - 1.66), and daytime exhaustion (aOR 1.41; 95% CI 1.12 - 1.78). None of the interactions between child atopic dermatitis and child comorbid atopic disease (asthma or allergic rhinitis), child age, child gender, and maternal education were statistically significant ($p < 0.05$).

Sub-analysis with child atopic dermatitis disease severity

When we examined the odds of maternal sleep disturbances according to the child's disease severity, we found larger effects among mothers of children with more severe disease (Figure 1 and Supplemental eTable2). For maternal sleep duration, we only found a statistically significant association for mothers of children with severe disease, who had 61% higher odds of reporting sleep duration less than 6 hours per night (aOR 1.61; 95% CI 1.05 - 2.48). While the odds were also higher for early morning awakening and difficulty falling asleep, these did not reach

statistical significance (aOR 1.53, 95% CI 0.96 - 2.45; aOR 1.53, 95% CI 0.90 - 2.58, respectively). The association with daytime exhaustion and subjectively insufficient sleep was stronger for mothers of children with severe disease (72-89% higher odds), but remained significant even for those with mild to moderate disease (31-39% higher odds).

Sub-analysis accounting for child sleep disturbances

Finally, we re-calculated the odds of maternal sleep disturbances while controlling for child sleep disturbances at each time point, to examine whether child sleep accounted for most of the association between child atopic dermatitis and maternal sleep. Overall, we found that the magnitude and significance of the associations was largely unchanged after adjusting for child sleep disturbances in model 2 (Table 3, Figure 1, and Supplemental eTable2).

Multiple imputation results

Imputed datasets were used to repeat all primary analyses (Supplemental eTables2-3). Primary analyses yielded results that were largely consistent with those estimated from the imputed data. Estimates using the imputed data were slightly attenuated towards the null; however, results remained qualitatively similar.

DISCUSSION

In a cohort of 11,649 mother-child pairs followed from birth through age 11, sleep duration was similar between mothers of children with and without atopic dermatitis. However, mothers of children with active atopic dermatitis reported subjectively insufficient sleep, difficulty falling

asleep, and daytime exhaustion throughout the first 11 years of childhood. These findings have important implications, given that atopic dermatitis is one of the most common chronic childhood conditions, affecting up to 20% of children in industrialized countries at any given age.²⁶

A strength of the current study is the use of a large prospective, longitudinal, population-based cohort in which children were followed from birth for over ten years. The few studies that have specifically examined the effect of child atopic dermatitis on parental sleep relative to parents of children without atopic dermatitis have been small, cross-sectional, and have been conducted among clinic-based populations.^{12-15,27} In our study, only mothers of children with severe disease were significantly more likely to report sleeping less than 6 hours per night. Similarly, Moore and colleagues found that parents of children with moderate to severe atopic dermatitis lost a median of 39 minutes of sleep per night,²⁷ and Meltzer *et al.* found that parents of children with atopic dermatitis were significantly more likely to report sleep duration less than 6 hours per night, compared to parents of healthy children.¹³

Although impaired parental sleep is thought to be related to the child's nighttime awakenings,^{12,13,27} adjusting for child sleep disturbances in our study did not change our conclusions. This suggests that maternal sleep disturbances may be explained by other factors, unrelated to the child's sleep disturbances. Recent work from the pediatric psychology literature in the setting of other chronic illnesses, including asthma, ventilator dependency, and cystic fibrosis, has supported caregiver stress and anxiety related to the child's condition as potential

contributors to parental sleep disruptions.^{7,8,13,28,29} Supporting this concept, other studies have found that parents of children with atopic dermatitis experience high rates of psychological distress and depression,^{12,30-32} which may explain some of their sleep disturbances. Further research is needed to better understand the exact causes of these sleep disruptions, and characterize their consequences on daytime functioning, wellbeing, and health outcomes in caregivers of children with atopic dermatitis.

