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A Real-World Study of Cumulative Steroid Burden in Patients with Newly Diagnosed Eosinophilic Esophagitis

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BACKGROUND

- Eosinophilic esophagitis (EoE) is a type 2 inflammatory disease of the esophagus that is chronic and gets worse over time. Cytokines and chemokines predominantly drive the pathophysiology of EoE.[1,2]
- The incidence of EoE is rising globally[3]; it may occur at any age, with a peak in adults aged 30–50 years.[4,5]
- EoE manifests symptoms of esophageal dysfunction and substantially impacts a patient's health-related quality of life.[4]
- After diagnosis, along with food-restriction diets, the most common off-label, first-line treatments in the United States are proton pump inhibitor monotherapy (52.8%) and topical corticosteroid monotherapy (21.5%).[6]
- Patients with EoE often suffer from other inflammatory diseases. For instance, about 25%–50% of the patients with EoE have concurrent asthma, which also requires treatment with topical and/or systemic steroids.[7]
- While data on the short-term use of swallowed topical corticosteroids (STCs) are abundant, the evidence of real-world burden of long-term cumulative exposure to corticosteroids in the management of EoE are sparse.

OBJECTIVE

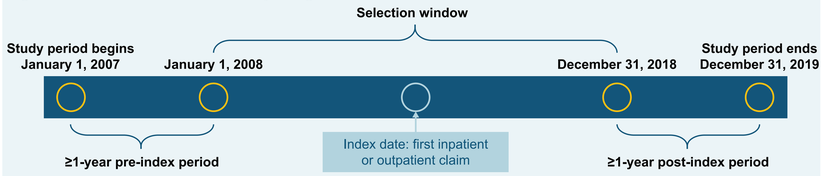
- **To describe the cumulative corticosteroid burden in patients with newly diagnosed EoE compared with a general patient population matched on age, sex, and history of asthma.**

METHODS

Data Source and Study Design

- A retrospective observational study was conducted using de-identified administrative claims data (2007–2019) from the Clinformatics® Data Mart (Optum, Inc.) (**Figure 1**).

Figure 1. Schematic overview of study design



Study Population

- Data from patients with newly diagnosed EoE were included in this study if
  - age was ≥ 1 year as of the index date (first claim of EoE diagnosis).
  - there were ≥ 2 medical claims (≥30 days to <365 days apart) with an EoE diagnosis (International Classification of Diseases [ICD]-9 530.13 or ICD-10 K20.0) during the identification period between January 01, 2008, and December 31, 2018.
  - there was 1-year washout period before the index date, and ≥1 year of continuous enrollment with an allowable gap of 31 days prior to the index date.
- Patients with eosinophilic gastritis/gastroenteritis/colitis in the baseline were excluded.
- Patients with EoE were matched with Optum patients who, on the EoE patient's index date, did not have EoE and satisfied the same enrollment, inclusion, and exclusion criteria.
  - Matching was done 1:1 on age (with a 1-year tolerance), sex, and baseline history of asthma.

Assessments

- Demographics were extracted during a 1-year pre-index period, and treatment history with systemic (SCS), oral (OCS), or inhaled corticosteroid (ICS) was identified by the National Drug Codes or Healthcare Common Procedure Coding System.
- All-cause cumulative corticosteroid exposure and treatment duration were measured during the follow-up period, a variable timeframe starting at the index date and ending at disenrollment or the end of the study.
  - The corticosteroid doses were converted to prednisone-equivalent doses based on active ingredients and the cumulative dose was calculated as the sum of the total dose for all dispensed prescriptions included in the drug class over the assessment period.
  - The cumulative SCS dose included oral and parenteral corticosteroids.

Statistical Analyses

- Unadjusted comparisons of the matched cohorts were performed using t-tests for continuous measures or chi-square tests for binary/categorical variables.
- A two-tailed *P*-value < 0.05 was considered statistically significant.

