Journal Pre-proof



Treatment Patterns of Pediatric Patients with Atopic Dermatitis: A Claims Data Analysis

Amy S. Paller, MD, Elaine C. Siegfried, MD, Francis Vekeman, MA, Abhijit Gadkari, PhD, Mandeep Kaur, MD, MS, Usha G. Mallya, PhD, Julie Héroux, MSc, Raymond Miao, MSc, Paola Mina-Osorio, MD, PhD

PII: S0190-9622(19)32500-9

DOI: https://doi.org/10.1016/j.jaad.2019.07.105

Reference: YMJD 13718

To appear in: *Journal of the American Academy of Dermatology*

Received Date: 21 January 2019

Revised Date: 24 July 2019

Accepted Date: 30 July 2019

Please cite this article as: Paller AS, Siegfried EC, Vekeman F, Gadkari A, Kaur M, Mallya UG, Héroux J, Miao R, Mina-Osorio P, Treatment Patterns of Pediatric Patients with Atopic Dermatitis: A Claims Data Analysis, *Journal of the American Academy of Dermatology* (2019), doi: https://doi.org/10.1016/j.jaad.2019.07.105.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2019 Published by Elsevier on behalf of the American Academy of Dermatology, Inc.

Journal Pre-proof

Article type: Original article

Title: Treatment Patterns of Pediatric Patients with Atopic Dermatitis: A Claims Data Analysis

Amy S. Paller, MD[1*]; Elaine C. Siegfried, MD[2*]; Francis Vekeman, MA[3]; Abhijit Gadkari, PhD[4]; Mandeep Kaur, MD, MS[5]; Usha G. Mallya, PhD[5]; Julie Héroux, MSc[3]; Raymond Miao, MSc[6]; Paola Mina-Osorio, MD, PhD[4]

[1] Departments of Dermatology and Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
[2] Department of Pediatrics, Division of Dermatology, Saint Louis University and Cardinal Glennon Children's Hospital, St. Louis, MO, USA
[3] StatLog, Inc., Montreal, Quebec, Canada
[4] Regeneron, Tarrytown, NY, USA
[5] Sanofi, Cambridge, MA, USA
[6] Sanofi, Bridgewater, NJ, USA

*Amy S. Paller and Elaine C. Siegfried contributed equally to the data analysis and interpretation, and drafting, and critical revision of the article.

Corresponding author:

Paola Mina-Osorio, MD, PhD
Medical Director, Immunology Medical Affairs
Regeneron Pharmaceuticals Inc.
777 Old Saw Mill River Road
Tarrytown, NY 10591
(941) 847-3228
Email: paola.minaosorio@regeneron.com

Funding sources: This study was funded by Regeneron Pharmaceuticals, Inc. and Sanofi.

Conflicts of Interest: A. Gadkari and P. Mina-Osorio, are employees of and stockholders in Regeneron Pharmaceuticals Inc. M. Kaur, U. Mallya, and R. Miao are employees and stockholder in Sanofi. F. Vekeman and J. Héroux are employees of StatLog Inc., which received research funding for the current study. A. S. Paller is an employee of Northwestern University. She has been a consultant with honorarium for Regeneron Pharmaceuticals and Sanofi and investigator for Regeneron Pharmaceuticals. E. C. Siegfried is an employee of Saint-Louis University. She has been a consultant with honorarium and an investigator for Regeneron Pharmaceuticals and Sanofi.

Reprint requests: Paola Mina-Osorio

Manuscript word count: 2,498 words (maximum 2,500)
Abstract word count: 200 (maximum 200)
Capsule summary word count: 47 (maximum 50)
References: 35 (no maximum)

Journal Pre-proof

Journal Pre-proof

Figures: 0 (maximum 5 figures/tables)
Tables: 4 (maximum 5 figures/tables)

Keywords: Atopic dermatitis; Eczema; Infants; Children; Adolescents; Topical corticosteroids; Topical calcineurin inhibitors; Topical treatment; Systemic treatment

Journal Pre-proof

Journal Pre-proof

Abstract

Background: Real-world evidence on treatment patterns of pediatric patients with atopic dermatitis (AD) is sparse.

Objective: To assess current treatment patterns in pediatric AD patients.

Methods: Retrospective observational analysis of commercial insurance and Medicaid administrative claims data (01/2011–12/2016) for pediatric AD patients, stratified by age and provider type.

Results: Analytic sample comprised 607,258 pediatric AD patients. Median observation period was 30.3 months; 78.6% were prescribed ≥1 AD medication. 86.7% were prescribed topical corticosteroids (TCS); 5.4% a calcineurin inhibitor. Systemic corticosteroids (SCS) were prescribed for 24.4% patients, of whom 51.8% had no asthma/allergic comorbidities. Of the 46.6% and 16.2% prescribed an antihistamine or montelukast, respectively, 62.0% and 41.3% had no asthma/allergic comorbidities. Systemic immunosuppressants were rarely prescribed (<0.5%). Higher potency TCS and SCS use increased with age. Treatment patterns varied by provider type; specialists were more likely to prescribe higher potency topicals and/or systemics, regardless of age. A minority of patients were treated by/referred to a specialist.

Limitations: Identification of AD patients relied on billing diagnoses; disease severity proxied based on treatment.

Conclusion: Results indicate that SCS, despite known risks, and other medications with disproven efficacy in AD are frequently prescribed, suggesting a need for safer and, more effective alternatives.

Journal Pre-proof

Capsule summary

- Pediatric AD treatments varied by provider type, with only a minority ever treated by a specialist.

- Pediatric patients with AD commonly used drugs without proven efficacy, as well as agents with an unfavorable safety profile, suggesting the need for safe and effective alternatives for long-term disease control.

Journal Pre-proof

Journal Pre-proof

INTRODUCTION

Atopic dermatitis (AD) is the most common chronic pediatric inflammatory skin disease.[1,2] It presents within the first year of life in the majority of patients and before age 5 in 85-95% of cases.[3,4] Given the early onset, primary care physicians, especially pediatricians, play a critical role in initial management and subsequent subspecialist referrals.[5]

Optimal AD management focuses on maintenance skin care and topical medications to minimize flares.[6] First-line topical prescription options include corticosteroids (TCS), calcineurin inhibitors (TCI), and a PDE4 inhibitor (crisaborole, FDA-approved in December, 2016). Skin care regimens are time-consuming and can be confusing, requiring education and monitoring.[7]

Off-label treatment, especially systemic immunosuppressants (IMM) and systemic (oral/ injectable) corticosteroids (SCS), are frequently prescribed for patients unresponsive to topical therapy.[8] Until recently, the only FDA approved systemic therapy for pediatric patients with AD was oral corticosteroid, despite potential adverse effects and known tendency to rebound.[9] In March 2019, the FDA approved dupilumab, an interleukin-4 receptor alpha antagonist, to treat patients aged 12 years and older with moderate-to-severe AD inadequately controlled by topical prescription treatments or when those therapies are not advisable.

