



**Fig 1.** Forest plot of the association between hidradenitis suppurativa and thyroid disorders. The forest plot shows a significantly higher prevalence of thyroid disorders among patients with hidradenitis suppurativa (odds ratio 1.88, 95% CI 1.25-2.81). *CI*, Confidence interval.

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### The frequency of off-label prescribing in the treatment of dermatologic diseases during 2006-2015



*To the Editor:* Off-label prescribing is the use of a drug for an indication not approved by the Food and Drug Administration (FDA); this practice is often driven by the low financial incentives to seek regulatory approval for every possible indication, particularly for uncommon diseases.<sup>1</sup> Off-label prescribing is often used in the treatment of skin diseases, with the frequency of off-label prescribing for several common skin diseases during the 1990s ranging 17%-73%.<sup>2</sup> However, little is known about the frequency of off-label prescribing for uncommon conditions and whether the frequency of off-label prescribing has changed with the introduction of new FDA-approved treatments.

To evaluate the frequency of off-label prescribing, we identified a representative set of common and uncommon dermatologic diagnoses from prior studies by International Classification of Diseases, 9th Revision, code.<sup>2,3</sup> Using the National Ambulatory Medical Care Survey, we identified medical encounters for these diagnoses during 2006-2015. To

improve accuracy of estimates, diagnoses from our initial representative list with <15 encounters were excluded; because of the limited number of surveyed encounters in the National Ambulatory Medical Care Survey, several uncommon conditions could not be evaluated (eg, dermatomyositis).

To minimize misclassification bias, only encounters with a single primary diagnosis code were included (ignoring codes for growths, which would not require prescription treatment and V-codes). From these encounters, the prescribed drugs were extracted and classified as on-label or off-label for their corresponding diagnoses by using IBM Micromedex (Armonk, NY).<sup>4</sup> Unrelated medications (eg, atorvastatin), vitamins, and over-the-counter medications without FDA approval for the diagnosis were excluded. The primary outcome was the frequency of encounters with  $\geq 1$  prescription for an off-label medication. Secondary analyses included the percentage of medications that were off-label for a given diagnosis. Statistical analyses were performed by using Stata 15 (StataCorp, College Station, TX).

The frequency of off-label prescribing ranged from 0.9% for herpes zoster to 58% for systemic lupus erythematosus (Table I). Of note, because some common treatments, such as topical and systemic steroids, have broadly labelled indications, our results might underestimate the true prevalence of off-label prescribing. Prescribing behavior was similar for dermatologists and nondermatologists, except for hidradenitis suppurativa, for which dermatologists prescribed off-label medications nearly twice as frequently as nondermatologists, although this difference was not statistically significant ( $P = .11$ ,  $\chi^2$ ).

