Sleep Disturbances in Adults with Eczema Are Associated with Impaired Overall Health: A US Population-Based Study

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Sleep disturbances are associated with poor health outcomes in adults. However, little is known about the sleep disturbances that occur in adult eczema. We studied the association between adult eczema and sleep disturbance and their impact on overall health and health care utilization. We used the 2012 National Health Interview Survey, a cross-sectional questionnaire of 34,613 adults. Eczema was associated with higher odds of fatigue (odds ratio (95% confidence interval): 2.97 (2.65–3.34)), regular daytime sleepiness (2.66 (2.34–3.01)), and regular insomnia (2.36 (2.11–2.64)), even after controlling for sleep duration, history of allergic disease, sociodemographics, and body mass index. There were significant interactions between eczema and fatigue, sleepiness, and insomnia as predictors of poorer overall health status, number of sick days, and doctor visits, such that eczema and each of the sleep symptoms were associated with higher odds of poorer outcomes than either eczema or sleep symptoms alone. Latent class analysis was used and identified five classes of fatigue, sleep disturbances, and allergic disorders. Two classes had high probabilities of eczema: one with high probabilities of asthma, hay fever, food allergy, and multiple sleep symptoms and the other with intermediate probability of insomnia alone. Future studies are warranted to better characterize sleep loss in eczema and develop strategies for treatment and prevention.

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INTRODUCTION

Sleep disorders are associated with poor performance in school and work, impaired overall health and safety, and considerable economic burden (Skaer and Sclar, 2010). Eczema is a common inflammatory skin condition that causes significant morbidity secondary to severe itch, sleep impairment, social embarrassment, and psychological distress (Carroll *et al.*, 2005). Sleep disturbance is attributed to the intense pruritus; it results in functional impairment (daytime fatigue, irritability, disturbed cognition, and decreased motor performance) and profoundly worsens the quality of life (QOL) in eczema patients (Bender *et al.*, 2003; Beattie and Lewis-Jones, 2006; Ricci *et al.*, 2007; Beikert *et al.*, 2014). Having eczema and concurrent sleep disturbance also significantly increases the risk of psychological disorders (Romanos *et al.*, 2010; Schmitt *et al.*, 2011), motor vehicle accidents, and workplace injury (Young *et al.*, 1997; Akerstedt *et al.*, 2002; Gander *et al.*, 2005).

Previous studies have demonstrated significantly worsened sleep quality in childhood eczema with less sleep, more frequent and prolonged awakening, and overall lower sleep efficiency (Monti *et al.*, 1989; Dahl *et al.*, 1995; Stores *et al.*, 1998; Chamlin *et al.*, 2005; Hon *et al.*, 2008; Camfferman *et al.*, 2010; Anuntaseree *et al.*, 2012; Camfferman *et al.*, 2013; Chang *et al.*, 2013). However, few studies have addressed the quality of sleep in the adult eczema population. Further, little is known about how different patterns of sleep disturbance affect the overall health in affected adults. Better understanding of the impact of adult eczema on sleep patterns could lead to new treatment and improve QOL. We hypothesized that adult eczema in the United States is associated with fatigue and disturbance of sleep patterns, which worsen overall health, independent of allergic airway disease.

RESULTS

Prevalence of eczema and other atopic disorders

Data were collected on 34,613 adults, representing all age, gender, and racial/ethnic groups. The US prevalence (95%

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Abbreviations: AD, atopic dermatitis; aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio

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confidence intervals (CIs)) of eczema in adults was 7.2% (6.9–7.6%). Eight percent (7.6–8.4%) currently had asthma, 7.5% (7.1–7.9%) had hay fever, 11.2% (10.8–11.7%) had respiratory allergies, and 3.9% (3.6–4.2%) had food or digestive allergies.

Prevalence of eczema was significantly associated with female sex (survey logistic regression; crude odds ratio (OR) (95% CIs): 1.52 (1.36–1.70)) and post-high school education (1.37 (1.13–1.66)) but inversely associated with African-American race (0.82 (0.70–0.96)), Hispanic origin (0.73 (0.62–0.85)), household income of $75,000–99,999 (0.76 (0.61–0.95)), families with children and either a single parent (0.79 (0.67–0.94)) or both parents living in the household (0.76 (0.65–0.89)) compared with those that had no children, and birthplace outside the United States (0.63 (0.54–0.73)). Prevalence was not associated with age (Table 1). Class II and III obesity, as defined by body mass index (BMI) of 35–39 and ⩾40, respectively, was also associated with eczema (class II: 1.31 (1.04–1.64); class III: 1.49 (1.18–1.88)).

Prevalence of fatigue and sleep disturbances

The 1-year prevalence of self-reported fatigue or lack of energy for more than 3 days was 15.8% (15.0–16.0%). Frequent excessive daytime sleepiness was described in 12.8% (12.3–13.2%), and 19.3% (18.8–19.9%) reported regularly having insomnia or trouble sleeping. Among adults who reported having regular insomnia, 43.6% (42.1–45.1%) also reported fatigue, and 36.8% (35.3–38.2%) had daytime sleepiness.

Prevalence of having more than 3 days of fatigue, regular daytime sleepiness, and/or insomnia was associated with age 50–69 (1.42 (1.29–1.55)) and ⩾70 years (1.59 (1.43–1.76)), female sex (1.67 (1.57–1.78)), and lower household income ($0–34,999: 2.15 (1.95–2.36); $35,000–74,999: 1.55 (1.40–1.71); $75,000–99,999: 1.19 (1.05–1.36)) and inversely associated with African–American (0.80 (0.74–0.87)) and Asian race (0.52 (0.45–0.60)), Hispanic origin (0.80 (0.74–0.87)), single (0.81 (0.74–0.89)) or multiple (0.67 (0.62–0.73)) children in the household, post-high school education (0.84 (0.76–0.92)), families that had children and either a single parent (0.83 (0.76–0.90)) or both parents in the household (0.60 (0.55–0.66)), and birthplace outside the United States (0.62 (0.57–0.67)). There was a U-shaped distribution of fatigue, daytime sleepiness, and/or insomnia associated with BMI, such that both, being underweight (1.57 (1.24–1.98)) and being obese (class I: 1.30 (1.19–1.42); class II: 1.90 (1.69–2.15); class III: 2.59 (2.25–2.99)), were associated with a higher prevalence of fatigue and sleep disturbance.

Association between eczema and sleep duration

History of eczema in the past year was associated with significantly higher odds of both short (1.35 (1.20–1.51)) and long (1.44 (1.19–1.74)) sleep duration (Table 2). These associations remained significant in multivariate models that controlled for the history of asthma, hay fever, respiratory allergy, food or digestive allergy, age, sex, race, Spanish origin, household income, level of education, US birthplace, number of children in the home, family structure, and BMI.