Published literature is scant on current pediatric-specific practice patterns.[10] The objective of this study was to assess current treatment patterns in a large population of insured pediatric patients with AD to identify opportunities for improved management.

Journal Pre-proof

METHODS

Study design, data, and patient population

The study used a retrospective observational design. Combined administrative medical and pharmacy claims from the IBM® MarketScan® Commercial Database and Multi-State Medicaid Database covering January 01, 2011 to December 31, 2016 were analyzed. Both databases include de-identified patient-level claims compliant with the Health Insurance Portability and Accountability Act.

Patients with ≥1 claim with a diagnosis of AD (International Classification of disease, ninth revision [ICD-9] 691.8 and ICD-10 L20.x) were included. The index date was defined as the first observed medical claim for AD. Other inclusion criteria were age <18 years on the index date and continuous health plan eligibility 6 months pre- (baseline period; up to 6 months for infants <1 year of age) and ≥12 months post-index date. Patients who received a diagnosis of an immune-mediated inflammatory disorder during the baseline period or on the index date were excluded to avoid ambiguity for medications used for these conditions rather than AD. The observation period spanned the patients' index date to the earliest of the end of health plan continuous eligibility or the data cut-off date.

Outcomes

The following medications were considered to be prescribed most likely to treat AD: TCS, TCI, antihistamines (topical and oral), montelukast sodium, SCS, IMM (azathioprine, cyclosporine A, methotrexate, mycophenolate mofetil, interferon gamma), intravenous immunoglobulin (IVIG), and phototherapy. Potential use for related conditions was explored with a subset analysis excluding patients with diagnostic codes for asthma and allergies. Although topical and oral

Journal Pre-proof

antibiotics are often prescribed for infected AD, these medications are also used for many unrelated, common childhood infections, so antibiotics were not included in the analysis. Crisaborole and dupilumab were not included because their approval did not coincide with the period of data availability. Class of AD medications received, total number of prescriptions filled, and combination therapies (overlap ≥3 months between ≥2 distinct AD treatments) were assessed.

A proxy for AD severity was developed using treatment regimens. TCS were classified by potency class (highest 1 to lowest 7).[11] The proxy for severity Level 1 included class 5-7 TCS or TCI used alone. The proxy for severity Level 2 included class 1-4 TCS, or TCI used with other AD therapies. Finally, the proxy for severity Level 3 included SCS and other IMM, IVIG, and phototherapy. Patients were categorized based on the treatment with the highest potency received. Untreated patients were categorized in the proxy for severity Level 1.

Statistical analyses

AD treatment patterns were reported among treated patients. Results were stratified by age group (<2 years, 2-5, 6-11, and 12-17) and by type of healthcare provider on the index date (dermatologist, allergists/immunologists [A/I], pediatrician, and other provider types [mainly primary care providers, family practices, acute care providers, and nurse practitioners). Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Journal Pre-proof

Journal Pre-proof

RESULTS

Patient characteristics

A total of 607,258 children were identified. Patients with Medicaid coverage represented 44.2% of the study population. Overall, 29.2% of patients had ≥1 atopic comorbidity, including allergic rhinitis (17.4%), asthma (12.1%), and allergic conjunctivitis (7.0%). Atopic comorbidities were more commonly observed among patients with the proxy for severity Level 3 (48.4%) compared to Level 1 (23.4%) and Level 2 (25.6%) (results not shown). Patients were observed for a median of 30.3 months (Table 1).

Treatment patterns

Most pediatric patients diagnosed with AD received ≥1 medication for AD during their observation period (78.6%; Table 1). Patients filled a mean (SD) of 2.7 (3.7) AD prescriptions annually; just under one-third (30.1%) received combination AD therapy (Table 2). Most patients (86.7%) received ≥1 prescription topical medication, mainly low (class 6-7: 36.5%) and medium (class 3-5: 63.8%) potency TCS. Antihistamines were the most commonly used systemic treatments (46.6%) and 16.2% received montelukast. SCS were prescribed in a quarter (24.4%) of the pediatric patients. Use of IMM and phototherapy was marginal (0.2% and 0.2%, respectively). Comorbid asthma and allergies were not present in most patients receiving antihistamines (62.0%) or SCS (51.8%), and in 41.3% of those prescribed montelukast sodium.

Stratifications

Patients across age groups had similar comorbid profiles (Table 3). Overall, younger patients were the least likely to have seen a dermatologist on the index date (Table 3). Proportions of patients with severity Level 3 increased with age (infants: 10.0%; adolescents: 34.5%). The

Journal Pre-proof

frequency of dispensed AD medications was consistent across all age groups (median: 1.3-1.4 annually), although specific treatments varied (Table 4). Notable differences were a positive relationship between TCS potency and age (low-/high-potency TCS, infants: 50.9%/10.1%; adolescents: 22.6%/24.3%). Use of SCS also increased with age (infants: 12.3%; adolescents: 40.7%). Regardless of age, IMM and phototherapy were very rarely used.

Referral to a dermatologist or A/I by pediatricians and other providers was infrequent (Table 3). Only 13.5% of patients had a visit with a dermatologist or A/I after seeing a pediatrician on the index date and 5.0% after seeing a provider other than a pediatrician.

Use of high-potency TCS was greatest among patients initially seen by a dermatologist (28.1%, 11.5%-14.5% among other provider categories), as was use of TCI (13.3%, 3.9%-7.8%) (Table 5). Conversely, use of oral antihistamines was lowest among those initially seen by a dermatologist (29.3%, 37.7%-58.4%). Use of SCS (44.0%, 21.0%-27.2%) and montelukast sodium (36.8%, 14.0%-15.7%) was highest among patients initially seen by an A/I. IMM and phototherapy were rarely prescribed, regardless of provider type.

Among patients treated by A/I, comorbid asthma and allergies were present in most patients receiving antihistamines (76.4%), SCS (84.8%), and montelukast sodium (86.5%); in contrast, these comorbidities were present in the minority of patients treated by dermatologists, pediatricians, and other providers receiving these treatments.