**Table I.** Data from National Ambulatory Medical Care Survey, 2006-2015

ICD-9 code	Diagnosis	All encounters			Encounters with dermatologists			Encounters with nondermatologists		
		% (95% CI) with $\geq 1$ off-label prescription	% (95% CI) medications off-label	Estimated no. visits in millions	% (95% CI) with $\geq 1$ off-label prescription	% (95% CI) medications off-label	Estimated no. visits in millions	% (95% CI) with $\geq 1$ off-label prescription	% (95% CI) medications off-label	Estimated no. visits in millions
692.6, 692.9	Contact dermatitis*	6.7 (5.1-8.3)	3.5 (2.5-4.6)	44	7.0 (4.7-9.4)	3.4 (1.9-4.8)	14	6.5 (4.4-8.6)	3.6 (2.3-4.9)	30
702.0	Actinic keratosis	1.1 (0.5-1.8)	0.6 (0.2-1.1)	39	1.3 (0.6-1.9) <sup>†</sup>	0.7 (0.2-1.2)	35	0.3 (0-0.7)	0.1 (0-0.1)	4.4
706.1	Acne	20 (17-23)	10 (8-12)	34	20 (17-23)	9.4 (8.0-10.9)	27	20 (12-27)	13 (6-21)	7.1
078.10, 078.12, 078.19	Viral warts	13 (9-16)	10 (7-12)	17	15 (9-21)	12 (8-16)	8.7	10 (5-15)	7.2 (3.6-10.8)	8.2
696.1	Psoriasis	13 (9-17)	4.5 (3.0-6.0)	10	13 (8-17)	4.5 (2.8-6.1)	8.9	16 (3-28)	4.6 (0.1-9.1)	1.2
053.9	Herpes zoster	0.9 (0-2.1)	0.4 (0-1.1)	7.2	0 (0-0)	0 (0-0)	0.5	0.9 (0-2.3)	0.5 (0-1.1)	6.7
695.3	Rosacea	33 (26-40)	20 (15-25)	6.5	34 (26-42)	19 (14-23)	5.4	27 (7-48)	24 (5-44)	1.2
691.8	Atopic dermatitis	10 (2-18)	3.9 (1.1-6.8)	6.0	6.3 (1.6-11.1)	2.6 (0.4-4.7)	1.9	12 (0-23)	4.6 (0.5-8.7)	4.0
690.10	Seborrheic dermatitis	5.4 (1.5-9.2)	2.9 (0.5-5.4)	3.5	8.4 (2.3-14.5)	4.6 (0.8-8.5)	2.2	0 (0-0)	0 (0-0)	1.3
694.5, 710.0, 710.8, 710.9	Lupus erythematosus	58 (45-72)	27 (18-36)	2.5	50 (19-80)	18 (3-34)	0.4	60 (45-75)	29 (19-39)	2.1
705.83	Hidradenitis suppurativa	45 (28-62)	33 (17-49)	1.1	72 (40-100)	50 (27-73)	0.2	40 (20-59)	30 (11-48)	0.9
701.0, 710.1	Scleroderma	16 (1-31)	5.9 (0-12.5)	1.0	16 (0-37)	12 (0-30)	0.3	16 (0-37)	3.0 (0-6.2)	0.6
443.0	Raynaud disease	29 (2-56)	25 (1-48)	0.8	NA	NA	NA	28 (1-54)	25 (0-48)	0.8
694.5	Bullous pemphigoid	43 (17-69)	26 (5-48)	0.4	43 (17-69)	26 (5-48)	0.4	NA	NA	NA

CI, Confidence interval; ICD-9, International Classification of Diseases, 9th Revision; NA, not applicable.

\*Including other eczemas of unspecified causes.

<sup>†</sup> $P < .05$  compared with nondermatologist encounters by using the  $\chi^2$  test.

Off-label prescribing remains a significant part of the care of patients with skin disease, even for common conditions, such as acne and rosacea. For instance, nearly a fifth of acne visits included off-label prescribing, which might be related to treatments, such as spironolactone.<sup>5</sup> Off-label prescribing was particularly frequent for uncommon skin diseases with few FDA-approved treatments, such as hidradenitis suppurativa, bullous pemphigoid, and systemic lupus erythematosus. These findings highlight a need for the continued development of FDA-approved treatments for skin diseases.

In addition, given the continued importance of off-label prescribing for the treatment of skin disease, it is concerning that a recent analysis of compendia used by Medicare to determine coverage revealed that many off-label skin disease treatments were not included.<sup>3</sup> Efforts to ensure consistent access to appropriate off-label medications are needed to ensure high-quality care for the unique needs of patients with skin disease.

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## Optimal timing of postoperative pharmacologic pain control in Mohs micrographic surgery: A prospective cohort study



*To the Editor:* The opioid epidemic has added pressure on physicians to limit the amount of narcotics prescribed. However, ensuring that patients have appropriate analgesics available when they are experiencing the greatest amount of pain is crucial. Accordingly, our study's objective was to determine the optimal timing and type of pharmacologic pain control after Mohs micrographic surgery (MMS).

This prospective cohort study was approved by the University of Missouri institutional review board. Each patient logged information in a pain diary starting on postoperative day (POD) 0 at 2 PM and continued in 8-hour increments until POD4 at 6 AM. Patients were asked to record their worst pain rating for each time frame on a scale of 0 through 10, pain medications taken, and whether they felt their pain was well controlled regardless of pain score. Each patient was prescribed 6 tramadol 50-mg tablets and told to take 1 tablet every 4 to 6 hours as needed for postoperative pain of 7 or greater out of 10. Patients were advised to take acetaminophen and/or nonsteroidal anti-inflammatory drugs for lesser pain.

A total of 253 out of 400 patients returned their surveys. The mean age was 71 years; 65% (165) were men and 35% (88) were women. Overall, 45 (115) of cases occurred on the eyelids, ears, noses, or lips; 46% (117) on other head and neck sites; 8% (20) on trunk and extremity sites; and fewer than 1% (1) on genital sites. The average postoperative defect size