Maternal emotional and psychosocial wellbeing is inextricably linked to the child's health, development, and cognitive and social functioning.^{1,2,33} In children with atopic dermatitis, chronically sleep-deprived, exhausted, or depressed caregivers may be less equipped to implement time-consuming treatment regimens, regulate their child's behavior, and help children cope with their illness.^{13,34} The American Academy of Pediatrics recommends that clinicians provide family-oriented care that addresses the needs of the entire family and promotes family functioning in order to optimize child outcomes.¹ These recommendations include screening for family circumstances that may negatively influence the wellbeing of the child. Our results suggest that clinicians caring for children with atopic dermatitis should screen for caregiver sleep disturbances and fatigue, engage mothers in discussion about their emotional health, and consider offering resources for psychosocial support, particularly in mothers of children with more severe disease. Clinicians may also consider formally screening mothers for sleep problems using the Pittsburgh Sleep Quality Index (PSQI), for depression using the Patient Health Questionnaire-9 (PHQ-9), and for anxiety using the Generalized Anxiety Disorder 7-item (GAD-7) scale, all of which are well-validated questionnaires.³⁵⁻³⁸ Additional research is needed to

understand how interventions targeted at both child atopic dermatitis and maternal wellness can improve the entire family's sleep.

Several limitations warrant discussion, including the potential for selection bias due to missing data and attrition, which is inherent to all large-scale longitudinal studies. To address this, we performed multiple imputation and reassuringly, found similar results. Another important limitation relates to the possibility for misclassification bias, because both exposure and outcome data were self-reported. While we cannot rule out the possibility of some misclassification, prior studies have found that self-report of atopic dermatitis closely approximates physician assessment of atopic dermatitis.³⁹ Although it is possible that mothers who are chronically exhausted may have a tendency to report more severe disease in their child, the associations remained significant even for mothers of children with mild disease. In addition, the estimates of moderate-severe disease match that of other population-based studies,^{25,40} and parent-reported disease severity has been shown to correlate well with objective disease-severity measures.^{41,42} In population-based studies comparing survey sleep duration to objective measures, self-report tends to overestimate total duration of sleep,⁴³ which would bias our results towards the null. An additional limitation relates to the fact that the sleep quality questions about difficulty falling asleep and early morning awakenings were not asked beyond the child's 5th year of age. Future work should investigate whether these maternal sleep quality disturbances persist into later childhood and adolescence. The current study focused on mothers' sleep, as mothers are often the primary caregivers; future research should consider the role of fathers and other caregivers.

Finally, while the cohort is fairly representative of the United Kingdom population,¹⁶ it is unclear the extent to which our results are generalizable to other populations.

CONCLUSION

Throughout the first 11 years of childhood, mothers of children with active atopic dermatitis experienced more difficulty falling asleep, subjectively insufficient sleep, and daytime exhaustion compared to mothers of children without atopic dermatitis, and the child's disease severity correlated with worse maternal sleep. Child sleep disturbances did not fully explain maternal sleep disturbances, and further research is needed to better understand these mechanisms. In caring for children with atopic dermatitis, clinicians should inquire about caregiver sleep disturbances and fatigue, and consider offering psychosocial support.

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Author contributions:

Dr. Abuabara and Ms. Ramirez had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Ms. Ramirez conceptualized and designed the study, carried out and takes responsibility for the data analyses, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Abuabara conceptualized and designed the study, supervised data analyses and interpretation, and critically reviewed and revised the manuscript for important intellectual content.

Ms. Chen, and Drs. Langan, Prather, Kidd, McCulloch, Cabana, and Chren contributed to the study design and interpretation of results, and critically reviewed and revised the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Potential Conflicts of Interest: Dr. Abuabara receives research funding for atopic dermatitis from the National Eczema Association, Dermatology Foundation, Robert Wood Johnson Foundation, NIAMS, and is a consultant to TARGETPharma, a company developing a

prospective atopic dermatitis registry. The other authors have no conflicts of interest relevant to this article to disclose.