RESULTS

- Overall, 17,777 patients with EoE (3095 patients aged 1–17 years and 14,682 patients aged ≥18 years) were matched with 17,777 patients from general patient population (3017 patients aged 1–17 years and 14,760 patients aged ≥18 years; **Table 1**).
  - Patients were more commonly male (aged 1–17 years: 71.0%; aged ≥18 years: 62.1%).
  - More than 25% of pediatric patients with EoE were diagnosed with concurrent asthma.
- Patients with EoE aged 1–17 years had significantly longer person-years of follow up than the matched patients (mean [standard deviation {SD}]: 2.91 [2.38] versus 2.73 [2.41]; *P*<0.01). Similarly, the patients with EoE aged ≥18 years had significantly longer person-years of follow-up than the matched patients (2.61 [2.08] versus 2.42 [2.06]; *P*<0.01).
- At baseline, patients with EoE across age groups had significantly (*P*<0.01) higher exposure and longer treatment duration with corticosteroids than their matched patient population (**Table 2**).

Table 1. Baseline demographic and clinical characteristics of patients with EoE and matched general patient population

	Age 1–17 years			Age ≥18 years		
Characteristic	Patients with EoE	Matched control patients	*P* value	Patients with EoE	Matched control patients	*P* value
Number of patients	3095	3017	–	14,682	14,760	–
Age; mean (SD) years	10.01 (4.84)	10.18 (4.76)	0.18	45.02 (15.18)	45.25 (15.27)	0.19
Female; *n* (%)	898 (29.0)	866 (28.7)	0.81	5567 (37.9)	5599 (37.9)	0.99
Race/Ethnicity; *n* (%)						
Asian	110 (3.6)	173 (5.7)	<0.01	264 (1.8)	842 (5.7)	<0.01
Black	167 (5.4)	263 (8.7)	<0.01	726 (4.9)	1436 (9.7)	<0.01
White	2399 (77.5)	1976 (65.5)	<0.01	12,420 (84.6)	9977 (67.6)	<0.01
Hispanic	180 (5.8)	368 (12.2)	<0.01	718 (4.9)	1821 (12.3)	<0.01
Unknown/Missing	239 (7.7)	237 (7.9)	0.88	554 (3.8)	684 (4.6)	<0.01
Any comorbidities; *n* (%)						
Allergic conjunctivitis	35 (1.1)	31 (1.0)	0.79	143 (1.0)	81 (0.5)	<0.01
Allergic rhinitis	1014 (32.8)	592 (19.6)	<0.01	2557 (17.4)	1454 (9.9)	<0.01
Asthma	822 (26.6)	807 (26.7)	0.89	1666 (11.3)	1681 (11.4)	0.92
Any type II condition	1367 (44.2)	755 (25.0)	<0.01	3385 (23.1)	2021 (13.7)	<0.01
Anxiety	209 (6.8)	77 (2.6)	<0.01	1207 (8.2)	788 (5.3)	<0.01
Depression	239 (7.7)	125 (4.1)	<0.01	1630 (11.1)	1282 (8.7)	<0.01
Gastroesophageal reflux disease	1115 (36.0)	61 (2.0)	<0.01	5693 (38.8)	1312 (8.9)	<0.01
Inflammatory bowel disease	42 (1.4)	2 (0.1)	<0.01	250 (1.7)	119 (0.8)	<0.01

EoE, eosinophilic esophagitis; SD, standard deviation.

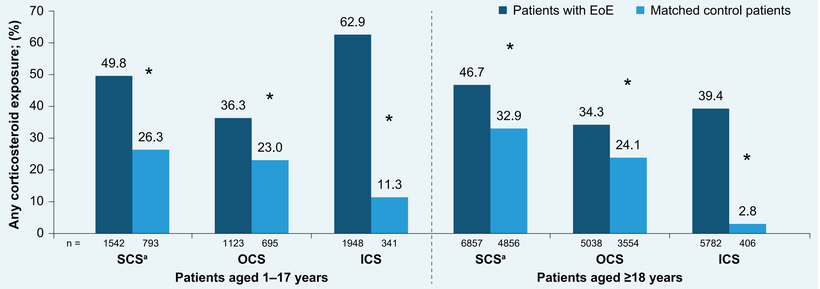
Table 2. Corticosteroid treatment patterns at baseline in patients with EoE and matched general patient population