Association between eczema, fatigue, and sleep disturbance

Adults with eczema had a higher 1-year prevalence of fatigue (5,580,472 people or 32.8% (30.4–35.2%)), regular daytime sleepiness (4,430,186 people or 26.0% (23.8–28.3%)), and insomnia (5,847,404 people or 34.4% (32.0–36.8%)) compared with those without eczema (27.5% (26.9–28.1%); Table 2). In particular, eczema was associated with higher odds of fatigue (OR (95% CIs): 2.97 (2.65–3.34)), regular daytime sleepiness (OR (95% CIs): 2.66 (2.34–3.01)), and regular insomnia (OR (95% CIs): 2.36 (2.11–2.64)). These associations remained significant in multivariate models that included the above-mentioned atopic disorders, sociodemographics, and BMI, as well as sleep duration (Table 2).

Significant two-way interactions were found between symptoms of insomnia and fatigue/daytime sleepiness and between insomnia and sleep duration. Therefore, contrast statements were used to generate estimates for OR and 95% CIs at each level of combination. Odds of eczema were higher in subjects with either fatigue/daytime sleepiness (2.67 (2.28–3.13)) or insomnia (1.96 (1.65–2.34)) and highest with both fatigue/daytime sleepiness and insomnia (3.61 (3.15–4.12); Table 2). Adults with insomnia had higher odds of eczema for all sleep durations (3–6 hours: 2.38 (2.05–2.76); 7–8 hours: 2.40 (2.02–2.85); 9–14 hours: 3.72 (2.73–5.05)). These interactions remained significant in multivariate models. In contrast, adults without insomnia did not have significant interactions with sleep duration as predictors of eczema.

There were no significant differences of association between eczema, asthma and/or hay fever, and sleep disturbance in obese (class I–III) versus normal weight adults (data not shown).

Association between eczema, fatigue, sleep disturbance, and overall health status

In univariate models, eczema (OR (95% CIs): 1.98 (1.74–2.26)), fatigue (6.21 (5.70–6.76)), daytime sleepiness (4.71 (4.29–5.16)), and insomnia (3.99 (3.68–4.33)) were all significant predictors of having only fair/poor overall health. However, there were significant two-way interactions between eczema and fatigue and sleep disturbances. In models of interaction between eczema and fatigue, eczema alone was associated with fair/poor health (OR (95% CIs): 1.29 (1.07–1.56)), whereas fatigue without eczema was associated with higher odds of fair/poor health (OR (95% CIs): 5.93 (5.42–6.50)); those with both eczema and fatigue had even higher odds of fair/poor health (OR (95% CIs): 8.63 (7.15–10.43); Table 3).

Similarly, in models of interaction between eczema and regular daytime sleepiness or insomnia, eczema alone was consistently associated with fair/poor health; regular daytime sleepiness or insomnia without eczema had even higher odds of fair/poor health; and both regular daytime sleepiness or insomnia and eczema had the highest odds of fair/poor health.

Associations between eczema, sleep disturbances, and number of sick days and doctor visits

Significant two-way interactions were found between eczema and sleep disturbances as predictors of the number of missed

Table 1. Determinants of eczema and sleep problems in adults ($n = 34,613$)

Variable—no. (%)	Eczema			Fatigue, daytime sleepiness, or insomnia		
	% Prev (95% CI)	Crude OR (95% CI)	*P*-value	% Prev (95% CI)	Crude OR (95% CI)	*P*-value
Age (years)						
18–29	6.6 (5.8–7.4)	1.00	—	25.6 (24.1–27.0)	1.00	—
30–49	7.4 (6.7–8.0)	1.12 (0.96–1.31)	0.14	26.2 (25.2–27.2)	1.03 (0.94–1.14)	0.47
50–69	7.6 (7.0–8.3)	1.17 (1.00–1.37)	0.05	32.7 (31.6–33.8)	1.42 (1.29–1.55)	<0.0001
⩾70	6.9 (6.0–7.8)	1.05 (0.87–1.27)	0.59	35.3 (33.6–37.0)	1.59 (1.43–1.76)	<0.0001
Sex						
Male	5.8 (5.3–6.3)	1.00	—	23.8 (22.9–24.6)	1.00	—
Female	8.6 (8.0–9.1)	1.52 (1.36–1.70)	<0.0001	34.3 (33.4–35.2)	1.67 (1.57–1.78)	<0.0001
Race						
Caucasian	7.4 (7.0–7.8)	1.00	—	30.4 (29.7–31.1)	1.00	—
African American	6.1 (5.3–7.0)	0.82 (0.70–0.96)	0.01	25.9 (24.4–27.4)	0.80 (0.74–0.87)	<0.0001
American Indian	8.2 (5.0–11.4)	1.12 (0.73–1.72)	0.59	34.3 (28.3–40.2)	1.20 (0.92–1.56)	0.19
Asian	6.6 (5.3–8.0)	0.89 (0.71–1.11)	0.31	18.4 (16.3–20.5)	0.52 (0.45–0.60)	<0.0001
Multiracial/other	13.3 (6.7–20.0)	1.93 (1.08–3.44)	0.03	29.3 (20.7–37.9)	0.95 (0.63–1.44)	0.81
Hispanic origin						
No	7.5 (7.1–7.9)	1.00	—	29.9 (29.2–30.6)	1.00	—
Yes	5.6 (4.8–6.3)	0.73 (0.62–0.85)	<0.0001	25.5 (24.0–26.9)	0.80 (0.74–0.87)	<0.0001
Household income (× $1,000)						
0–34	7.3 (6.8–7.9)	0.97 (0.83–1.12)	0.65	36.8 (35.8–37.8)	2.15 (1.95–2.36)	<0.0001
35–74	7.8 (7.1–8.5)	1.03 (0.88–1.21)	0.72	29.6 (28.4–30.7)	1.55 (1.40–1.71)	<0.0001
75–99	5.9 (4.9–6.8)	0.76 (0.61–0.95)	0.01	24.5 (22.6–26.3)	1.19 (1.05–1.36)	0.008
⩾100	7.6 (6.7–8.5)	1.00	—	21.4 (20.0–22.7)	1.00	—
Children in household						
None	7.8 (7.3–8.2)	1.00	—	31.4 (30.7–32.2)	1.00	—
Single	6.3 (5.4–7.2)	0.80 (0.68–0.94)	0.008	27.2 (25.5–28.9)	0.81 (0.74–0.89)	<0.0001
Multiple	6.1 (5.4–6.9)	0.78 (0.67–0.90)	0.0009	23.5 (22.2–24.8)	0.67 (0.62–0.73)	<0.0001
Highest level of household education						
<High school	5.8 (4.8–6.7)	1.00	—	33.1 (31.2–35.0)	1.00	—
High school or GED	5.7 (5.0–6.3)	0.98 (0.79–1.22)	0.85	31.4 (30.0–32.7)	0.92 (0.83–1.03)	0.15
>High school	7.7 (7.2–8.2)	1.37 (1.13–1.66)	0.001	29.2 (28.4–30.1)	0.84 (0.76–0.92)	0.0002
Family structure						
No children	7.8 (7.3–8.2)	1.00	—	31.4 (30.7–32.2)	1.00	—
Both parents	6.3 (5.4–7.2)	0.76 (0.65–0.89)	0.0004	21.6 (20.3–23.0)	0.60 (0.55–0.66)	<0.0001
Single parent	7.5 (4.6–10.4)	0.79 (0.67–0.94)	0.007	27.5 (25.8–29.1)	0.83 (0.76–0.90)	<0.0001
Other adult, no parents	6.0 (5.2–6.8)	0.96 (0.63–1.46)	0.84	34.7 (29.4–40.0)	1.16 (0.92–1.47)	0.22
Birthplace in the United States						
No	5.0 (4.3–5.6)	0.63 (0.54–0.73)	<0.0001	21.6 (20.3–22.8)	0.62 (0.57–0.67)	<0.0001
Yes	7.7 (7.3–8.1)	1.00	—	30.8 (30.1–31.5)	1.00	—
Body mass index						
<18.5	7.8 (4.9–10.6)	1.11 (0.74–1.67)	0.62	35.6 (30.4–40.9)	1.57 (1.24–1.98)	0.0002
18.5–24.9	7.1 (6.5–7.7)	1.00	—	26.1 (25.1–27.1)	1.00	—
25–29.9	6.6 (6.0–7.2)	0.93 (0.81–1.06)	0.29	26.2 (25.2–27.3)	1.01 (0.93–1.09)	0.87
30–34.9	7.3 (6.4–8.2)	1.04 (0.89–1.22)	0.63	31.4 (29.9–32.9)	1.30 (1.19–1.42)	<0.0001
35–39.9	9.0 (7.3–10.7)	1.31 (1.04–1.64)	0.02	40.2 (37.6–42.8)	1.90 (1.69–2.15)	<0.0001
⩾40	10.1 (8.2–12.1)	1.49 (1.18–1.88)	0.0009	47.8 (44.5–51.1)	2.59 (2.25–2.99)	<0.0001