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Table 1. Maternal sleep outcome measurements by child age

Child age	21 months (1 year, 9 months)	33 months (2 years, 9 months)	47 months (3 years, 11 months)	61 months (5 years, 1 month)	73 months (6 years, 1 month)	85 months (7 years, 1 month)	110 months (9 years, 2 months)	134 months (11 years, 2 months)
Sleep duration	x	x		x		x		x
Early morning awakening	x	x		x				
Difficulty falling asleep	x	x		x				
Subjectively insufficient sleep	x	x		x		x		
Daytime exhaustion	x	x	x	x	x		x	x

Table 2. Cohort characteristics

			No atopic dermatitis (n=5,599; 54.0%)	Atopic dermatitis* (n=4,767; 46.0%)	p-value**
	Total	n (%)	n (%)	n (%)	
Maternal characteristics					
Mother race/ethnicity (white)	12,324	12,001 (97.4)	5,039 (97.7)	4,500 (97.9)	0.51
Maternal age at delivery					< 0.001
≤ 20 years old	13,972	1,004 (7.2)	376 (6.7)	202 (4.2)	
21-34 years old	13,972	11,585 (82.9)	4,630 (82.7)	4,061 (85.2)	
≥ 35 years old	13,972	1,383 (9.9)	593 (10.6)	504 (10.6)	
Maternal history of atopic condition ^a	12,454	5,659 (45.4)	2,179 (42.0)	2,318 (50.3)	< 0.001
Household smoking exposure ^b	10,188	3,683 (36.2)	1,661 (37.4)	1,435 (33.7)	< 0.001
Maternal highest education ^c					< 0.001
CSE/None	12,412	2,504 (20.2)	1,106 (21.3)	701 (15.2)	
Vocational	12,412	1,224 (9.9)	513 (9.9)	435 (9.4)	
O level	12,412	4,294 (34.6)	1,860 (35.8)	1,595 (34.6)	
A level	12,412	2,791 (22.5)	1,149 (22.1)	1,141 (24.8)	
Degree	12,412	1,599 (12.9)	563 (10.9)	736 (16.0)	
Social class ^d					< 0.001
Unskilled	12,254	227 (1.9)	87 (1.7)	53 (1.2)	
Partly skilled	12,254	920 (7.5)	381 (7.5)	274 (6.2)	
Skilled manual	12,254	1,666 (13.6)	717 (14.2)	502 (11.3)	
Skilled non-manual	12,254	3,780 (30.8)	1,601 (31.7)	1,340 (30.2)	
Managerial and technical	12,254	4,566 (37.3)	1,878 (37.1)	1,779 (40.0)	
Professional	12,254	1,095 (8.9)	395 (7.8)	493 (11.1)	
Financial difficulties quartile					0.06
Lowest	12,083	4,337 (35.9)	1,819 (36.0)	1,722 (38.5)	
Mild	12,083	3,006 (24.9)	1,272 (25.1)	1,104 (24.7)	
Moderate	12,083	2,324 (19.2)	973 (19.2)	832 (18.6)	
Highest	12,083	2,416 (20.0)	995 (19.7)	817 (18.3)	
Crowding index ^e					< 0.001
≤ 0.5	12,799	5,329 (41.6)	2,085 (40.0)	2,146 (46.7)	
> 0.5 - 0.75	12,799	4,013 (31.3)	1,644 (31.6)	1,456 (31.7)	
> 0.75 - 1	12,799	2,579 (20.2)	1,111 (21.3)	788 (17.2)	
> 1	12,799	878 (6.9)	370 (7.1)	203 (4.4)	
Maternal sleep problems during pregnancy ^f	13,406	4,535 (33.8)	1,886 (34.6)	1,486 (31.5)	0.001

