Health Care Resource Use and Costs Associated With Side Effects of Oral Corticosteroid Use in Chronic Idiopathic Urticaria (CIU): A Claims-Based Analysis

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INTRODUCTION

- Oral corticosteroids (OCS) are a common therapy in patients with chronic idiopathic urticaria (CIU) who remain symptomatic on H_1-antihistamine therapy.[1]
- OCS are associated with side effects that may lead to negative health outcomes[2,3] and may contribute to a higher health care burden.
- Data on costs associated with possible OCS-related side effects in patients with CIU are lacking.

OBJECTIVE

- To quantify risks and costs associated with possible side effects (PSE) related to OCS use in patients with CIU.

METHODS

Study Population

- We used data from a commercial claims database (January 1, 2008–December 31, 2012, inclusive).
- Patients with CIU were identified in calendar years 2008–2011 (baseline years) by the following criteria (met during ≥1 full calendar year):
  - Inclusion criteria
    - 2 outpatient diagnoses of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 708.1, 708.8, or 708.9 (idiopathic urticaria, other specified urticaria, and unspecified urticaria, respectively) ≥6 weeks apart in the calendar year; or
    - 1 outpatient diagnosis of ICD-9-CM code 708.1, 708.8, or 708.9, plus 1 diagnosis of 995.1 (nonhereditary angioedema) ≥6 weeks from the 708.x diagnosis in the calendar year
  - Exclusion criteria
    - Not continuously enrolled in a health plan in the baseline year and enrolled <12 months after the index date; or
    - <18 years of age at the end of the baseline year.
- The index date of identified patients was defined as January 1 of the next calendar year.
- For patients who were identified in multiple calendar years, the earliest index date was used.
- The baseline year was defined as 1 year immediately before the index date. The follow-up period began on the index date and continued for ≥1 year until the end of enrollment or study end (December 31, 2012).

Study Variables

- First, we estimated the hazard associated with developing a new instance of OCS-related side effects, depending on the OCS exposure.
  - OCS exposure was measured as cumulative prednisone-equivalent exposure[4] based on pharmacy claims.
  - OCS-related PSEs were identified based on ICD-9-CM codes and Current Procedural Terminology codes listed in claims with the selected procedure or diagnosis in any coding field.
  - PSEs were defined as new instances of the following conditions: diabetes mellitus, hypertension, lipid disorders,[5] cataracts, neuropsychiatric conditions (depression[6,7] or mania), skeletal conditions (nonvertebral or vertebral fractures or osteoporosis), and infectious diseases (pneumonia or opportunistic infections including herpes zoster).
- We compared changes from the baseline year to the post-index period (increment) in claims-based mean total adjusted annualized health care costs (in 2012 USD) between patients with and without PSEs (adjusted for the covariates age, sex, Charlson Comorbidity Index [CCI] score, and use of immunosuppressive and miscellaneous agents [cyclosporine, dapsone, doxepin, hydroxychloroquine, methotrexate, mycophenolate, and sulfasalazine]).

Statistical Analyses

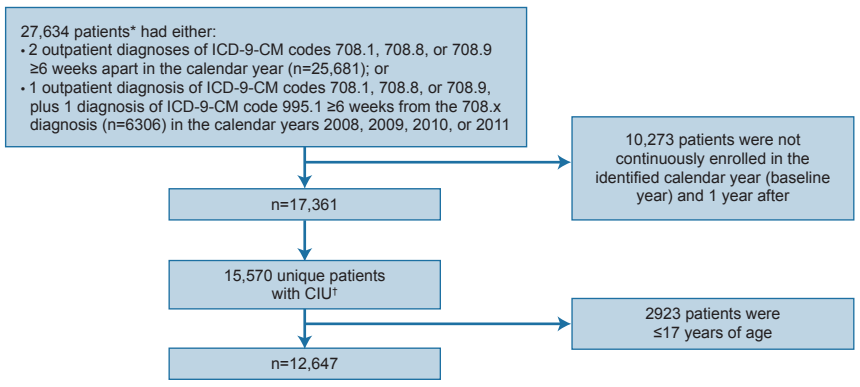
- The unadjusted rate per 100 patient-years was estimated for any PSE (combined) and each PSE separately. OCS exposure in the unadjusted analysis included baseline exposure.
- We used time-dependent Cox regression to separately model cumulative oral prednisone-equivalent exposure in grams (updated daily) and risk of developing PSEs as outlined above.
- For comparing costs, a multivariable linear regression model was used to obtain adjusted parameter estimates, adjusted for the same variables as above.