Abbreviations: CI, confidence interval; GED, graduate equivalent degree; OR, odds ratio; Prev, prevalence.
Refusal to answer a particular question or response of ''don't know'' occurred for the questions pertaining to eczema in 25 (0.07%), fatigue in 20 (0.05%), daytime sleepiness in 14 (0.04%), insomnia in 9 (0.02%), current asthma in 37 (0.1%), hay fever in 25 (0.07%), respiratory allergies in 48 (0.1%) and digestive allergies in 37 (0.1%), age in 0 (0.0%), sex in 0 (0.0%), race in 0 (0.0%), Hispanic/Spanish origin in 0 (0.0%), household income in 1,928 (5.6%), highest level of education in the household in 69 (0.2%), US birthplace in 10 (0.03%), number of children in home in 0 (0.0%), family structure in 4 (0.01%), and body mass index in 1,361 (3.9%), respectively.

Table 2. Eczema as a predictor of sleep duration, fatigue, daytime sleepiness, and insomnia in adults ($n = 34,613$)

Variable		No eczema	Eczema				
		% Prev (95% CI)[1]	% Prev (95% CI)[2]	OR (95% CI)	*P*-value	aOR (95% CI)	*P*-value
Sleep duration (h)							
Short: 3–6		28.9 (28.2–29.5)	34.3 (31.9–36.7)	1.35 (1.20–1.51)	<0.0001	1.30 (1.14–1.79)	0.0001
Average: 7–8		62.8 (62.1–63.5)	55.2 (52.6–57.7)	1.00 (ref)	—	1.00 (ref)	—
Long: 9–14		8.3 (7.9–8.7)	10.5 (8.8–12.2)	1.44 (1.19–1.74)	0.0002	1.43 (1.14–1.79)	0.002
Fatigue							
No		85.9 (85.4–86.4)	67.2 (64.8–69.6)	1.00	—	1.00	—
Yes		14.1 (13.6–14.6)	32.8 (30.4–35.2)	2.97 (2.65–3.34)	<0.0001	2.23 (1.93–2.58)	<0.0001
Daytime sleepiness							
No		88.3 (87.8–88.7)	74.0 (71.7–76.2)	1.00	—	1.00	—
Yes		11.7 (11.3–12.2)	26.0 (23.8–28.3)	2.66 (2.34–3.01)	<0.0001	2.04 (1.75–2.38)	<0.0001
Insomnia overall							
No		81.8 (81.3–82.4)	65.6 (63.2–68.0)	1.00	—	1.00	—
Yes		18.2 (17.6–18.7)	34.4 (32.0–36.8)	2.36 (2.11–2.64)	<0.0001	1.83 (1.59–2.12)	<0.0001
Insomnia	*Fatigue*						
No	No	75.3 (74.7–75.9)	52.7 (50.1–55.3)	1.00	—	1.00	—
No	Yes	6.6 (6.2–6.9)	12.9 (11.1–14.7)	2.80 (2.34–3.35)	<0.0001	2.22 (1.80–2.74)	<0.0001
Yes	No	10.6 (10.2–11.0)	14.5 (12.7–16.3)	1.94 (1.66–2.28)	<0.0001	1.65 (1.35–2.00)	<0.0001
Yes	Yes	7.5 (7.1–7.9)	19.9 (17.9–21.9)	3.78 (3.28–4.35)	<0.0001	2.74 (2.28–3.29)	<0.0001
Insomnia	*Daytime sleepiness*						
No	No	76.5 (76.0–77.1)	55.5 (53.0–58.1)	1.00	—	1.00	—
No	Yes	5.3 (5.0–5.6)	10.1 (8.5–11.8)	2.63 (2.16–3.21)	<0.0001	2.22 (1.77–2.78)	<0.0001
Yes	No	11.7 (11.3–12.2)	18.4 (16.5–20.4)	2.17 (1.88–2.50)	<0.0001	1.78 (1.48–2.13)	<0.0001
Yes	Yes	6.4 (6.1–6.8)	15.9 (14.2–17.7)	3.42 (2.95–3.98)	<0.0001	2.47 (2.04–2.99)	<0.0001
Insomnia	*Sleep duration (h)*						
No	3–6	23.3 (22.6–24.0)	25.1 (22.4–27.9)	1.14 (0.97–1.32)	0.11	1.18 (0.98–1.41)	0.07
No	7–8	68.2 (67.5–68.9)	64.9 (61.8–68.0)	1.00	—	1.00	—
No	9–14	8.5 (8.1–9.0)	10.0 (8.0–12.0)	1.23 (0.97–1.56)	0.08	1.30 (0.99–1.71)	0.06
Yes	3–6	54.5 (52.9–56.1)	51.9 (47.6–56.1)	2.38 (2.05–2.76)	<0.0001	1.94 (1.63–2.32)	<0.0001
Yes	7–8	38.1 (36.5–39.7)	36.6 (32.5–40.8)	2.40 (2.02–2.85)	<0.0001	1.93 (1.57–2.37)	<0.0001
Yes	9–14	7.4 (6.5–8.3)	11.5 (8.6–14.4)	3.86 (2.83–5.26)	<0.0001	3.07 (2.08–4.51)	<0.0001