Child characteristics					
Child gender (male)	13,978	7,220 (51.7)	3,022 (54.0)	2,319 (48.7)	< 0.001
Child race/ethnicity (white)	12,077	11,468 (95.0)	4,812 (95.5)	4,335 (95.6)	0.82
Child asthma ever ^g	12,612	3,237 (25.7)	1,078 (19.3)	1,745 (36.6)	< 0.001
Child allergic rhinitis ever ^g	10,156	1,375 (13.5)	356 (8.1)	872 (20.2)	< 0.001
Child asthma or allergic rhinitis ever ^g	12,620	3,919 (31.1)	1,300 (23.2)	2,120 (44.5)	< 0.001
Child asthma and allergic rhinitis ever ^g	12,620	693 (5.5)	134 (2.4)	497 (10.4)	< 0.001

Table 2:

* Children who ever reported atopic dermatitis through age 11 years (i.e. had at least two reports of flexural dermatitis)

** Chi-squared test comparing mother-child pairs who never reported atopic dermatitis to those who ever reported atopic dermatitis through age 11 years

^a Including atopic dermatitis, asthma, or allergic rhinitis

^b When child was 1.75 years of age

^c United Kingdom education levels: CSE or 'Certificate of Secondary Education' (national school examinations at 16 years); 'Vocational'; 'O level' (national school examinations at 16 years, higher than CSE); 'A level' (national school examinations at 18 years); 'Degree' (university degree or higher)

^d Highest of either parent, based on occupation

^e Defined as the number of persons living in the household divided by the number of rooms in the household

^f Defined as difficulty falling asleep "often" or "very often" at 18 or 32 weeks of gestation

^g Defined as at least 2 reports of symptoms throughout childhood

Table 3. Odds of maternal sleep disturbances across time points among mothers of children with active atopic dermatitis compared to mothers of children who never reported atopic dermatitis

	Sleep duration < 6 hours per night ¹	Early morning awakening ²	Difficulty falling asleep ³	Subjectively insufficient sleep ⁴	Daytime exhaustion ⁵
	Odds Ratio (95% Confidence Interval)				
Unadjusted	0.92 (0.78 - 1.09)	1.27 (1.06 - 1.52)	1.17 (0.96 - 1.43)	1.45 (1.27 - 1.66)	1.38 (1.13 - 1.69)
Model 1	1.09 (0.90 - 1.32)	1.16 (0.93 - 1.46)	1.36 (1.01 - 1.83)	1.43 (1.24 - 1.66)	1.41 (1.12 - 1.78)
Model 2	1.06 (0.85 - 1.33)	1.15 (0.91 - 1.44)	1.33 (0.99 - 1.79)	1.42 (1.23 - 1.65)	1.43 (1.12 - 1.83)

Table 3: For each of the maternal sleep outcomes, results from an unadjusted and two separate adjusted multivariable mixed models examining the association between child active atopic dermatitis and maternal sleep disturbances at multiple time points. Model 1 adjusted for child gender, child age, mother race/ethnicity, child atopy (asthma and/or allergic rhinitis), household smoking exposure, maternal education, social class, crowding index, financial difficulties score, maternal sleep problems during pregnancy, maternal atopy, and maternal age at delivery. Model 2 adjusted for the same variables as Model 1, as well as child sleep disturbances at each time point. Model 2 excluded the 134-month time point from analyses for the outcomes of sleep duration and daytime exhaustion as data on child sleep disturbances was not available at this time point.

