The Patient-Reported Disease Burden in Pediatric Patients with Atopic Dermatitis (AD): A Cross-Sectional Study in the United States (US), Canada, Europe, and Japan

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BACKGROUND

- Atopic dermatitis (AD) is a common inflammatory skin disease characterized by eczematous lesions, intense itch, and a chronic or relapsing disease course.
- AD negatively affects sleep, health-related quality of life (HRQoL), and overall health.[1]
- AD affects all age groups, although pediatric and adult AD may differ in terms of risk factors and clinical presentation, which is of importance for the impact of symptoms on the daily lives of children and their families.[2–6]
- AD typically manifests in early childhood between 2 months and 2 years of age.[7,8]
- Few multinational studies have previously published on the self-reported disease burden in children with AD.

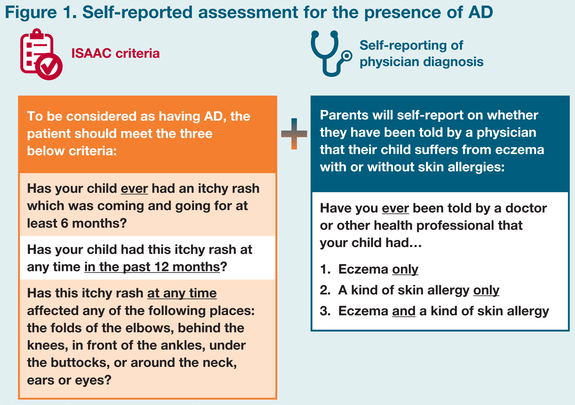
OBJECTIVE

- **This study aimed to assess the disease burden in children with AD aged 6–11 years, stratified by disease severity in the United States (US), Canada, Europe (France, Germany, Italy, Spain, and the United Kingdom [UK]), and Japan.**

METHODS

- This was a cross-sectional, web-based, self-report survey of children (aged 6–11 years) with AD conducted in the US, Canada, Europe, and Japan.
- The study was conducted in accordance with the European Pharmaceutical Market Research Association, Marketing Research Association, the British Healthcare Business Intelligence Association, and additional local country codes of conduct, as well as data protection legislation.
- Data were collected from September 26, 2018 to February 20, 2019.
- In each country, members of online panels (LightSpeed Health, all countries; Research Now/SSI, all countries; Toluna, all countries except Japan; AIP, Japan) who met the inclusion criteria (parents/guardians of children aged 6–11 years) received an e-mail invitation to participate in the survey. The e-mail did not mention skin disease or AD.
  - Members of online panels were recruited through broad-reach portals, special interest sites, and direct e-mailing campaigns.
  - All members:
    - agreed to be part of the online panel and their e-mail was confirmed through a double opt-in registration process
    - registered with demographic information, passed quality checkpoints, and agreed to country-specific terms and conditions and privacy policies.
- All parents/guardians provided informed consent prior to participation.
- The presence of diagnosed AD in the respondents was determined by means of the International Study of Asthma and Allergies in Childhood (ISAAC) criteria and through self-reported physician diagnosis of eczema (**Figure 1**).
- Patients with AD were stratified by disease severity (mild, moderate, or severe) in the past week based on Patient Global Assessment.

Figure 1. Self-reported assessment for the presence of AD



AD, atopic dermatitis; ISAAC, International Study of Asthma and Allergies in Childhood.

METHODS (CONT.)