Journal Pre-proof

DISCUSSION

This study provides a comprehensive overview of medications prescribed for more than half a million pediatric patients with AD and characterizes their clinical management. Key differences in how pediatric patients with AD are treated across provider types were observed. Furthermore, only one in four patients were initially evaluated or subsequently referred to a specialist (dermatologist or A/I) by a pediatrician or other provider types. In addition to insurance restricted access, shortages of pediatric dermatologists in the United States, particularly outside of metropolitan areas, may be a contributing factor in this low observed rate of dermatology clinic visits.[12,13] This database included 44.2% insured by Medicaid, a group most severely impacted by access to specialist care, with dermatology among the most restricted.[14–18]

With an observed utilization above 85%, topical treatments was the mainstay for the management of AD, consistent with current guidelines' recommendations.[6] TCS were most widely used, dispensed in 85.9% of patients. These proportions are higher than recently reported use of TCS by 72.0% of females and 56.7% of males aged 0-19 years who saw a dermatologist for a primary diagnosis of AD.[19] Similarly, an analysis of visits for AD from the U.S. National Ambulatory Medical Care Survey (NAMCS) from 2003-2012 indicated that around 61% of patients aged 0-15 years old received TCS.[20] The probable explanation for this higher reported utilization of TCS is the longer patient follow-up.

While low- and medium-potency TCS were equally prescribed by all types of providers, use of high-potency TCS was more common among patients initially seen by a dermatologist. This finding supports greater comfort and familiarity with prescribing higher potency agents among

Journal Pre-proof

dermatologists.[20] Infants and young children were also least likely to receive high-potency TCS and to see a dermatologist. Primary care physicians are often hesitant to prescribe stronger than low-potency TCS, even for flaring AD.

The observed utilization of TCI by 13.3% of patients seen by a dermatologist is consistent with that reported in a recent analysis of the NAMCS data for patients under 15 years old.[20] Notably, this proportion was three times higher than that observed among patients cared for by providers other than A/I or pediatricians. As for TCS, dermatologists may have more comfort with the risk-benefit profile of this class of treatments, when used as prescribed.[10]

There was widespread use of medications not recommended by published AD guidelines, consistent with a previously published observational study.[21] Oral antihistamines were the most commonly used agents after TCS, despite concerns over adverse effects, such as undesired sedation, dry mouth, and blurred vision, which may be particularly detrimental for school-aged children.[21–23] Furthermore, there has been a recently identified potential association between sedating antihistamine use in AD patients and ADHD in a single report.[23] There is a lack of evidence supporting their benefit in AD, although physicians may be prescribing them for the soporific effect.[22,24,25] Moreover, this widespread use may be partially explained by the documented misperception of parents that antihistamines are useful in reducing AD-related itch.[19] Similar results were observed with montelukast, despite the absence of evidence supporting its efficacy in patients with AD[26–28] and potential risk of neuropsychiatric adverse effects in children, including depression, aggression, and nightmares.[29]

Journal Pre-proof

A limitation of our study design was the inherent inability to assess the widespread use of oral antibiotics to treat AD, rather than unrelated infections. Furthermore, over-the-counter AD treatments such as emollients and topical 1% hydrocortisone, typically used for maintenance therapy for milder forms of AD, were not captured in the database. This may help to explain why 21.4% of these patients did not have any filled prescriptions for AD medication. These data are in line with a recently published study, in which >30% of patients did not report use of any topical medications within the past week.[31]

Until the approval of dupilumab in March 2019 to treat patients aged 12 years and older with moderate-to-severe AD inadequately controlled by topical prescription treatments or when those therapies are not advisable, corticosteroids were the only FDA-approved systemic medication for AD in children. However, guidelines and a consensus from the International Eczema Council recommending against this approach, with perhaps the exception of short-term transitional administration for acute, severe exacerbations.[22,24,25,32] Long-term utilization of SCS has been associated with rebound worsening after treatment discontinuation and side effects, including growth suppression in children, osteoporosis, osteonecrosis, adrenal insufficiency, Cushing syndrome, hypertension, glucose intolerance, and diabetes, to name a few.[9] Yet, in the present study 24.4% of patients had ≥1 filled prescription for SCS during the observation period (12.6% when excluding patients with concomitant asthma or allergies).

The prevalence of SCS use was highest for adolescent patients (40.7%) and those treated by A/I (44.0%) and dermatologists (27.2%). A retrospective study using national survey data between 1997 and 2004 reported SCS rates of 17% for all AD-related visits, excluding those for patients with concomitant asthma or allergies. However, this visit-level rate is difficult to compare to the

Journal Pre-proof

patient-level results from the current analysis.[33] Previously reported utilization rates in US clinical practices were lower;[14,28] likely due to the longer average observation period in the present study. The high prevalence of SCS use in pediatric patients with AD emphasizes the need for safe and effective therapies to treat the disease.

A survey among North American pediatric dermatologists cited cyclosporine, methotrexate, and mycophenolate mofetil as the systemic first-line treatments of choice for AD, not systemic steroids.[36] Yet, filled prescriptions for systemic IMM other than corticosteroids were marginal across all age groups and provider types. At less than 1%, the utilization of IMM in the present study is less than expected for patients in the most severe group, previously documented at around 7%.[37] Despite safety concerns which limit their acceptance, for many patients with severe AD, the benefits of IMM often outweigh the risks. Still, a recent survey of adult patients with moderate-to-severe AD treated with systemic agents, including IMM, indicated that the lack of disease control was a concern, with patients reporting a substantial number, prolonged duration of, and recurrent flares.[38]

One key challenge with the identification of patients with AD in administrative health care claims stems from the fact that a variety of ICD diagnostic codes have been assigned to “AD”, “eczema” or “dermatitis” and a clinician’s choice of code may vary for a patient seen for AD. Thus, restricting the sample to those with a specific diagnostic code for AD may inadvertently exclude some ‘true AD” patients who were misdiagnosed. However, the objective here was not to measure the prevalence of pediatric AD, but rather to characterize treatment patterns in patients with AD. Thus, a conservative approach in selecting patients with a specific diagnosis of AD was favored. A sensitivity analysis using a broader set of codes for AD and AD-related

Journal Pre-proof

conditions (dyshidrosis, other erythematosquamous dermatosis, infective dermatitis, other specified dermatitis, dermatitis unspecified, contact dermatitis and other eczema, unspecified cause, and nummular dermatitis) yielded similar results, supporting the findings.