¹Unadjusted model: N = 10,691 individuals [mean of 3.7 observations per individual (range 1-5)]; Model 1: N = 8,961 individuals [mean of 3.7 observations per individual (range 1-5)]; Model 2: N = 8,837 individuals [mean of 3.1 observations per individual (range 1-4)]

²Unadjusted model: N = 10,449 individuals [mean of 2.5 observations per individual (range 1-3)]; Model 1: N = 8,796 individuals [mean of 2.5 observations per individual (range 1-3)]; Model 2: N = 8,771 individuals [mean of 2.4 observations per individual (range 1-3)]

³Unadjusted model: N = 10,443 individuals [mean of 2.5 observations per individual (range 1-3)]; Model 1: N = 8,794 individuals [mean of 2.5 observations per individual (range 1-3)]; Model 2: N = 8,768 individuals [mean of 2.4 observations per individual (range 1-3)]

⁴Unadjusted model: N = 10,546 individuals [mean of 3.1 observations per individual (range 1-4)]; Model 1: N = 8,883 individuals [mean of 3.1 observations per individual (range 1-4)]; Model 2: N = 8,831 individuals [mean of 3.0 observations per individual (range 1-4)]

⁵Unadjusted model: N = 10,886 individuals [mean of 5.1 observations per individual (range 1-7)]; Model 1: N = 9,061 individuals [mean of 5.0 observations per individual (range 1-7)]; Model 2: N = 9,003 individuals [mean of 4.4 observations per individual (range 1-6)]

Figure 1, Panel A-E. Adjusted odds and 95% confidence intervals for maternal sleep disturbances across time points among mothers of children with active atopic dermatitis according to disease severity compared to mothers of children who never reported atopic dermatitis

Legend: For each of the maternal sleep outcomes, results from two separate adjusted multivariable mixed models examining the association between child active atopic dermatitis and maternal sleep disturbances at multiple time points. Model 1 adjusted for child gender, child age, mother race/ethnicity, child atopy (asthma and/or allergic rhinitis), household smoking exposure, maternal education, social class, crowding index, financial difficulties score, maternal sleep problems during pregnancy, maternal atopy, and maternal age at delivery. Model 2 adjusted for the same variables as Model 1, as well as child sleep disturbances at each time point. Model 2 excluded the 134-month time point from analyses for the outcomes of sleep duration and daytime exhaustion as data on child sleep disturbances was not available at this time point.

Online-only Supplement

Online-only figures

Supplemental eFigure1. Directed Acyclic Graph

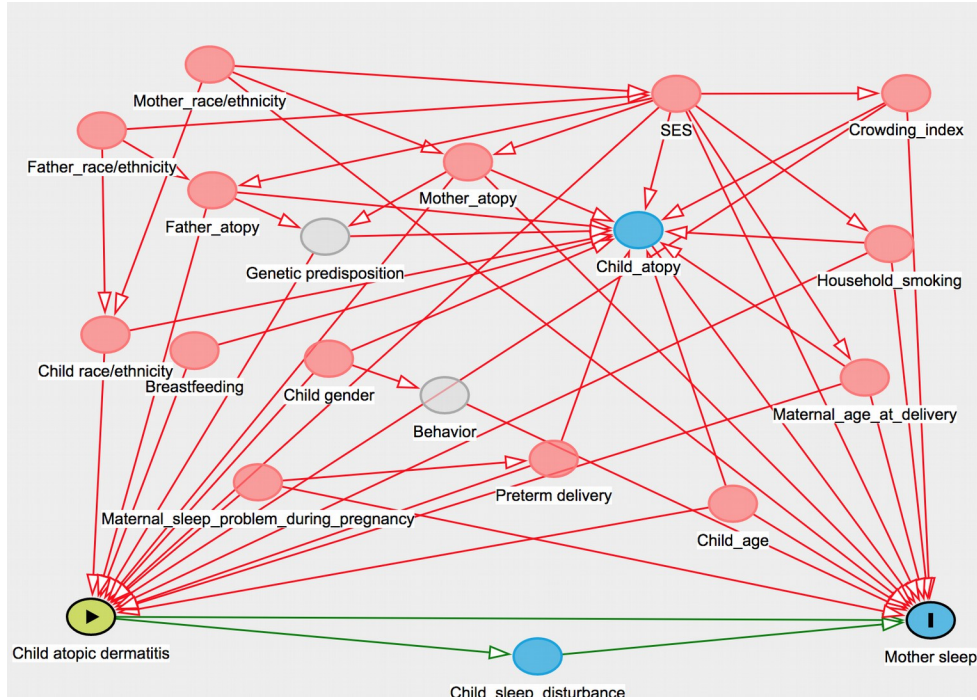
Online-only tables

Supplemental eTable1. Unadjusted odds of sleep disturbances among mothers of children with active atopic dermatitis by child age compared to mothers of children who never reported atopic dermatitis