- The following outcomes were captured during the survey:
  - Level of AD severity according to the Patient-Oriented Eczema Measure (POEM; 0–28, higher scores indicate worse disease severity).
  - Patient-reported worst itch and worst skin pain severity in the past 24 h,and overall sleep disturbance in the past 24 h, assessed with the Numerical Rating Scale (NRS; 0–10, higher scores indicate worse symptom severity).
  - HRQoL in the past 7 days assessed with the Children's Dermatology Life Quality Index (CDLQI; 0–30, higher scores indicate worse QoL).[9]
  - Presence of atopic comorbidities.
  - Total number of missed school days during the past 4 weeks.
- Parents responded to all survey questions, except for questions related to HRQoL, sleep, skin pain, and itch, when parents were asked to pass control to their child.
  - If parents agreed to pass control to their child, questions related to HRQoL (assessed with CDLQI), sleep, skin pain, and itch (assessed with NRS) were answered by the child.
- The response rate was determined based on the number of individuals who clicked on the survey link. To obtain a representative population for each country, quotas were set for numbers of respondents in specific categories relating to age and sex (https://www.census.gov), geographical regions (United States Census Bureau for US, Statistics Canada for Canada, Statistics Bureau of Japan for Japan, and Eurostat for Europe), and urban/rural split (United States Census Bureau for US and https://knoema.fr for Canada, Japan, and Europe).
  - When quota objectives were not met, a weighting adjustment was applied to obtain a representative population with respect to sociodemographic characteristics for each country.
- Descriptive analyses (mean, standard deviation [SD], median, and range) are provided for continuous variables, and data are presented as percentages for categorical variables. Z-test or t-test were used for comparisons between two groups and P<0.05 was taken to denote statistical significance.

RESULTS

- A total of 1681 children with AD were surveyed across the US, Canada, Europe, and Japan, stratified by disease severity (mild AD, n=1112; moderate AD, n=506; severe AD, n=63).
  - Parents of children with AD responded to all survey questions for 70.2–84.1% of survey responses across the US, Canada, Europe, and Japan, whereas children responded to HRQoL-related questions for 15.9–29.8% of survey responses.
- Baseline demographics for respondents with diagnosed AD were similar across disease severity levels. At the time of the survey, patients with diagnosed AD had a mean (SD) age of approximately 9.0 (1.7) years, and males and females were generally equally distributed (**Table 1**).
- Mean scores of itch (**Figure 2**), sleep disturbance (**Figure 3**), skin pain (**Figure 4**), and HRQoL (**Figure 5**) increased (ie, worse itch, sleep, skin pain, and HRQoL) with higher levels of AD severity.
- Children with severe AD reported up to 10.9 missed school days during the past 4 weeks, compared with 4.5 and 6.5 for those with mild and moderate AD, respectively (**Figure 6**).
- Overall, atopic comorbidities were reported more frequently among children with severe AD; hay fever and asthma were the most common (**Table 2**).

Limitations

- Potential misclassification and recall bias, as outcomes were based on self-report by parents/guardians (and children in some cases).
- Selection bias due to method of data collection (ie, online survey) and potential differences between individuals who agreed to participate and those who did not.

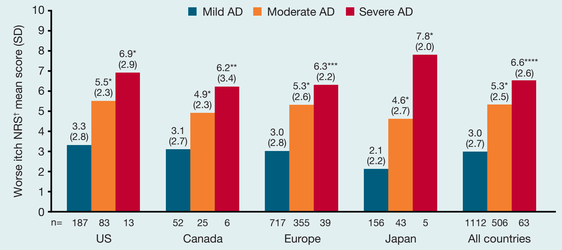
RESULTS (CONT.)

Table 2. Proportion of children with AD in the US, Canada, Europe, and Japan with self-reported history of atopic comorbidities, by disease severity