Additional limitations include the fact that diagnostic codes used for billing may reflect suspected, rather than confirmed clinical diagnoses. AD severity was defined based on treatments received rather than on clinical data. As such, the proportion of patients with higher severity may be underestimated due to reluctance of health care providers to treat with more potent therapies. Finally, claims data only provide information on filled prescriptions, not medications actually used.

CONCLUSION

Despite high prevalence and disease burden of pediatric AD in the US, there is no consensus on a uniform approach to disease management. Results from this claims data analysis indicate that most patients were not seen by a specialist; moreover, treatment varied greatly by provider type, with specialists more likely to treat with higher potency topicals and/or systemics. Oral antihistamines and montelukast were frequently prescribed in patients with AD without asthma and allergic comorbidities, especially in younger children, despite their lack of demonstrated efficacy. Systemic immunosuppressants were very rarely prescribed, despite the potential benefit of these drugs for severe AD patients. Instead, systemic corticosteroids were far more commonly prescribed, especially for adolescents, despite their known risks. These results emphasize the need for effective therapies that are well tolerated by pediatric patients for long-term control of the disease.

Journal Pre-proof

Journal Pre-proof

ACKNOWLEDGEMENTS

Writing/editorial assistance in the preparation of this article was provided by Éric Gravel from StatLog Inc and was payed for by Regeneron and Sanofi. Dr. Paller and Dr. Siegfried provided equal contribution to the study.

Journal Pre-proof

Journal Pre-proof

References

1. Avena-Woods C. Overview of atopic dermatitis. *Am J Manag Care*. 2017;23(8 Suppl):S115-S123. http://www.ncbi.nlm.nih.gov/pubmed/28978208. Accessed September 6, 2018.

2. Nutten S. Atopic Dermatitis: Global Epidemiology and Risk Factors. *Ann Nutr Metab*. 2015;66(1):8-16. doi:10.1159/000370220

3. Williams HC. Clinical practice. Atopic Dermatitis. *N Engl J Med*. 2005;352(22):2314-2324. doi:10.1056/NEJMcp042803

4. Illi S, von Mutius E, Lau S, et al. The natural course of atopic dermatitis from birth to age 7 years and the association with asthma. *J Allergy Clin Immunol*. 2004;113(5):925-931. doi:10.1016/j.jaci.2004.01.778

5. Saavedra JM, Boguniewicz M, Chamlin S, et al. Patterns of Clinical Management of Atopic Dermatitis in Infants and Toddlers: A Survey of Three Physician Specialties in the United States. *J Pediatr*. 2013;163(6):1747-1753. doi:10.1016/j.jpeds.2013.06.073

6. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: Part 2. Management and Treatment of Atopic Dermatitis with Topical Therapies. *J Am Acad Dermatol*. 2014;71(1):116-132. doi:10.1016/j.jaad.2014.03.023

7. Eichenfield LF, Boguniewicz M, Simpson EL, et al. Translating Atopic Dermatitis Management Guidelines Into Practice for Primary Care Providers. *Pediatrics*. 2015;136(3):554-565. doi:10.1542/peds.2014-3678

8. Krejci-Manwaring J, Tusa MG, Carroll C, et al. Stealth monitoring of adherence to topical medication: adherence is very poor in children with atopic dermatitis. *J Am Acad Dermatol*. 2007;56(2):211-216. doi:10.1016/j.jaad.2006.05.073

9. Yu SH, Drucker AM, Lebwohl M, Silverberg JI. A systematic review of the safety and efficacy of systemic corticosteroids in atopic dermatitis. *J Am Acad Dermatol*. December 2017. doi:10.1016/j.jaad.2017.09.074

10. Siegfried EC, Jaworski JC, Mina-Osorio P. A Systematic Scoping Literature Review of Publications Supporting Treatment Guidelines for Pediatric Atopic Dermatitis in Contrast to Clinical Practice Patterns. *J Pediatr*. 2018;Submitted.

11. WHO Model Prescribing Information: Drugs Used in Skin Diseases: Annex: Classification of topical corticosteroids. http://apps.who.int/medicinedocs/en/d/Jh2918e/32.html. Accessed March 7, 2018.

12. Prindaville B, Horii KA, Siegfried EC, Brandling-Bennett H. Pediatric dermatology workforce in the United States. *Pediatr Dermatol*. 2019;36(1):166-168. doi:10.1111/pde.13684

13. Prindaville B, Antaya RJ, Siegfried EC. Pediatric Dermatology: Past, Present, and Future. *Pediatr Dermatol*. 2015;32(1):1-12. doi:10.1111/pde.12362

14. Group TMAS. Access of Medicaid Recipients to Outpatient Care. *N Engl J Med*. 1994;330(20):1426-1430. doi:10.1056/NEJM199405193302007

Journal Pre-proof

15. Bisgaier J, Rhodes K V. Auditing Access to Specialty Care for Children with Public Insurance. *N Engl J Med*. 2011;364(24):2324-2333. doi:10.1056/NEJMsa1013285

16. Skinner AC, Mayer ML. Effects of insurance status on children's access to specialty care: a systematic review of the literature. *BMC Health Serv Res*. 2007;7:194. doi:10.1186/1472-6963-7-194

17. Resneck J, Pletcher MJ, Lozano N. Medicare, Medicaid, and access to dermatologists: the effect of patient insurance on appointment access and wait times. *J Am Acad Dermatol*. 2004;50(1):85-92. doi:10.1016/S0190

18. Siegfried EC, Paller AS, Vekeman F, et al. *Differences in Treatment Patterns and Healthcare Resource Utilization between Medicaid and Commercially Insured Children with Atopic Dermatitis*.; 2019.

19. Alexander T, Maxim E, Cardwell LA, Chawla A, Feldman SR. Prescriptions for atopic dermatitis: oral corticosteroids remain commonplace. *J Dermatolog Treat*. October 2017:1-3. doi:10.1080/09546634.2017.1365112

20. He A, Feldman SR, Fleischer AB. Trends in Atopic Dermatitis Management: Comparison of 1990-1997 to 2003-2012. *J Drugs Dermatol*. 2018;17(2):135-140. http://www.ncbi.nlm.nih.gov/pubmed/29462220. Accessed February 26, 2018.