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio; Prev, prevalence.

Binary survey logistic regression models were constructed with sleep duration (3–6, 7–8, and 9–14 hours) and 1-year history of more than 3 days with fatigue or tiredness and regular daytime sleepiness and insomnia as the independent variables and 1-year history of eczema as the dependent variable. OR and 95% CIs were estimated. Multivariate logistic regression models were constructed that included current asthma, hay fever, respiratory and digestive allergies, age, race, Hispanic/Spanish origin, household income, highest level of education in the household, US birthplace, number of children in home, family structure, and body mass index. Models of fatigue, daytime sleepiness, and insomnia also included sleep duration as a covariate. A significant two-way interaction was found between insomnia and fatigue, daytime sleepiness, and sleep duration ($P<0.0001$). Contrast statements were used to estimate various combinations of insomnia, fatigue, daytime sleepiness, and sleep duration.

Refusal to answer a particular question or response of ''don't know'' occurred for the questions pertaining to eczema in 25 (0.07%), sleep duration in 497 (1.3%), fatigue in 20 (0.05%), daytime sleepiness in 14 (0.04%), insomnia in 9 (0.02%), current asthma in 37 (0.1%), hay fever in 25 (0.07%), respiratory allergies in 48 (0.1%) and digestive allergies in 37 (0.1%), age in 0 (0.0%), sex in 0 (0.0%), race in 0 (0.0%), Hispanic/Spanish origin in 0 (0.0%), household income in 1,928 (5.6%), highest level of education in the household in 69 (0.2%), US birthplace in 10 (0.03%), number of children in home in 0 (0.0%), family structure in 4 (0.01%), and body mass index in 1,361 (3.9%), respectively.

[1]Data are presented as the percent prevalence of sleep duration and/or disturbance in subjects with no history of eczema.

[2]Data are presented as the percent prevalence of sleep duration and/or disturbance in subjects with a history of eczema.

Table 3. Association between eczema and overall health status is related to sleep disturbance in adults ($n = 34,613$)

Variable	Eczema	Poor/fair vs. excellent/very good/good health				
		% Poor/fair (95% CI)	OR (95% CI)	*P*-value	aOR (95% CI)	*P*-value
Fatigue						
No	No	8.5 (8.1–8.9)	1.00	—	1.00	—
No	Yes	10.7 (9.0–12.5)	1.29 (1.07–1.56)	0.009	1.41 (1.13–1.76)	0.002
Yes	No	35.6 (33.8–37.3)	5.93 (5.42–6.50)	<0.0001	5.23 (4.68–5.85)	<0.0001
Yes	Yes	44.5 (40.0–49.0)	8.63 (7.15–10.43)	<0.0001	7.53 (5.97–9.49)	<0.0001
Sleepiness						
No	No	9.6 (9.2–10.0)	1.00	—	1.00	—
No	Yes	14.7 (12.7–16.8)	1.62 (1.37–1.92)	<0.0001	1.71 (1.40–2.09)	<0.0001
Yes	No	32.7 (30.8–34.6)	4.57 (4.15–5.05)	<0.0001	4.00 (3.55–4.50)	<0.0001
Yes	Yes	41.9 (36.9–46.9)	6.78 (5.49–8.36)	<0.0001	5.23 (4.08–6.71)	<0.0001
Insomnia						
No	No	9.0 (8.6–9.4)	1.00	—	1.00	—
No	Yes	12.9 (10.6–15.2)	1.50 (1.21–1.85)	0.0002	1.58 (1.26–1.99)	<0.0001
Yes	No	27.4 (25.9–28.0)	3.81 (3.49–4.16)	<0.0001	3.27 (2.95–3.62)	<0.0001
Yes	Yes	38.8 (34.8–42.9)	6.43 (5.37–7.68)	<0.0001	5.18 (4.12–6.51)	<0.0001

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.
Binary survey logistic regression models were constructed with overall health status as the dependent variable (fair/poor vs. excellent/very/good) and 1-year history of eczema and fatigue, daytime sleepiness, and/or insomnia as the independent variable. Significant interactions found between history of eczema and sleep disturbances. Contrast statements were used to estimate OR and 95% CIs at each level of interaction. Multivariate logistic regression models were constructed that included current asthma, hay fever, respiratory and digestive allergies, age, race, Hispanic/Spanish origin, household income, highest level of education in the household, US birthplace, number of children in home, family structure, body mass index, and sleep duration.
Refusal to answer a particular question or response of "don't know" occurred for the questions pertaining to eczema in 25 (0.07%), sleep duration in 497 (1.3%), fatigue in 20 (0.05%), daytime sleepiness in 14 (0.04%), insomnia in 9 (0.02%), overall health in 0 (0.0%), current asthma in 37 (0.1%), hay fever in 25 (0.07%), respiratory allergies in 48 (0.1%) and digestive allergies in 37 (0.1%), age in 0 (0.0%), sex in 0 (0.0%), race in 0 (0.0%), Hispanic/Spanish origin in 0 (0.0%), household income in 1,928 (5.6%), highest level of education in the household in 69 (0.2%), US birthplace in 10 (0.03%), number of children in home in 0 (0.0%), family structure in 4 (0.01%), and body mass index in 1,361 (3.9%), respectively.

workdays, days in bed, and doctor visits. Adults who had eczema as well as fatigue, daytime sleepiness, and/or insomnia had even higher numbers of missed workdays and days in bed than those with either eczema or fatigue/sleep disturbances (general linear models, $P<0.0001$ for all; Figure 1a–f). In contrast, adults with eczema and insomnia had a higher number of doctor visits than those with either eczema or insomnia ($P<0.0001$), but a similar number to those with fatigue or daytime sleepiness and no eczema ($P\geqslant0.66$; Figure 1g–i). Similar results were also found with the Wilcoxon rank sum test and Poisson regression models (data not shown).