Supplemental eTable2. Odds and 95% confidence intervals for maternal sleep disturbances across time points among mothers of children with active atopic dermatitis according to disease severity compared to mothers of children who never reported atopic dermatitis (non-imputed data)

Supplemental eTable3. Odds and 95% confidence intervals for maternal sleep disturbances across time points among mothers of children with active atopic dermatitis according to disease severity compared to mothers of children who never reported atopic dermatitis (imputed data)

Supplemental eFigure1. Directed Acyclic Graph



eFigure1: Directed acyclic graph representing relationships between covariates and primary predictor and outcome. Red circles represent ancestors of the exposure and outcome (i.e. confounders), blue circles represent ancestors of the outcome (i.e. causal determinants of the outcome), and grey circles represent unobserved (i.e. latent) variables. Green lines represent causal paths, and red lines represent biasing paths. The minimally sufficient adjustment set (MSAS) was determined using DAGitty, a software for creating causal diagrams to minimize confounding bias in epidemiology.³⁴ Child atopy (asthma or allergic rhinitis) was considered to be a collider which was appropriately accounted for by adjusting for additional variables contained on the backdoor paths shared by this collider. The final MSAS was determined to be the following: child gender, child age, mother race/ethnicity, maternal age at delivery, social class, maternal education, financial difficulties score, crowding index, presence of comorbid atopic diseases in the child (asthma or allergic rhinitis), maternal history of any atopic condition (atopic dermatitis, asthma, or allergic rhinitis), household smoking exposure, and maternal sleep problems during pregnancy.

Supplemental eTable1. Unadjusted odds of sleep disturbances among mothers of children with active atopic dermatitis by child age compared to mothers of children who never reported atopic dermatitis

Child age	Sleep duration < 6 hours per night	Early morning awakening	Difficulty falling asleep	Subjectively insufficient sleep	Daytime exhaustion
	Odds Ratio (95% Confidence Interval)				
21 months	0.96 (0.78 - 1.18)	1.20 (1.01 - 1.42)	1.09 (0.90 - 1.33)	1.37 (1.20 - 1.57)	1.55 (1.26 - 1.90)
33 months	1.14 (0.92 - 1.42)	1.09 (0.91 - 1.30)	1.11 (0.89 - 1.38)	1.43 (1.24 - 1.65)	1.33 (1.06 - 1.68)
47 months	-	-	-	-	1.37 (1.06 - 1.78)
61 months	1.06 (0.82 - 1.38)	1.17 (0.96 - 1.43)	1.17 (0.91 - 1.50)	1.29 (1.09 - 1.52)	1.79 (1.31 - 2.44)
73 months	-	-	-	-	0.97 (0.72 - 1.31)
85 months	1.15 (0.86 - 1.55)	-	-	1.38 (1.15 - 1.65)	-
110 months	-	-	-	-	1.28 (0.82 - 2.00)
134 months	1.02 (0.62 - 1.69)	-	-	-	1.60 (1.12 - 2.27)

eTable1: For each of the maternal sleep outcomes, results from unadjusted logistic regression models examining the association between child active atopic dermatitis and maternal sleep outcomes based on cross-sectional data at different child ages.