21. He A, Feldman SR, Fleischer AB. An assessment of the use of antihistamines in the management of atopic dermatitis. *J Am Acad Dermatol*. January 2018. doi:10.1016/j.jaad.2017.12.077

22. Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: Section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol*. 2014;71(2):327-349. doi:10.1016/j.jaad.2014.03.030

23. Schmitt J, Buske-Kirschbaum A, Tesch F, et al. Increased attention-deficit/hyperactivity symptoms in atopic dermatitis are associated with history of antihistamine use. *Allergy*. 2018;73(3):615-626. doi:10.1111/all.13326

24. Ring J, Alomar A, Bieber T, et al. Guidelines for treatment of atopic eczema (atopic dermatitis) Part I. *J Eur Acad Dermatology Venereol*. 2012;26(8):1045-1060. doi:10.1111/j.1468-3083.2012.04635.x

25. Ring J, Alomar A, Bieber T, et al. Guidelines for treatment of atopic eczema (atopic dermatitis) Part II. *J Eur Acad Dermatology Venereol*. 2012;26(9):1176-1193. doi:10.1111/j.1468-3083.2012.04636.x

26. Roekevisch E, Spuls PI, Kuester D, Limpens J, Schmitt J. Efficacy and safety of systemic treatments for moderate-to-severe atopic dermatitis: A systematic review. *J Allergy Clin Immunol*. 2014;133(2):429-438. doi:10.1016/j.jaci.2013.07.049

27. Lee AY. Is Montelukast Benefical in Children With Atopic Dermatitis? *Allergy Asthma Immunol Res*. 2016;8(4):279-281. doi:10.4168/aair.2016.8.4.279

28. Chin WK. Leukotriene receptor antagonism may not be effective in atopic dermatitis treatment after all. *J Clin Pharm Ther*. 2018;43(1):159-162. doi:10.1111/jcpt.12648

Journal Pre-proof

29. Haarman MG, van Hunsel F, de Vries TW. Adverse drug reactions of montelukast in children and adults. *Pharmacol Res Perspect*. 2017;5(5):e00341. doi:10.1002/prp2.341

30. Yamamoto-Hanada K, Yang L, Narita M, Saito H, Ohya Y. Influence of antibiotic use in early childhood on asthma and allergic diseases at age 5. *Ann Allergy, Asthma Immunol*. 2017;119(1):54-58. doi:10.1016/j.anai.2017.05.013

31. Simpson EL, Guttman-Yassky E, Margolis DJ, et al. Association of Inadequately Controlled Disease and Disease Severity With Patient-Reported Disease Burden in Adults With Atopic Dermatitis. *JAMA dermatology*. 2018;154(8):903-912. doi:10.1001/jamadermatol.2018.1572

32. Drucker AM, Eyerich K, de Bruin-Weller MS, et al. Use of systemic corticosteroids for atopic dermatitis: International Eczema Council consensus statement. *Br J Dermatol*. 2018;178(3):768-775. doi:10.1111/bjd.15928

33. Horii KA, Simon SD, Liu DY, Sharma V. Atopic Dermatitis in Children in the United States, 1997 2004: Visit Trends, Patient and Provider Characteristics, and Prescribing Patterns. *Pediatrics*. 2007;120(3):e527-e534. doi:10.1542/peds.2007-0289

34. Manthripragada AD, Pinheiro SP, MaCurdy TE, et al. Off-label topical calcineurin inhibitor use in children. *Pediatrics*. 2013;132(5):e1327-32. doi:10.1542/peds.2013-0931

35. Horii KA, Simon SD, Liu DY, Sharma V. Atopic Dermatitis in Children in the United States, 1997 2004: Visit Trends, Patient and Provider Characteristics, and Prescribing Patterns. *Pediatrics*. 2007;120(3):e527-e534. doi:10.1542/peds.2007-0289

36. Totri CR, Eichenfield LF, Logan K, et al. Prescribing practices for systemic agents in the treatment of severe pediatric atopic dermatitis in the US and Canada: The PeDRA TREAT survey. *J Am Acad Dermatol*. 2017;76(2):281-285. doi:10.1016/j.jaad.2016.09.021

37. Silverberg JI, Simpson EL. Associations of childhood eczema severity: a US population-based study. *Dermat contact, atopic, Occup drug*. 2014;25(3):107-114. doi:10.1097/DER.0000000000000034

38. Silverberg JI, Ghorayeb E, Chen Z. *A Real-World Study Evaluating AdeQUacy of Existing Systemic Treatments for Patients with Moderate-to-Severe Atopic Dermatitis (AD-QUEST): 6-Month Survey Data on Flares*. Presented at the International Investigative Dermatology/Society for Investigative Dermatology Annual Meeting (IID/SID), May 16–19, 2018, Orlando, Florida

427 Table 1. "Demographic and Clinical Characteristics of Patients with AD"

	n = 607,258
Demographics	
Age, mean ± SD | median	5.4 ± 5.0 | 4.0
Male, n (%)	307,992 (50.7%)
Commercial insurance plan type, n (%)	338,678 (55.8%))
Medicaid coverage, n (%)	268,580 (44.2%)
Comorbidities during the 6-month baseline period[1]	
Combined Charlson/Elixhauser comorbidity index, mean ± SD | median	0.2 ± 0.4 | 0.0
Patients with ≥ 1 comorbidity, n (%)	289,104 (47.6%)
Patients with ≥ 1 atopic comorbidity, n (%)	177,212 (29.2%)
Allergic conjunctivitis	42,405 (7.0%)
Allergic rhinitis	105,537 (17.4%)
Allergic urticaria	4,798 (0.8%)
Asthma	73,351 (12.1%)
Chronic rhinosinusitis	9,693 (1.6%)
Eosinophilic esophagitis	471 (0.1%)
Food allergy	9,572 (1.6%)
Nasal polyps	159 (0.0%)
Patients with ≥ 1 other comorbidity, n (%)	157,872 (26.0%)
Autoimmune disorders	1,920 (0.3%)
Bacterial infections	20,007 (3.3%)
Fungal infections	80,410 (13.2%)
Obesity	10,257 (1.7%)
Psychiatric comorbidities	29,511 (4.9%)
Anxiety	6,614 (1.1%)
Attention deficit hyperactivity disorder	19,978 (3.3%)
Depression	6,804 (1.1%)
Sleep disorders	1,582 (0.3%)
Viral infections and disorders	36,856 (6.1%)
Patients who received ≥ 1 treatment for AD during the observation period[2], n (%)	477,484 (78.6%)