RESULTS

Patient Characteristics

- 12,647 patients were included in the cohort (**Figure 1**); mean (SD) age was 49.2 (15.9) years (median [range], 49 [18–83] years) and 71.0% were female (**Table 1**).

Figure 1. Patient Disposition



CIU, chronic idiopathic urticaria; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification. *Some patients were identified as meeting study inclusion criteria in >1 calendar year. †When patients were identified as having met study inclusion criteria in multiple years, the earliest year was used.

Table 1. Baseline Patient Demographics

Characteristic	All Patients With CIU n=12,647	Patients With CIU (OCS*) n=7009	Patients With CIU (No OCS*) n=5638
Mean (SD) age, y	49.2 (15.9)	49.2 (15.4)	49.3 (16.5)
Female, n (%)	8979 (71.0)	5042 (71.9)	3937 (69.8)
Baseline year, n (%)			
2008	3434 (27.2)	1832 (26.1)	1602 (28.4)
2009	3024 (23.9)	1639 (23.4)	1385 (24.6)
2010	3020 (23.9)	1698 (24.2)	1322 (23.4)
2011	3169 (25.1)	1840 (26.3)	1329 (23.6)
Mean (SD) days of follow-up	756.3 (378.9)	749.6 (377.0)	764.6 (381.2)
Mean (SD) CCI score	0.90 (1.54)	0.95 (1.54)	0.85 (1.53)
Mean (SD) no. of chronic conditions	3.38 (2.12)	3.49 (2.18)	3.23 (2.05)

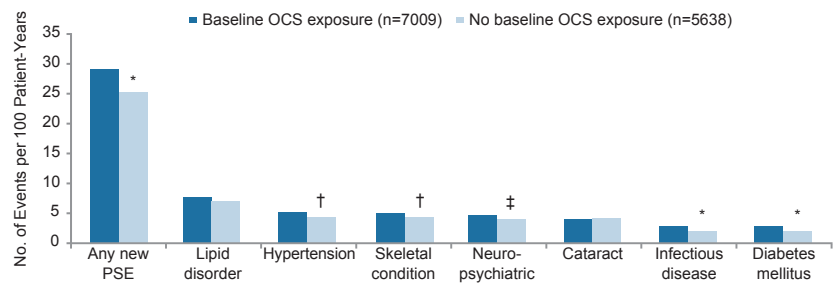
CCI, Charlson Comorbidity Index; CIU, chronic idiopathic urticaria; OCS, oral corticosteroids. *In the baseline year.

Patient Descriptive Characteristics

- Patient baseline demographics are presented in **Table 1**.
- During the baseline year, 55.4% of patients with CIU used OCS.
  - Mean (SD) days supply of OCS was 16.2 (36.0).
  - Mean (SD) per-patient cumulative prednisone-equivalent exposure was 0.367 (0.799) grams.

- The unadjusted rate of new PSEs was 27.3 per 100 patient-years.
  - The unadjusted rate of PSEs was higher in patients with baseline OCS exposure (**Figure 2**).

Figure 2. Unadjusted PSEs per 100 Patient-Years



OCS, oral corticosteroids; PSE, possible side effect. For patients with events of interest, person-years were calculated as years from index date to the event. For patients without events of interest, person-years were calculated as years from index date to end of follow-up. *P* values indicate comparison between the baseline year OCS exposure and no baseline OCS exposure groups. **P*<0.001; †*P*<0.01; ‡*P*<0.05.