Supplemental eTable2. Odds and 95% confidence intervals for maternal sleep disturbances across time points among mothers of children with active atopic dermatitis according to disease severity compared to mothers of children who never reported atopic dermatitis (non-imputed data)

	Child atopic dermatitis disease activity and severity	Sleep duration < 6 hours*	Early morning awakening	Difficulty falling asleep	Subjectively insufficient sleep	Daytime exhaustion*
	Never reported atopic dermatitis	Ref.	Ref.	Ref.	Ref.	Ref.
Unadjusted	No problem	0.68 (0.48 - 0.95)	1.18 (0.83 - 1.66)	0.91 (0.61 - 1.36)	1.28 (1.01 - 1.62)	1.10 (0.78 - 1.53)
	Mild	0.70 (0.59 - 0.84)	1.07 (0.89 - 1.28)	1.02 (0.83 - 1.24)	1.33 (1.17 - 1.51)	1.22 (1.01 - 1.48)
	Moderate	1.02 (0.81 - 1.28)	1.16 (0.92 - 1.47)	1.31 (1.02 - 1.68)	1.36 (1.15 - 1.61)	1.42 (1.11 - 1.80)
	Severe	1.49 (1.02 - 2.16)	1.79 (1.20 - 2.67)	1.55 (1.00 - 2.40)	1.92 (1.42 - 2.61)	1.92 (1.32 - 2.79)
Model 1	No problem	0.86 (0.59 - 1.27)	1.09 (0.73 - 1.62)	1.13 (0.70 - 1.82)	1.27 (0.98 - 1.65)	1.19 (0.82 - 1.73)
	Mild	0.95 (0.79 - 1.15)	1.03 (0.82 - 1.30)	1.29 (0.96 - 1.73)	1.34 (1.17 - 1.54)	1.39 (1.12 - 1.74)
	Moderate	1.06 (0.82 - 1.36)	1.06 (0.80 - 1.39)	1.53 (1.10 - 2.12)	1.31 (1.09 - 1.57)	1.38 (1.06 - 1.81)
	Severe	1.61 (1.05 - 2.48)	1.53 (0.96 - 2.45)	1.53 (0.90 - 2.58)	1.89 (1.34 - 2.66)	1.72 (1.12 - 2.64)
Model 2	No problem	0.84 (0.55 - 1.29)	1.17 (0.79 - 1.74)	1.12 (0.70 - 1.81)	1.32 (1.01 - 1.71)	1.16 (0.78 - 1.73)
	Mild	0.92 (0.74 - 1.15)	1.01 (0.80 - 1.26)	1.24 (0.92 - 1.66)	1.37 (1.19 - 1.57)	1.42 (1.12 - 1.79)
	Moderate	1.03 (0.78 - 1.36)	1.01 (0.76 - 1.33)	1.49 (1.07 - 2.07)	1.30 (1.08 - 1.56)	1.43 (1.07 - 1.89)
	Severe	1.60 (1.01 - 2.54)	1.47 (0.91 - 2.36)	1.51 (0.89 - 2.56)	1.76 (1.23 - 2.50)	1.80 (1.15 - 2.82)

eTable2: For each of the maternal sleep outcomes, results from an unadjusted and two separate adjusted multivariable mixed models examining the association between child atopic dermatitis disease severity and maternal sleep disturbances at multiple time points. Model 1 adjusted for child gender, child age, mother race/ethnicity, child atopy (asthma and/or allergic rhinitis), household smoking exposure, maternal education, social class, crowding index, financial difficulties score, maternal sleep problems during pregnancy, maternal atopy, and maternal age at delivery. Model 2 adjusted for the same variables as Model 1, as well as child sleep disturbances at each time point. * Model 2 excluded the 134-month time point from analyses for the outcomes of sleep duration and daytime exhaustion as data on child sleep disturbances was not available at this time point. Results using non-imputed original data.