Journal Pre-proof

Proxy for AD severity during the observation period[3], n (%)	
Severity level 1	261,335 (43.0%)
Severity level 2	224,864 (37.0%)
Severity level 3	121,059 (19.9%)
Duration of observation period (months), mean ± SD | median	33.6 ± 16.1 | 30.3

Notes:

1. The baseline period includes the index date. For infants, the baseline period includes up to 6 months of follow-up.

2. Patients considered in the analysis of treatment patterns.

3. Patients are categorized based on the treatment with the highest potency received.
Level 1: no treatment for AD, topical cortisosteroid (TCS) Class 7 – least Potent, TCS Class 6 – mild, TCS Class 5 – lower mid-strength, topical calcineurin inhibitors (TCI) used alone.
Level 2: TCS Class 4 – mid-strength, TCS Class 3 – upper mid-strength, TCS Class 2 – potent, TCS Class 1 – superpotent, TCI (when used with any other treatment for AD).
Level 3: SCS, azathioprine, cyclosporine A, methotrexate, mycophenolate mofetil, interferon gamma, intravenous immunoglobulin (IVIG), phototherapy.

Journal Pre-proof

Journal Pre-proof

429 Table 2. "Treatment Patterns of Patients with AD – Entire Observation Period"

	n = 477,484
Total filled prescriptions for AD treatment per year, mean ± SD | median	2.7 ± 3.7 | 1.3
Combination therapy with ≥2 distinct AD treatments, n (%)	143,614 (30.1%)
Topical treatments, n (%)	413,965 (86.7%)
Topical antihistamines	24 (0.0%)
Any topical corticosteroids (TCS)	410,134 (85.9%)
TCS low potency	174,444 (36.5%)
TCS medium potency	304,462 (63.8%)
TCS high potency	70,083 (14.7%)
Topical calcineurin inhibitors (TCI)	25,577 (5.4%)
Systemic treatments, n (%)	297,313 (62.3%)
Systemic antihistamines[1]	222,328 (46.6%)
Systemic corticosteroids (SCS)[1]	116,635 (24.4%)
Any systemic immunosuppressants (IMM)	1,106 (0.2%)
Azathioprine	147 (0.0%)
Cyclosporine A	252 (0.1%)
Interferon gamma	1 (0.0%)
Methotrexate	600 (0.1%)
Mycophenolate mofetil	276 (0.1%)
Intravenous immunoglobulin (IVIG)	5,123 (1.1%)
Montelukast sodium[1]	77,529 (16.2%)
Phototherapy, n (%)	938 (0.2%)

Notes:

1. The proportion of patients without comorbid asthma or allergies was 62.0% among patients prescribed systemic antihistamines, 51.8% among patients prescribed SCS, and 41.3% among patients prescribed montelukast sodium.

430

Journal Pre-proof

431 Table 3. "Demographic and Clinical Characteristics of Patients with AD – Stratified by Age Group and Provider Type"

	Age Group				Provider Type			
	0-1 yr	**2-5 yr**	**6-11 yr**	**12-17 yr**	**Dermatology**	**Allergy/ Immunology**	**Pediatrics**	**Other Provider**
	n = 195,591 (32.2%)	n = 152,270 (25.1%)	n = 165,113 (27.2%)	n = 94,284 (15.5%)	n = 71,899 (11.8%)	n = 39,238 (6.5%)	n = 233,342 (38.4%)	n = 262,779 (43.3%)
Demographics								
Age, mean ± SD | median	0.3 ± 0.4 | 0.0	3.4 ± 1.1 | 3.0	8.3 ± 1.7 | 8.0	14.2 ± 1.7 | 14.0	7.8 ± 5.3 | 8.0	6.0 ± 4.5 | 5.0	4.3 ± 4.7 | 3.0	5.6 ± 5.1 | 5.0
Male, n (%)	109,240 (55.9%)	77,052 (50.6%)	81,051 (49.1%)	40,649 (43.1%)	34,035 (47.3%)	21,910 (55.8%)	120,382 (51.6%)	131,665 (50.1%)
Commercial insurance plan type, n (%)	106,255 (54.3%)	82,290 (54.0%)	91,400 (55.4)	58,733 (62.3)	63.354 (88.1%)	31,626 (80.6%)	166,009 (71.1%)	77,689 (29.6%)
Medicaid coverage, n (%)	89,336 (45.7%)	69,980 (46.0%)	73,713 (44.6%)	35,551 (37.7%)	8,545 (11.9%)	7,612 (19.4%)	67,333 (28.9%)	185,090 (70.4%)
Comorbidities during the 6-month baseline period[1]								
Combined Charlson/Elixhauser comorbidity index, mean ± SD | median	0.1 ± 0.3 | 0.0	0.2 ± 0.4 | 0.0	0.2 ± 0.4 | 0.0	0.2 ± 0.5 | 0.0	0.1 ± 0.3 | 0.0	0.4 ± 0.5 | 0.0	0.1 ± 0.4 | 0.0	0.2 ± 0.5 | 0.0
Patients with ≥ 1 comorbidity, n (%)	76,992 (39.4%)	74,496 (48.9%)	91,206 (55.2%)	46,410 (49.2%)	33,484 (46.6%)	30,615 (78.0%)	93,171 (39.9%)	131,834 (50.2%)
Patients with ≥ 1 atopic comorbidity, n (%)	31,357 (16.0%)	54,410 (35.7%)	62,762 (38.0%)	28,683 (30.4%)	13,678 (19.0%)	28,992 (73.9%)	53,340 (22.9%)	81,202 (30.9%)
Allergic conjunctivitis	13,716 (7.0%)	13,225 (8.7%)	11,147 (6.8%)	4,317 (4.6%)	3,417 (4.8%)	5,547 (14.1%)	15,372 (6.6%)	18,069 (6.9%)
Allergic rhinitis	10,589 (5.4%)	32,263 (21.2%)	43,273 (26.2%)	19,412 (20.6%)	7,078 (9.8%)	22,930 (58.4%)	27,494 (11.8%)	48,035 (18.3%)
Allergic urticaria	1,269 (0.6%)	1,589 (1.0%)	1,301 (0.8%)	639 (0.7%)	312 (0.4%)	1,716 (4.4%)	965 (0.4%)	1,805 (0.7%)
Asthma	7,308 (3.7%)	21,965 (14.4%)	30,296 (18.3%)	13,782 (14.6%)	5,315 (7.4%)	12,324 (31.4%)	19,525 (8.4%)	36,187 (13.8%)
Chronic rhinosinusitis	1,458 (0.7%)	3,301 (2.2%)	3,088 (1.9%)	1,846 (2.0%)	1,067 (1.5%)	1,572 (4.0%)	2,582 (1.1%)	4,472 (1.7%)
Eosinophilic esophagitis	46 (0.0%)	139 (0.1%)	183 (0.1%)	103 (0.1%)	46 (0.1%)	160 (0.4%)	80 (0.0%)	185 (0.1%)
Food allergy	3,035 (1.6%)	3,093 (2.0%)	2,586 (1.6%)	858 (0.9%)	463 (0.6%)	3,899 (9.9%)	1,988 (0.9%)	3,222 (1.2%)
Nasal polyps	6 (0.0%)	21 (0.0%)	59 (0.0%)	73 (0.1%)	18 (0.0%)	36 (0.1%)	39 (0.0%)	66 (0.0%)
Patients with ≥ 1 other comorbidity, n (%)	55,916 (28.6%)	31,079 (20.4%)	44,858 (27.2%)	26,019 (27.6%)	25,080 (34.9%)	6,237 (15.9%)	52,693 (22.6%)	73,862 (28.1%)