	Age 1–17 years			Age ≥18 years		
Corticosteroid treatment pattern	Patients with EoE	Matched control patients	*P* value	Patients with EoE	Matched control patients	*P* value
Any SCS[a] exposure; *n* (%)	840 (27.1)	577 (19.1)	<0.01	3983 (27.1)	3065 (20.8)	<0.01
SCS[a] cumulative dose[b]; mean (SD) mg	235.78 (1109.26)	144.46 (549.37)	<0.01	114.53 (779.72)	70.65 (474.60)	<0.01
Annualized SCS[a] treatment duration; mean (SD) days[b]	3.82 (20.07)	2.04 (12.45)	<0.01	4.08 (23.01)	2.92 (19.14)	<0.01
Any OCS exposure; *n* (%)	653 (21.1)	526 (17.4)	<0.01	2719 (18.5)	2078 (14.1)	<0.01
OCS cumulative dose[b]; mean (SD) mg	236.18 (1109.72)	143.95 (547.85)	<0.01	105.26 (768.51)	63.10 (455.66)	<0.01
Annualized OCS treatment duration; mean (SD) days[b]	3.82 (20.07)	2.03 (12.43)	<0.01	4.02 (22.99)	2.88 (19.11)	<0.01
Any ICS exposure; *n* (%)	754 (24.4)	344 (11.4)	<0.01	1309 (8.9)	343 (2.3)	<0.01
Annualized ICS treatment duration; mean (SD) days[b]	21.88 (56.36)	9.37 (35.66)	<0.01	6.17 (30.12)	2.21 (19.89)	<0.01

EoE, eosinophilic esophagitis; ICS, inhaled corticosteroid; OCS, oral corticosteroid; SCS, systemic corticosteroid; SD, standard deviation.
[a]Oral and parenteral corticosteroids; [b]Amongst all patients.

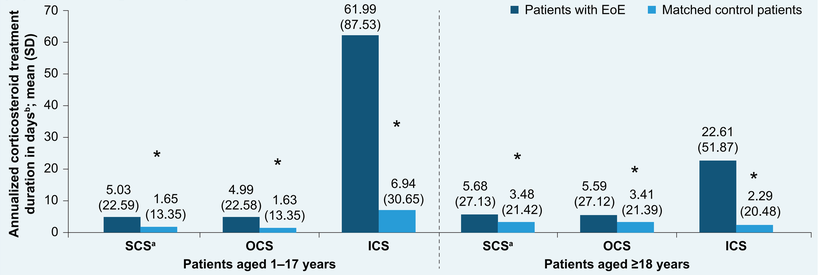
- During the follow-up, patients with EoE aged 1–17 years had significantly (*P*<0.01) higher exposure to SCS, OCS, and ICS than their matched general patient population (**Figure 2**).
- Similarly, significantly higher exposure to SCS, OCS, and ICS was observed in patients with EoE aged ≥18 years, than in their matched cohort (all *P*<0.01; **Figure 2**).
- Compared with the matched general patient population, the mean annualized treatment duration with SCS, OCS, and ICS was also significantly (*P*<0.01) longer in patients with EoE aged 1–17 years and ≥18 years; **Figure 3**).

Figure 2. Any corticosteroid exposure in patients with EoE and matched general patient population during follow-up



EoE, eosinophilic esophagitis; ICS, inhaled corticosteroid; n, number of patients with steroid exposure in the respective cohorts; OCS, oral corticosteroid; SCS, systemic corticosteroid; SD, standard deviation.
[a]Oral and parenteral corticosteroids; *P<0.01.

Figure 3. Annualized corticosteroid treatment duration in days in patients with EoE and matched general patient population during follow-up



EoE, eosinophilic esophagitis; ICS, inhaled corticosteroid; OCS, oral corticosteroid; SCS, systemic corticosteroid; SD, standard deviation.
[a]Oral and parenteral corticosteroids; [b]Amongst all patients; *P<0.01.

CONCLUSIONS

- This study demonstrated that patients with EoE, across all age groups, had considerably more prescriptions, higher cumulative steroid exposure, and longer treatment duration with SCS, OCS, and ICS than their matched general patient population.
- Prescribing corticosteroids to pediatric patients with EoE is of particular concern since they are more susceptible to adverse events related to corticosteroids, with a potential impact on their growth,[8] and have an increased likelihood of cumulative exposure throughout their lifetime.
- When administering STCs for EoE, gastroenterologists should examine historical and current exposure since the cumulative steroid burden rises with a chronic disease, especially in patients with coexisting inflammatory conditions.

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Conflicts of interest: **SN**, **TP**, **JJN**, **AN**, and **STT** are employees and stockholders of Sanofi. **AR** and **RBT** are employees and stockholders of Regeneron Pharmaceuticals, Inc.

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