Supplemental eTable3. Odds and 95% confidence intervals for maternal sleep disturbances across time points among mothers of children with active atopic dermatitis according to disease severity compared to mothers of children who never reported atopic dermatitis (imputed data)

	Child atopic dermatitis disease activity and severity	Sleep duration < 6 hours*	Early morning awakening	Difficulty falling asleep	Subjectively insufficient sleep	Daytime exhaustion*
	Never reported atopic dermatitis	Ref.	Ref.	Ref.	Ref.	Ref.
Unadjusted	No problem	0.89 (0.71 - 1.11)	1.12 (0.92 - 1.36)	1.00 (0.79 - 1.28)	1.20 (1.04 - 1.37)	1.19 (0.97 - 1.45)
	Mild	0.90 (0.81 - 1.01)	1.08 (0.97 - 1.20)	1.11 (0.98 - 1.25)	1.24 (1.14 - 1.34)	1.31 (1.18 - 1.45)
	Moderate	1.08 (0.91 - 1.27)	1.13 (0.98 - 1.30)	1.23 (1.05 - 1.45)	1.27 (1.14 - 1.40)	1.43 (1.22 - 1.67)
	Severe	1.28 (1.00 - 1.65)	1.36 (1.06 - 1.75)	1.34 (1.01 - 1.78)	1.49 (1.26 - 1.76)	1.64 (1.28 - 2.08)
Model 1	No problem	1.01 (0.81 - 1.27)	1.13 (0.92 - 1.39)	1.06 (0.82 - 1.38)	1.21 (1.06 - 1.39)	1.22 (0.99 - 1.50)
	Mild	1.01 (0.90 - 1.13)	1.07 (0.96 - 1.19)	1.14 (1.00 - 1.30)	1.24 (1.14 - 1.35)	1.34 (1.21 - 1.49)
	Moderate	1.11 (0.94 - 1.32)	1.11 (0.95 - 1.28)	1.25 (1.05 - 1.48)	1.24 (1.11 - 1.37)	1.43 (1.21 - 1.67)
	Severe	1.28 (0.99 - 1.65)	1.31 (1.01 - 1.68)	1.29 (0.96 - 1.73)	1.44 (1.21 - 1.72)	1.60 (1.25 - 2.04)
Model 2	No problem	1.00 (0.79 - 1.28)	1.13 (0.91 - 1.39)	1.06 (0.82 - 1.37)	1.21 (1.05 - 1.39)	1.17 (0.94 - 1.45)
	Mild	0.99 (0.87 - 1.12)	1.07 (0.96 - 1.19)	1.14 (1.00 - 1.30)	1.24 (1.14 - 1.34)	1.32 (1.18 - 1.48)
	Moderate	1.10 (0.93 - 1.31)	1.10 (0.95 - 1.28)	1.24 (1.05 - 1.47)	1.22 (1.10 - 1.36)	1.39 (1.19 - 1.64)
	Severe	1.27 (0.99 - 1.63)	1.29 (1.00 - 1.66)	1.28 (0.95 - 1.71)	1.41 (1.19 - 1.68)	1.57 (1.23 - 2.02)

eTable3: For each of the maternal sleep outcomes, results from an unadjusted and two separate adjusted multivariable generalized estimating equation (GEE) models examining the association between child atopic dermatitis disease severity and maternal sleep disturbances at multiple time points. Model 1 adjusted for child gender, child age, mother race/ethnicity, child atopy (asthma and/or allergic rhinitis), household smoking exposure, maternal education, social class, crowding index, financial difficulties score, maternal sleep problems during pregnancy, maternal atopy, and maternal age at delivery. Model 2 adjusted for the same variables as Model 1, as well as child sleep disturbances at each time point. * Model 2 excluded the 134-month time point from analyses for the outcomes of sleep duration and daytime exhaustion as data on child sleep disturbances was not available at this time point. Results using imputed data. Due to the extremely large size of the imputed dataset, mixed models were not computationally feasible and GEE models were used instead. Robust standard errors were used in the GEE models.