Autoimmune disorders	194 (0.1%)	412 (0.3%)	734 (0.4%)	580 (0.6%)	652 (0.9%)	90 (0.2%)	376 (0.2%)	802 (0.3%)
Bacterial infections	5,446 (2.8%)	6,298 (4.1%)	5,735 (3.5%)	2,528 (2.7%)	3,439 (4.8%)	984 (2.5%)	7,286 (3.1%)	8,298 (3.2%)
Fungal infections	49,291 (25.2%)	13,130 (8.6%)	10,808 (6.5%)	7,181 (7.6%)	9,617 (13.4%)	2,223 (5.7%)	29,985 (12.9%)	38,585 (14.7%)
Psychiatric comorbidities	819 (0.4%)	2,663 (1.7%)	15,258 (9.2%)	10,771 (11.4%)	2,892 (4.0%)	1,658 (4.2%)	7,802 (3.3%)	17,159 (6.5%)
Anxiety	80 (0.0%)	818 (0.5%)	2,771 (1.7%)	2,945 (3.1%)	1,016 (1.4%)	505 (1.3%)	1,972 (0.8%)	3,121 (1.2%)
Attention deficit hyperactivity disorder	35 (0.0%)	1,469 (1.0%)	12,370 (7.5%)	6,104 (6.5%)	1,641 (2.3%)	1,126 (2.9%)	5,586 (2.4%)	11,625 (4.4%)
Depression	705 (0.4%)	492 (0.3%)	1,730 (1.0%)	3,877 (4.1%)	687 (1.0%)	264 (0.7%)	1,112 (0.5%)	4,741 (1.8%)
Obesity	312 (0.2%)	1,532 (1.0%)	4,737 (2.9%)	3,676 (3.9%)	658 (0.9%)	445 (1.1%)	2,901 (1.2%)	6,253 (2.4%)
Sleep disorders	163 (0.1%)	346 (0.2%)	629 (0.4%)	444 (0.5%)	98 (0.1%)	98 (0.2%)	403 (0.2%)	983 (0.4%)
Viral infections and disorders	3,987 (2.0%)	12,452 (8.2%)	15,086 (9.1%)	5,331 (5.7%)	11,918 (16.6%)	1,510 (3.8%)	9,755 (4.2%)	13,673 (5.2%)
Provider type on the index date, n (%)								
Dermatology	11,390 (5.8%)	16,184 (10.6%)	23,570 (14.3%)	20,755 (22.0%)	-	-	-	-
Allergy/Immunology	7,296 (3.7%)	12,957 (8.5%)	13,513 (8.2%)	5,472 (5.8%)	-	-	-	-
Pediatrics	95,717 (48.9%)	58,820 (38.6%)	54,461 (33.0%)	24,344 (25.8%)	-	-	-	-
Other	81,188 (41.5%)	64,309 (42.2%)	73,569 (44.6%)	43,713 (46.4%)	-	-	-	-
Patients with ≥1 visit with a dermatologist or an allergist/immunologist after the index visit, n (%)[2]					33,046 (46.0%)	20,061 (51.1%)	31,516 (13.5%)	13,144 (5.0%)
0-1 yr	-	-	-	-	6,719 (59.0%)	4,139 (56.7%)	14,230 (14.9%)	3,874 (4.8%)
2-5 yr	-	-	-	-	7,405 (45.8%)	6,382 (49.3%)	7,288 (12.4%)	3,119 (4.9%)
6-11 yr	-	-	-	-	9,819 (41.7%)	6,860 (50.8%)	6,620 (12.2%)	3,415 (4.6%)
12-17 yr	-	-	-	-	9,103 (43.9%)	2,680 (49.0%)	3,378 (13.9%)	2,736 (6.3%)
Patients who received ≥ 1 treatment for AD during the observation period[3], n (%)	145,683 (74.5%)	120,070 (78.9%)	133,472 (80.8%)	78,259 (83.0%)	58,758 (81.7%)	29,994 (76.4%)	169,455 (72.6%)	219,277 (83.4%)
Proxy for AD severity during the observation period[4], n (%)								
Severity level 1	104,428 (53.4%)	67,066 (44.0%)	61,754 (37.4%)	28,087 (29.8%)	26,062 (36.2%)	15,730 (40.1%)	115,465 (49.5%)	104,078 (39.6%)

Journal Pre-proof

Severity level 2	71,613 (36.6%)	59,726 (39.2%)	59,828 (36.2%)	33,697 (35.7%)	29,087 (40.5%)	10,061 (25.6%)	80,698 (34.6%)	105,018 (40.0%)
Severity level 3	19,550 (10.0%)	25,478 (16.7%)	43,531 (26.4%)	32,500 (34.5%)	16,750 (23.3%)	13,447 (34.3%)	37,179 (15.9%)	53,683 (20.4%)
Duration of observation period (months), mean ± SD | median	32.9 ± 16.6 | 28.7	34.9 ± 16.2 | 32.5	33.9 ± 15.8 | 31.2	32.1 ± 15.1 | 28.9	34.1 ± 16.1 | 31.3	32.1 ± 15.6 | 28.4	33.1 ± 16.0 | 29.5	34.1 ± 16.2 | 31.3

Notes:
1. The baseline period includes the index date. For infants, the baseline period includes up to 6 months of follow-up.
2. Percentages for the age groups are calculated out of the total number of patients in the corresponding age group.
3. Patients considered in the analysis of treatment patterns.
4. Patients are categorized based on the treatment with the highest potency received.
Level 1: no treatment for AD, topical cortisosteroid (TCS) Class 7 – least Potent, TCS Class 6 – mild, TCS Class 5 – lower mid-strength, topical calcineurin inhibitors (TCI) used alone.
Level 2: TCS Class 4 – mid-strength, TCS Class 3 – upper mid-strength, TCS Class 2 – potent, TCS Class 1 – superpotent, TCI (when used with any other treatment for AD).
Level 3: SCS, azathioprine, cyclosporine A, methotrexate, mycophenolate mofetil, interferon gamma, intravenous immunoglobulin (IVIG), phototherapy.