We tested whether the association between eczema and overall health status is mediated by fatigue and/or sleep disturbance using three different approaches. All approaches indicated there was significant mediation (the Sobel test (95% CIs): 0.042 (0.038–0.046), $P<0.0001$; bootstrapping approach, indirect effects OR (95% CIs): 1.10 (1.09–1.11)), although only partial mediation ($\beta(yx,m)=0.02$, $P=0.003$; $R^2=0.002$). Similarly, partial mediation was found for the number of missed workdays (the Sobel test (95% CIs): 0.02 (0.015–0.027), $P<0.0001$; bootstrapping approach, indirect effects OR (95% CIs): 1.05 (1.03–1.07); $\beta(yx,m)=0.06$, $P=0.01$; $R^2=0.0003$) and doctor visits (the Sobel test (95% CIs): 0.28 (0.23–0.33), $P<0.0001$; bootstrapping approach, indirect effects OR (95% CIs): 1.92 (1.70–2.19); $\beta(yx,m)=1.02$, $P<0.0001$; $R^2=0.003$).

Latent class analysis of fatigue, sleep disturbance, and allergic disorders

LCA was used to identify patterns of fatigue, sleep disturbances, and allergic disorders. The best-fit model had five classes based on minimal Bayesian information criteria, corrected Akaike information criteria, and adjusted Bayesian information criteria (Supplementary Table 2 online). Conditional probabilities of having fatigue, sleep disturbance, or allergic disease in each class are plotted in Figure 2. Two classes had high probabilities of sleep disturbance (classes 3 and 4). Class 4 had high probabilities of eczema, asthma, hay fever, and food allergy, whereas class 3 had low probabilities of these disorders. Class 1 had an intermediate probability of insomnia but not fatigue or sleepiness; this group also had an intermediate probability of eczema. Class 2 included those with a high probability of hay fever and respiratory allergies but low probability of fatigue and sleep disturbances. Finally, class 5 included those with a low probability of fatigue, sleep disturbance, and allergic disease.

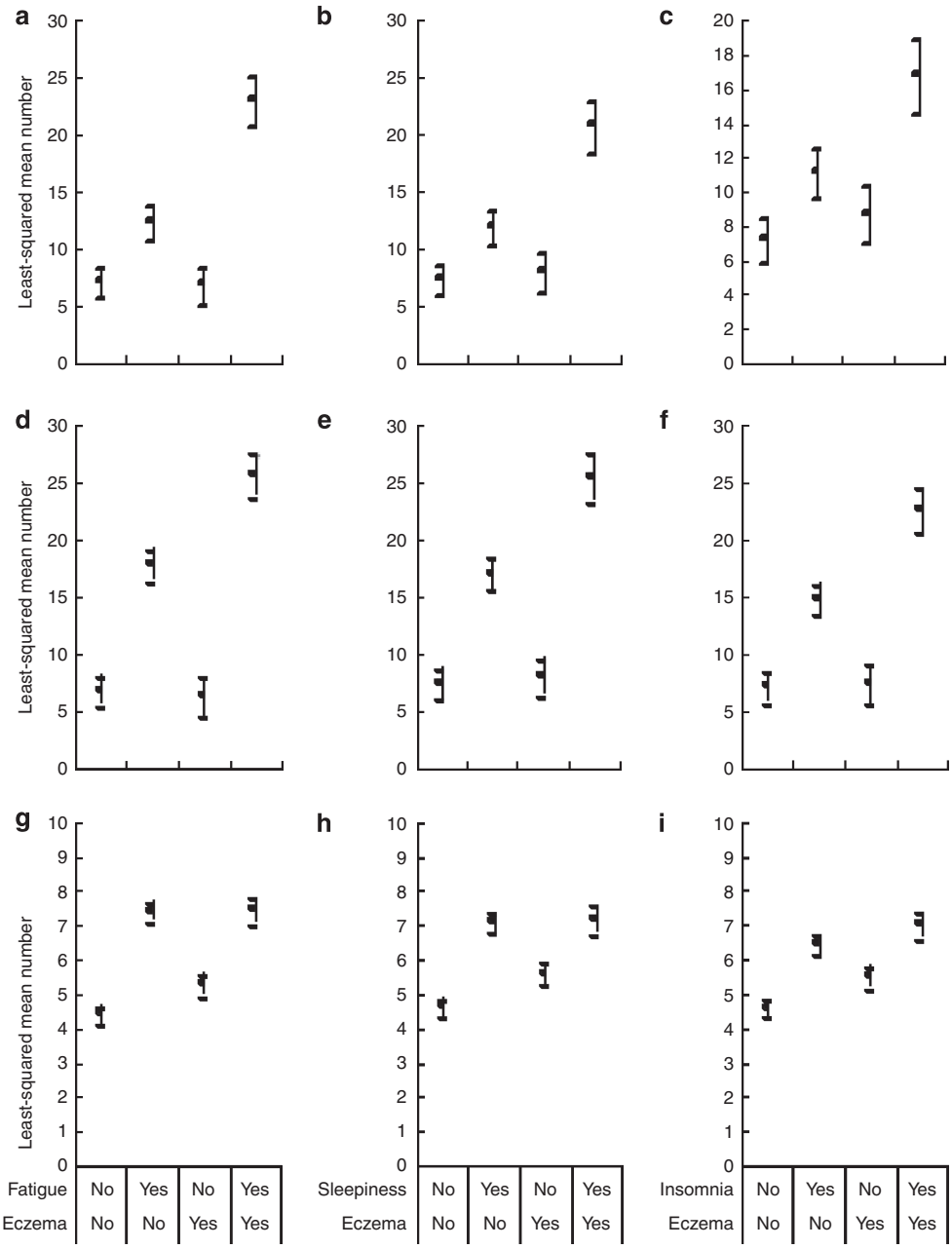

Figure 1. Association between eczema, sleep disturbance, and number of sick days, days in bed, and doctor visits. General linear models were constructed with number of sick days (**a**–**c**), days in bed (**d**–**f**), and doctor visits (**g**–**i**) as the dependent variables using a normal link function. The dependent variables were eczema, as well as fatigue (left column), daytime sleepiness (middle column), or insomnia (right column), and a two-way interaction term between them. *Post hoc* analyses were conducted of differences among the levels of one factor at a fixed level of the other factor. Least-square means (95% confidence intervals (CIs)) are plotted for each combination of factors included in the interaction effects. In addition, β values (95% CIs) for comparisons between each group and those without eczema or sleep disturbance are presented as text.