	US			Canada			Europe			Japan			All countries		
Proportion of patients by comorbidity, %	Mild AD (n=187)	Moderate AD (n=83)	Severe AD (n=13)	Mild AD (n=52)	Moderate AD (n=25)	Severe AD (n=6)	Mild AD (n=717)	Moderate AD (n=355)	Severe AD (n=39)	Mild AD (n=156)	Moderate AD (n=43)	Severe AD (n=5)	Mild AD (n=1112)	Moderate AD (n=506)	Severe AD (n=63)
≥1 atopic comorbidity	88.2	88.9	91.9	84.8	88.0	100.0	81.3	87.5***	94.3***	84.6	95.2	100	85.5	89.7***	93.9
Asthma	51.2	51.7	69.9	50.7	56.2	84.0	46.3	57.1*	66.5***	32.2	60.0*	59.7	46.6	55.3*	68.7****
Hay fever	60.1	63.9	69.9	59.3	35.6	65.4	57.5	68.0*	64.9	49.9	60.4	80.0	57.6	64.9*	68.2
Allergic rhinitis	28.9	30.0	46.1	24.8	8.0	16.3	25.6	35.5*	33.5	44.6	48.9	80.1	29.2	33.6	41.2***
Allergic conjunctivitis	13.8	12.8	15.1	18.9	0.0	34.7	17.0	20.6	33.9*	18.0	18.2	20.0	16.0	16.9	24.5
Seasonal allergies	54.5	48.8	53.8	40.2	39.7	32.4	35.1	48.2*	38.3	31.3	34.9	60.2	42.1	47.2	46.4
Food allergies	18.3	33.6*	54.2*	26.7	31.8	33.3	16.6	24.3*	21.4	20.6	32.2	80.1****	18.0	28.6*	40.8****
Chronic rhinosinusitis	8.5	11.7	22.1	11.5	0.0	16.1	4.2	5.8	8.9	8.8	6.9	20.0	6.6	7.9	16.1****
Nasal polyps	1.1	3.5	30.0**	9.2	0.0	0.0	2.6	3.7	7.2	0.0	0.0	20.0	1.9	3.2	17.9**
Eosinophilic esophagitis	1.1	1.3	31.0**	2.0	0.0	0.0	1.2	3.0***	5.9***	–	–	–	1.0	2.1	16.5**
Atopic kerato-conjunctivitis	0.5	5.0	7.0	1.9	0.0	0.0	2.1	2.1	4.7	0.0	0.0	20.0	1.3	3.0***	6.5*

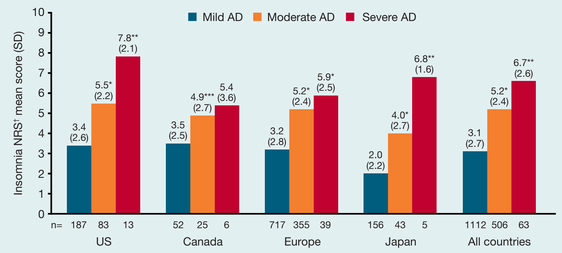
*P<0.01 compared with mild AD. **P<0.01 compared with mild AD and with moderate AD. ***P<0.05 compared with mild AD. ****P<0.01 compared with mild AD and P<0.05 compared with moderate AD.
AD, atopic dermatitis; US, United States.

Figure 2. Worst itch NRS mean scores (in the past 24 h) reported by children with AD in the US, Canada, Europe, and Japan, by disease severity



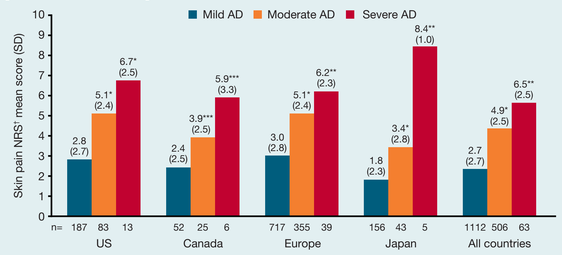
*P<0.01 compared with mild AD. **P<0.05 compared with mild AD. ***P<0.01 compared with mild AD and P<0.05 compared with moderate AD. ****P<0.01 compared with mild and with moderate AD.
†0–10, higher scores indicate worse itch severity.
AD, atopic dermatitis; NRS, Numerical Rating Scale; SD, standard deviation; US, United States.