- OCS exposure was associated with increased adjusted risk of developing any of the PSE (combined together) and hypertension, skeletal condition, neuropsychiatric conditions, infectious diseases, and diabetes mellitus individually (**Table 2**).
- Controlling for age, sex, CCI score, and use of immunosuppressive and miscellaneous agents, at any given point in time, for an additional 1 gram of prednisone-equivalent exposure, patients with CIU experienced a 7% higher hazard of developing any of the studied side effects (combined) than their counterparts without OCS exposure (**Table 2**).

Table 2. Adjusted HRs (95% CI) per Additional 1 Gram Cumulative (Prednisone Equivalent) Exposure

PSE	HR (95% CI)	*P* Value
Combined PSE		
First PSE	1.07 (1.05–1.08)	<0.001
Individual PSE		
Diabetes mellitus	1.07 (1.04–1.10)	<0.001
Hypertension	1.05 (1.01–1.08)	0.004
Lipid disorders	1.03 (1.00–1.06)	0.049
Cataract	1.02 (0.98–1.05)	0.318
Neuropsychiatric conditions	1.05 (1.02–1.08)	0.001
Skeletal conditions	1.08 (1.06–1.11)	<0.001
Infectious diseases	1.07 (1.05–1.10)	<0.001

CI, confidence interval; HR, hazard ratio; PSE, possible side effect.

Health Care Costs

- In both the baseline year and post-index period, the unadjusted health care costs were higher in patients with claims indicating possible OCS-related side effects than in patients without such claims (**Table 3**).

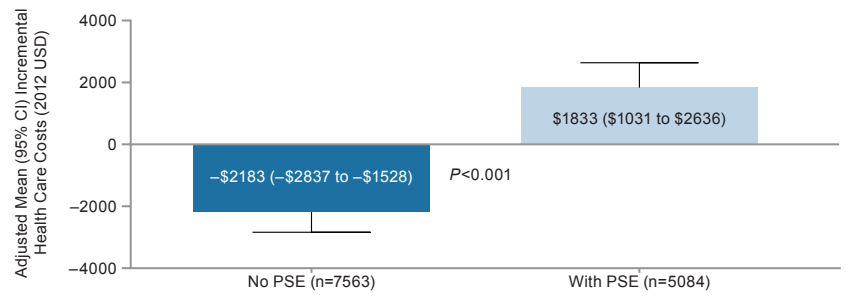
Table 3. Unadjusted Total Annualized Health Care Costs Stratified by OCS-Associated PSE in the Post-index Period

		Total Costs in Baseline Year (PRE)	Annualized Total Costs in the Post-index Period (POST)	Incremental Annual Costs (POST – PRE)
	n (%)	Mean (SD)	Mean (SD)	Mean (SD)
All patients with CIU	12,647 (100.0)	$13,023.40 ($27,182.90)	$12,455.11 ($28,209.00)	–$568.29 ($28,871.90)
No PSE	7563 (59.8)	$10,776.47 ($20,913.00)	$8726.18 ($19,844.80)	–$2050.29 ($22,920.70)
With PSE	5084 (40.2)	$16,365.95 ($34,190.70)	$18,002.28 ($36,638.70)	$1636.33 ($35,835.30)

CIU, chronic idiopathic urticaria; PSE, possible side effect. All costs adjusted to 2012 USD using the medical care components of the Consumer Price Index.

- Linear regression modeling showed that age, CCI score, and presence of a PSE were significantly associated with incremental health care costs (*P*<0.001).
- Adjusted incremental annual health care costs were higher for patients who had a PSE (**Figure 3**).

Figure 3. Adjusted Incremental Annual Health Care Costs With or Without OCS-Associated PSE*



CI, confidence interval; OCS, oral corticosteroid; PSE, possible side effect. *Adjusted by age, sex, Charlson Comorbidity Index score, and medication use (immunosuppressant and miscellaneous); annualized costs in post-index period minus costs in the baseline year.

LIMITATIONS

- Although we controlled for age, sex, CCI score, and use of immunosuppressive and other agents, unobserved confounders (an inevitable shortcoming of claims database analyses) still may have influenced the outcomes of the study.
- PSEs were not confirmed clinically.

CONCLUSION

- Although OCS may help control CIU symptoms, real-world evidence suggests that OCS are associated with side effects, resulting in significant additional health care costs.

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