DISCUSSION

In the present study, we demonstrate that eczema in adults is associated with both short and long sleep durations. Short duration is likely due to difficulty falling asleep and premature awakening secondary to itch, whereas long duration is likely due to poor sleep efficiency, excessive fatigue, and sleepiness and perhaps the use of sedating antihistamines. Even after controlling for sleep duration, other atopic diseases, and sociodemographic factors, eczema was associated with fatigue, daytime sleepiness, and insomnia. In particular, adults with insomnia as well fatigue and/or daytime sleepiness had the highest odds of eczema. Adults with eczema were more likely to have fair/poor overall health, even without fatigue or sleep disturbances. However, the presence of fatigue or sleep

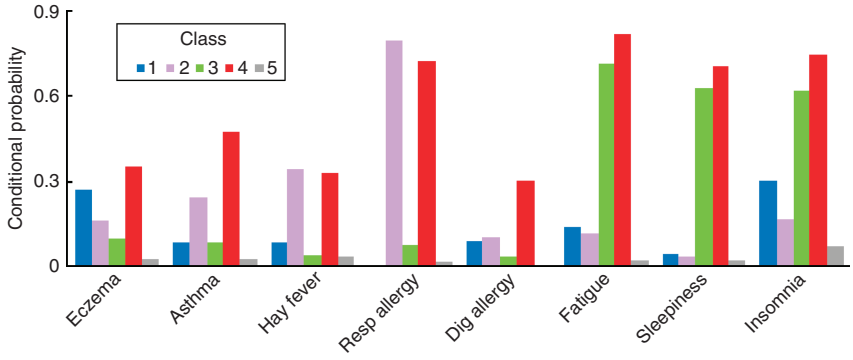

Figure 2. Conditional probability plot for sleep disturbance, eczema, and allergic disease within latent classes. Latent class analysis (LCA) was used to examine patterns of binary variables of sleep disturbance and the occurrence of eczema, asthma, hay fever, and respiratory and/or food (digestive (Dig)) allergy. LCA used the observed binary data to identify homogeneous patterns, i.e., $n=5$ latent classes. Conditional probabilities were estimated using maximum likelihood to characterize the latent classes. Conditional probability plots are presented, where probabilities closer to 0 or 1 indicate lower or higher chances, respectively.

disturbance and eczema led to significantly higher rates of self-reported fair/poor health, as well as higher numbers of missed workdays, days in bed, and doctor visits. The associations between eczema and poorer health outcomes were only partially mediated by fatigue and/or sleep disturbance, suggesting that there are additional factors at play. Finally, there were two distinct groups of subjects that had sleep disturbance with eczema: one with other allergic disease who had higher probabilities of insomnia, fatigue, and daytime sleepiness and the other with a higher probability of insomnia alone. Of note, there were other latent classes observed with similar probabilities of eczema and low probabilities of fatigue, insomnia, and/or sleepiness, indicating there are subsets of eczema without major sleep disturbances. Together, the results of this study suggest that adults with eczema have high rates of fatigue and sleep disturbances, which severely impact on overall health and increase health care utilization. With almost 9 million US adults with eczema reporting fatigue or sleep disturbance, our study demonstrates the considerable public health burden of eczema. A previous study of childhood atopic dermatitis (AD) found that having more severe disease was associated with increased health care utilization, including seeing a specialist and using more health-related services (Silverberg and Simpson, 2013). The results of the present study suggest that fatigue and sleep disturbances are major drivers of lost workdays and increased health care utilization and weigh heavily on the public health burden of eczema. It would therefore be prudent to improve our understanding of sleep disturbance in eczema and why some eczema patients are particularly affected by sleep problems, whereas others are not. Ultimately, this will lead to targeted interventions for prevention and treatment and improved care of eczema.

Previous smaller-scale studies also found high rates of sleep disturbances among adults with eczema (Bender *et al.*, 2003; Zuberbier *et al.*, 2006; Hanifin *et al.*, 2007; Bender *et al.*, 2008; Torrelo *et al.*, 2012). A case-control study of 14 eczema patients and 14 control patients without skin disease assessed sleep impairment using the Pittsburgh sleep quality index and actigraphy (Bender *et al.*, 2003). Questionnaires revealed lower sleep quality, more awakening, and daytime dysfunction among eczema patients. Similarly, actigraphic assessment revealed that eczema patients slept less, awoke more often, and spent more time awake during waking episodes, with resultant lower overall sleep efficiency (Bender *et al.*, 2003). Another study administered questionnaires, actigraphy, and polysomnography to 20 adult eczema patients and found that greater disease severity was associated with poorer sleep (Bender *et al.*, 2008). A multicenter questionnaire–based study from the International Study of Life with Atopic Eczema, including 1,098 adults, found that a typical AD flare disrupts the sleep of patients for an average of 8.4 nights per flare, which extrapolated to ~81 days per year per patient (Zuberbier *et al.*, 2006).

An important limitation of the above-mentioned studies is the lack of control for comorbid asthma and rhinoconjunctivitis, which are common confounding factors in adults with eczema (Silverberg and Hanifin, 2013) and can independently cause sleep disturbances. Approximately 40% of asthma patients experience night-time awakenings every night (Turner-Warwick, 1988), leading to shortened sleep duration and increased daytime sleepiness (Dales *et al.*, 1992; Fitzpatrick *et al.*, 1993; Janson *et al.*, 1996; Vir *et al.*, 1997; Craig *et al.*, 2004; Leger *et al.*, 2006; Mastronarde *et al.*, 2008). In addition, the prevalence of early morning awakenings and difficulty inducing sleep was twice as high, and the prevalence of daytime sleepiness 50% higher, in European asthmatic adults compared with non-asthmatics (Janson *et al.*, 1996). Similarly, allergic rhinitis sufferers experience interruption of the sleep cycle leading to increased daytime somnolence and decreased QOL, attributed to nasal obstruction and linked to increased night-time microarousals (Lavie *et al.*, 1981; Craig *et al.*, 2004; Leger *et al.*, 2006; Bender and Leung, 2005; Leger *et al.*, 2006). We now demonstrate an association between eczema, fatigue, and sleep disturbances, even after controlling for the history of respiratory allergies, as well as for food and digestive allergies and other potentially confounding sociodemographic factors. Moreover, LCA models revealed a

latent class of adults with eczema that had higher probability of insomnia even in the absence of other allergic disorders.