Figure 3. Sleep disturbance NRS mean scores (in the past 24 h) reported by children with AD in the US, Canada, Europe, and Japan, by disease severity



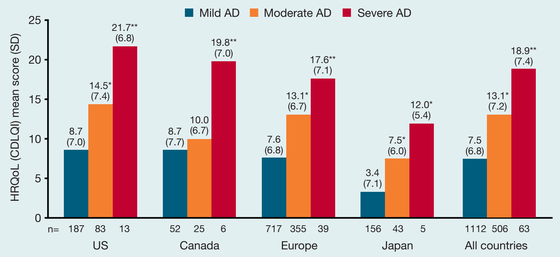
*P<0.01 compared with mild AD. **P<0.01 compared with mild AD and with moderate AD. ***P<0.05 compared with mild AD.
†0–10, higher scores indicate worse sleep severity.
AD, atopic dermatitis; NRS, Numerical Rating Scale; SD, standard deviation; US, United States.

Figure 4. Worst skin pain NRS mean scores (in the past 24 h) reported by children with AD in the US, Canada, Europe, and Japan, by disease severity



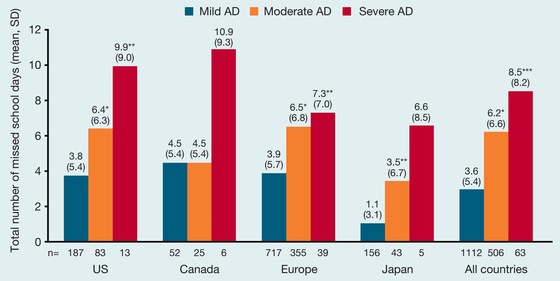
*P<0.01 compared with mild AD. **P<0.01 compared with mild AD and with moderate AD. ***P<0.05 compared with mild AD.
†0–10, higher scores indicate worse skin pain severity.
AD, atopic dermatitis; NRS, Numerical Rating Scale; SD, standard deviation; US, United States.

Figure 5. HRQoL in the past week assessed by CDLQI† mean score for children with AD in the US, Canada, Europe, and Japan, by disease severity



*P<0.01 compared with mild AD. **P<0.01 compared with mild AD and with moderate AD.
†0–30, higher score indicates a worse HRQoL, bands are 0–1 = no effect on child's life; 2–6 = small effect; 7–12 = moderate effect; 13–18 = very large effect; 19–30 = extremely large effect.[9]
AD, atopic dermatitis; CDLQI, Children Dermatology Life Quality Index; HRQoL, health-related quality of life; SD, standard deviation; US, United States.

Figure 6. Total number of missed school days during past 4 weeks for children with AD in the US, Canada, Europe, and Japan, by disease severity



*P<0.01 compared with mild AD. **P<0.05 compared with mild AD and with moderate AD. ***P<0.01 compared with mild and with moderate AD.
AD, atopic dermatitis; SD, standard deviation; US, United States.

Table 1. Baseline demographics of children with AD in the US, Canada, Europe, and Japan

	US			Canada			Europe			Japan			All countries		
	Mild AD (n=187)	Moderate AD (n=83)	Severe AD (n=13)	Mild AD (n=52)	Moderate AD (n=25)	Severe AD (n=6)	Mild AD (n=717)	Moderate AD (n=355)	Severe AD (n=39)	Mild AD (n=156)	Moderate AD (n=43)	Severe AD (n=5)	Mild AD (n=1112)	Moderate AD (n=506)	Severe AD (n=63)
Female, %	53.3	40.9	55.0	50.4	59.8	66.9	42.6	46.1	42.7	51.7	49.2	60.3	48.0	44.8	50.9
Age, mean years (SD)	8.8 (1.7)	9.2 (1.7)	9.3 (1.4)	8.8 (1.8)	9.2 (1.5)	8.9 (1.4)	9.0 (1.7)	9.2 (1.7)	9.1 (1.8)	8.8 (1.8)	8.8 (1.7)	9.3 (1.8)	8.9 (1.7)	9.2 (1.7)	9.2 (1.6)
POEM score, mean (SD)	6.2 (4.8)	11.9 (5.2)	20.9 (4.2)	6.0 (4.2)	11.8 (5.0)	20.7 (5.6)	5.2 (4.1)	10.7 (4.9)	17.0 (5.6)	5.1 (4.2)	10.1 (4.5)	18.2 (5.3)	5.6 (4.4)	11.1 (5.0)	19.1 (5.4)

AD, atopic dermatitis; POEM, Patient-Oriented Eczema Measure; SD, standard deviation; US, United States.