Journal Pre-proof

Journal Pre-proof

434 Table 4. "Treatment Patterns of Patients with AD (Entire Observation Period) – Stratified by Age Group and Provider Type"

	Age Group				Provider Type			
	0-1 yr	**2-5 yr**	**6-11 yr**	**12-17 yr**	**Dermatology**	**Allergy/ Immunology**	**Pediatrics**	**Other Provider**
	n = 145,683	n = 120,070	n = 133,472	n = 78,259	n = 58,758	n = 29,994	n = 169,455	n = 219,277
Total filled prescriptions for AD treatment per year, mean ± SD | median	2.4 ± 3.1 | 1.3	2.7 ± 3.8 | 1.3	2.9 ± 4.1 | 1.4	2.6 ± 3.7 | 1.3	2.4 ± 3.4 | 1.2	4.2 ± 5.2 | 2.2	2.2 ± 3.0 | 1.1	2.9 ± 3.9 | 1.5
Combination therapy with ≥2 distinct AD treatments, n (%)	35,611 (24.4%)	38,042 (31.7%)	45,092 (33.8%)	24,869 (31.8%)	16,881 (28.7%)	11,273 (37.6%)	40,085 (23.7%)	75,375 (34.4%)
Topical treatments, n (%)	129,920 (89.2%)	103,829 (86.5%)	113,325 (84.9%)	66,891 (85.5%)	53,780 (91.5%)	21,757 (72.5%)	149,268 (88.1%)	189,160 (86.3%)
Topical antihistamines	8 (0.0%)	5 (0.0%)	7 (0.0%)	4 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.0%)	22 (0.0%)
Any topical corticosteroids (TCS)	129,515 (88.9%)	102,953 (85.7%)	111,826 (83.8%)	65,840 (84.1%)	52,428 (89.2%)	21,430 (71.4%)	148,309 (87.5%)	187,967 (85.7%)
TCS low potency	74,122 (50.9%)	43,820 (36.5%)	38,837 (29.1%)	17,665 (22.6%)	20,139 (34.3%)	7,913 (26.4%)	63,210 (37.3%)	83,182 (37.9%)
TCS medium potency	90,466 (62.1%)	77,545 (64.6%)	86,126 (64.5%)	50,325 (64.3%)	38,597 (65.7%)	17,001 (56.7%)	109,289 (64.5%)	139,575 (63.7%)
TCS high potency	14,771 (10.1%)	15,052 (12.5%)	21,249 (15.9%)	19,011 (24.3%)	16,539 (28.1%)	4,347 (14.5%)	19,538 (11.5%)	29,659 (13.5%)
Topical calcineurin inhibitors (TCI)	5,157 (3.5%)	6,171 (5.1%)	8,217 (6.2%)	6,032 (7.7%)	7,843 (13.3%)	2,344 (7.8%)	6,809 (4.0%)	8,581 (3.9%)
Systemic treatments, n (%)	83,566 (57.4%)	77,036 (64.2%)	86,829 (65.1%)	49,882 (63.7%)	30,123 (51.3%)	23,283 (77.6%)	91,502 (54.0%)	152,405 (69.5%)
Systemic antihistamines[1]	69,659 (47.8%)	60,430 (50.3%)	61,226 (45.9%)	31,013 (39.6%)	17,195 (29.3%)	13,146 (43.8%)	63,904 (37.7%)	128,083 (58.4%)
Systemic corticosteroids (SCS)[2]	17,914 (12.3%)	24,230 (20.2%)	42,616 (31.9%)	31,875 (40.7%)	15,998 (27.2%)	13,207 (44.0%)	35,522 (21.0%)	51,908 (23.7%)
Any systemic immunosuppressants (IMM)[3]	124 (0.1%)	218 (0.2%)	399 (0.3%)	365 (0.5%)	289 (0.5%)	75 (0.3%)	263 (0.2%)	479 (0.2%)
Intravenous immunoglobulin (IVIG)	1,851 (1.3%)	1,379 (1.1%)	1,096 (0.8%)	797 (1.0%)	688 (1.2%)	351 (1.2%)	1,936 (1.1%)	2,148 (1.0%)
Montelukast sodium[4]	16,895 (11.6%)	23,125 (19.3%)	26,608 (19.9%)	10,901 (13.9%)	8,374 (14.3%)	11,049 (36.8%)	23,756 (14.0%)	34,350 (15.7%)
Phototherapy, n (%)	62 (0.0%)	184 (0.2%)	346 (0.3%)	346 (0.4%)	363 (0.6%)	80 (0.3%)	173 (0.1%)	322 (0.1%)

Notes:
1. The proportion of patients without comorbid asthma or allergies was 80.9% among 0-1 yr, 55.2% among 2-5 yr, 49.3% among 6-11 yr, 57.7% among 12-17 yr, 74.9% for dermatology, 23.6% for A/I, 67.9% for pediatrics, and 61.2% for other provider types.
2. The proportion of patients without comorbid asthma or allergies was 77.0% among 0-1 yr, 41.4% among 2-5 yr, 42.0% among 6-11 yr, 58.9% among 12-17 yr, 69.8% for dermatology, 15.2% for A/I, 58.7% for pediatrics, and 51.0% for other provider types.
3. Immunosuppressants included azathioprine, cyclosporine A, interferon gamma, methotrexate, and mycophenolate mofetil.
4. The proportion of patients without comorbid asthma or allergies was 72.1% among 0-1 yr, 36.0% among 2-5 yr, 29.0% among 6-11 yr, 34.7% among 12-17 yr, 59.0% for dermatology, 13.5% for A/I, 52.1% for pediatrics, and 38.4% for other provider types.

435