Allergic airway disorders that often accompany eczema, such as asthma and hay fever, are associated with obstructive sleep apnea (OSA) and its sequelae. A study of OSA syndrome found a higher risk of perennial allergic rhinitis (Canova *et al.*, 2004). Similarly, our study found significant associations between obesity and each of the sleep disturbances (consistent with OSA) in adults with asthma and hay fever. Yet, there were no such associations between obesity, sleep disturbances, and eczema, suggesting that the sleep disturbances in adult eczema patients were not due to OSA or comorbid airway disease. Rather, pruritus is likely the major contributor to sleep disturbance in eczema. Further studies are needed to identify the specific patterns of sleep disturbance in eczema and distinguish them from those found in atopic airway disorders.

Our results also confirm past observations in the United States (Karacan *et al.*, 1976) and Japan (Doi *et al.*, 2000) showing the association of sleep disturbance with female gender, older age, and lower household income. The lower prevalences of sleep disturbances among African-Americans, Asians, and Hispanics with eczema are consistent with previously described racial/ethnic differences in sleep disturbances regardless of eczema (Ruiter *et al.*, 2011; Ralls and Grigg-Damberger, 2012; Chapman *et al.*, 2013; Grandner *et al.*, 2013; Jackson *et al.*, 2013; Knutson, 2013; Pranathiageswaran *et al.*, 2013). They may be related to differential self-reporting and household income, and reflect socioeconomic differences of adult sleep patterns, including differences in sleep behavior and duration, social pressures and psychosocial stress, poor environmental conditions, noise, air, and light pollution, more nightshift work, etc. Future studies with objective measurements of sleep disturbance are needed to verify these associations.

Growing evidence suggests an association of eczema with obesity, including the results of our study. Obesity has previously been associated with increased prevalence and severity of eczema and higher prevalence of atopic asthma in 2,090 adults aged $\geqslant$19 (Silverberg *et al.*, 2012). Another study associated prolonged obesity ($>$2.5 years) in early childhood and increased odds and severity of eczema (Silverberg *et al.*, 2011), suggesting that obesity and its chronic pro-inflammatory effects (Jin and Flavell, 2013) may be a modifiable risk factor for eczema. In the present study, obesity was also associated with higher prevalence of eczema but not with greater sleep disturbances in eczema.

Eczema is known to have a significant and negative impact on health-related QOL (Bender *et al.*, 2003; Beattie and Lewis-Jones, 2006; Ricci *et al.*, 2007; Hon *et al.*, 2008; Beikert *et al.*, 2014), and our study supports this notion by demonstrating that sleep disturbance is a major driver of poor overall health status, lost workdays, and increased health care utilization. In 384 adult eczema patients, sleep disturbance was strongly associated with decreased QOL using Dermatology Life Quality Index (Beikert *et al.*, 2014). In childhood eczema, sleep disturbance was the second highest scoring item, alongside itching (Hon *et al.*, 2008). Other studies in children similarly demonstrate that sleep disturbance is among the top contributing factors to reduced QOL (Beattie and Lewis-Jones, 2006; Ricci *et al.*, 2007). Together, these studies suggest that interventions targeting sleep disturbance are of utmost importance and likely to improve the overall health and QOL of adults and children with eczema.

The present study found the 1-year prevalence of adult eczema to be 7.2%, which is lower than the 10.2% prevalence recently demonstrated by Silverberg and Hanifin (2013). There are a number of differences between the questions used to measure eczema prevalence in these studies. The question used in the study of Silverberg and Hanifin (a) did not specify health care diagnosis of eczema and (b) assessed for ''eczema, dermatitis, or red inflamed rash'', which is less specific but more sensitive than the question used in the present study. Of note, many adult eczema patients either underutilize or do not utilize health care for their eczema (data not shown). Thus, the health care-diagnosed eczema outcome used in the present study may introduce a selection bias toward those who have higher household income and greater access to health care and are more likely to utilize health care for their eczema. This may explain why the previously demonstrated inverse association between eczema prevalence and household income was not found in the present study. It is therefore possible that the present study actually underestimates the prevalence of sleep disturbances in US adults with eczema. Regardless, we believe that the eczema question used in this study is sufficiently sensitive and specific to examine the burden of sleep disturbances in adult eczema.

The mechanisms underlying the association between eczema and sleep disturbance are not fully understood. The itch-scratch cycle of eczema interferes with initiation and maintenance of sleep (Camfferman *et al.*, 2010). Actigraphy and infrared video evidence reveals fragmented sleep with increased scratch time and restless nocturnal movement in both adults and children with eczema (Camfferman *et al.*, 2010). In addition, evidence for circadian rhythm–induced modification of itch exists, as studies have shown greater transepidermal water loss at night time along with decreased cortisol secretion (Gupta and Gupta, 2013). Both processes may lead to increased night time itch and fragmented sleep. Inflammatory cytokines implicated in sleep regulation are also elevated in patients with allergy (Bender and Leung, 2005). However, patients with eczema, even when in clinical remission, exhibit more sleep impairment than do healthy patients (Reuveni *et al.*, 1999), suggesting a more complex etiology beyond itch and inflammatory pathway activation. In a study of five children with eczema, regular antihistamine use had no effect on sleep latency, total sleep time, or other sleep parameters, determined by polysomnography (Camfferman *et al.*, 2013). However, the role of learned abnormal sleeping patterns or medication use (e.g., antihistamines or corticosteroids, which may interfere with sleep-wake regulation) deserves exploration in larger-scale studies.