CONCLUSIONS

- **This self-report, cross-sectional, real-world study on the burden of AD in children aged 6–11 years demonstrated a substantial and multidimensional impact of AD, including itch, sleep disturbance, skin pain, and HRQoL impact, as well as comorbidities and productivity losses; the results were generally consistent across countries.**
- **The burden associated with AD was remarkable and increased with increasing disease severity.**
- **The high disease burden observed in children aged 6–11 years implies that there is a major unmet therapeutic need in the management of children with moderate-to-severe AD.**

References: 1. Ricci G et al. Dermatol Reports. 2012;4:e1. 2. Vakharia PP et al. Am J Clin Dermatol. 2019;20:771–779. 3. Chamlin SL. Dermatol Ther. 2006;19:104–107. 4. Chamlin SL, Chren MM. Immunol Allergy Clin North Am. 2010;30:281–288. 5. Balkrishnan R et al. Pediatr Dermatol. 2003;20:5–10. 6. Yang EJ et al. Pediatr Dermatol. 2019;36:66–71. 7. Eichenfield LF et al. J Am Acad Dermatol. 2014;70:338–351. 8. Barbarot S et al. Allergy. 2018;73:1284–1293. 9. Waters A et al. Br J Dermatol. 2010;163(Suppl 1):121.

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Conflicts of interest: SW is co-principal investigator of the German Atopic Dermatitis Registry TREATgermany. He has received institutional research grants from Novartis, Pfizer, L'Oreal, and LEO Pharma, has performed consultancies for Sanofi-Genzyme, Regeneron Pharmaceuticals, Inc., LEO Pharma, Incyte, and Novartis, has lectured at educational events sponsored by Sanofi-Genzyme, Regeneron Pharmaceuticals, Inc., LEO Pharma, Abbvie, and Galderma, and is involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of psoriasis and atopic eczema. ELS has received grants/research support from Amgen, Celgene, Chugai, Galderma, Genentech, Medimmune, Sanofi/Regeneron Pharmaceuticals, Inc., Tioga, Vanda, and Eli Lilly and Company, and is a consultant for Anacor, Celgene, Galderma, Genentech, Medicis, Sanofi/Regeneron Pharmaceuticals, Inc., and Merck. JIS has acted as a consultant for and/or received grants/honoraria from AbbVie, AnaptysBio, Asana Biosciences, LLC, Eli Lilly and Company, Galderma Research and Development, LLC, GlaxoSmithKline, Glenmark Generics Inc., Kiniksa Pharmaceuticals, Ltd., LEO Pharma, Medimmune, Menlo Therapeutics, Pfizer Inc., PuriCore, Inc., Regeneron Pharmaceuticals, Inc., and Sanofi. SB has received research grants from Pierre Fabre Laboratory and Fondation pour la Dermatite Atopique; personal fees from Bioderma, Laboratoire La Roche Posay, Sanofi-Genzyme, Novalac, and Ferring; and non-financial support from AbbVie, Novartis, and Janssen. PMO is an employee of and stockholder in Regeneron Pharmaceuticals, Inc. AG was an employee of and stockholder in Regeneron Pharmaceuticals, Inc. at the time of the study. LE, IG, and AR are employees of and stockholders in Sanofi. MP is an employee of Kantar Health, who received funding from Sanofi to conduct the study.

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