This study has several strengths, including having prospective data collection, US population-based, and having a very large, randomly sampled and diverse sample. In addition, the

study had sufficient numbers for subset analyses and was controlled for a large number of potential confounding factors using logistic regression. The use of latent class analysis (LCA) allowed for identification of two distinct patterns of sleep disturbance in adult eczema. The random sampling, large sample size across all states, with representation of a host of racial and ethnic groups and complex weighting indicate that the results are likely generalizable to the entire US population. However, this study has potential limitations. Eczema history was based on a self-report of health care diagnosis and neither assessed clinically nor verified with any diagnostic testing. The specific question used in this study has not been previously validated; however, self-report of eczema using other instruments has been validated and found to have good correlation with clinical exam (Susitaival *et al.*, 1995; Flohr *et al.*, 2009). Moreover, the waxing and waning course and more variable presentation of adult eczema argue in favor of a broader question related to the history of eczema in the past 12 months. Nevertheless, there may be more than one type of eczema in adults (Abuabara and Margolis, 2013) that are detected by the question used in this study, including irritant, allergic contact, and xerotic dermatitis. We do not consider this to be a limitation because adult eczema often has a variable phenotype compared with childhood eczema and may present with overlapping atopic, irritant, and/or allergic contact dermatitis, rather than flexural eczema alone (Katsarou and Armenaka, 2011; Silverberg, 2014). Previous studies found a strong correlation between self-report of fatigue and sleepiness and objective measures of sleep disturbance: i.e., actigraphy and polysomnography (Bender *et al.*, 2008; Braley *et al.*, 2012). Further, self-reported measures of sleep disturbance have been the mainstay of epidemiologic study of sleep in cardiovascular disease (Shankar *et al.*, 2010; Westerlund *et al.*, 2013), diabetes (Plantinga *et al.*, 2012), chronic kidney disease (Plantinga *et al.*, 2011), etc. Family history of eczema may be an important confounding factor but was not assessed in National health interview survey (NHIS). The accuracy of self-reported family history by adults with eczema has not previously been studied and, based on the authors' clinical experience, is likely not very reliable. Finally, the cross-sectional nature of the study does not allow for the determination of causality of the association between eczema and sleep. That is, eczema may cause sleep impairment or perhaps underlying sleep disorders trigger eczema in predisposed individuals. Future longitudinal studies with objective measures of sleep disturbance are needed to verify these associations.

In conclusion, adult eczema is associated with altered sleep duration, fatigue, and sleep disturbances, including daytime sleepiness and insomnia. Although adults with eczema were more likely to report fair/poor health, the presence of sleep disturbances in combination with eczema significantly increased the rates of fair/poor health. This study suggests that sleep disturbances weigh heavily on adults with eczema and that treatments targeting sleep loss are likely to improve the overall health of eczema patients. Future studies are warranted to better characterize sleep loss in eczema and develop strategies for treatment and prevention.

MATERIALS AND METHODS

National health interview survey

After approval by Northwestern University's institutional review board, data were assessed using 2012 NHIS, a database collected by the National Center for Health Statistics and the principal source of health information on US noninstitutionalized civilians. Waiver of informed consent was obtained by the National Center for Health Statistics, as the survey posed minimal risk and respondents were not identifiable by the recorded data. The survey included a separate questionnaire about adult health to estimate the prevalence of physical, emotional, and behavioral health issues. The survey was administered in-person to selected households by the Bureau of the Census using ~400 trained interviewers with computer-assisted personal interviewing in English and Spanish. Using data from the US Census Bureau, sample weights were created that factored age, sex, race, ethnicity, household size, and educational attainment of the most educated household member using a multi-stage area probability sampling design by NHIS. These sample weights are needed to provide nationally representative prevalence estimates for each state's population of noninstitutionalized adults. All frequency data are presented as raw values, whereas prevalence estimates presented reflect this complex weighting. Questions used in the survey pertaining to history of eczema, sleep problems, and overall health are listed in Supplementary Table 1 online.

All data processing and statistical analyses were performed in SAS version 9.3. Outlier detection was performed for sleep duration revealing that responses of $\geqslant$15 hours duration were outliers. Models that incorporated sleep duration were tested with and without the exclusion of outliers, and no significant differences were found. Therefore, we only present models that excluded outliers. Bivariate and multivariate analyses of survey responses were performed using SURVEY procedures. Bivariate associations were tested with Rao-Scott χ^2 tests. Multivariate logistic regression models were constructed for fatigue, daytime sleepiness, and insomnia (binary outcomes) using two different approaches. First, we included all significant predictors from bivariate analyses in the models. Two- and three-way interaction terms between other covariates were also tested. Our *a priori* hypothesis was that adult eczema is associated with specific patterns of insomnia with sleep duration, fatigue, and sleepiness. Therefore, models were constructed that tested interaction terms between insomnia and either sleep duration, fatigue, or daytime sleepiness. We used stepwise and backward selection for multivariate logistic regression models to determine whether eczema would be selected consistently as a predictor and identify other significant predictors of sleep problems. Adjusted ORs (aORs) and 95% CIs were determined.

Multivariate logistic regression models were also constructed with personal health status as the dependent variable. Personal health status was modeled as the binary dependent variable. This approach was used over ordinal logistic regressions because the data did not meet the proportional odds assumption (Score test, $P<0.01$). Our *a priori* hypothesis was that adults with eczema, fatigue, and sleep disturbances have worse overall health than those with eczema alone. Therefore, models were constructed that tested interaction terms between eczema and sleep problems. Significant predictors from bivariate analyses were also included in the models.

Number of sick days, days in bed, and doctor visits were modeled using generalized linear models with a normal (linear regression) and

log (poisson regression) link function in SAS PROC GLIMMIX. The independent variables were history of eczema, as well as fatigue, daytime sleepiness, or insomnia and a two-way interaction term between them. *Post hoc* analyses were conducted of differences among the levels of one factor at a fixed level of the other factor. Least-square means and aORs (95% CIs) were estimated for each combination of factors included in the interaction effects.

Two- and three-way interactions between other covariates were tested and included in the above models if *P*-value <0.01 and modification of estimates by $>20\%$. The best models were selected using the Bayesian information criterion, which penalizes for extra parameters and takes into account the large sample size. To test whether any associations between eczema and poor personal health status, lost workdays, and health care utilization were mediated by fatigue and/or sleep disturbance (composite binary variable), mediation was tested using the approaches of Baron and Kenny, the Sobel test, and the bootstrap method described by Preacher and Hayes ($n=5{,}000$ bootstrapping samples; Preacher and Hayes, 2008). Complete data analysis was performed, i.e., subjects with missing data were excluded.

LCA was performed in SAS as previously described (Yang *et al.*, 2012; Supplementary Methods online).

CONFLICT OF INTEREST

PCZ is a consultant for Merck, Jazz, Vanda, and Aptalis Pharmaceuticals and owns stock in Teva Pharmaceuticals. The remaining authors state no conflict of interest.

AUTHOR CONTRIBUTIONS

JIS had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. JIS, ASP, AF, and PCZ were responsible for study concept and design. JIS and NG were responsible for acquisition of data. JIS, NG, ASP, AF, and PCZ were responsible for analysis and interpretation of data. JIS, NG, ASP, AF, and PCZ were responsible for drafting of the manuscript. JIS, NG, ASP, AF, and PCZ were responsible for critical revision of the manuscript for important intellectual content. JIS and NG were responsible for statistical analysis.

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/jid

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