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The frequency of off-label prescribing in the treatment of dermatologic disease: 2006–2015

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Off-label prescribing is the use of a drug for an indication not approved by the Food and Drug Administration (FDA), often driven by low financial incentives to seek regulatory approval for every possible indication, particularly for uncommon diseases.¹ Off-label prescribing is often used in the treatment of skin diseases, with the frequency of off-label prescribing for several common skin diseases ranging from 17–73% during the 1990s.² 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, a representative set of common and uncommon dermatologic diagnoses was identified from prior studies.^{2,3} Using the National Ambulatory Medical Care Survey (NAMCS), encounters for these diagnoses between 2006–2015 were identified using International Classification of Diseases, 9th Revision, codes. To improve accuracy of estimates, diagnoses from our initial representative list with fewer than 15 encounters were excluded; due to the limited number of surveyed encounters in NAMCS, several uncommon conditions could not be evaluated (e.g. 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 using IBM Micromedex.⁴ Unrelated medications (e.g. atorvastatin), vitamins, and over-the-counter medications without FDA approval for the diagnosis were excluded. The primary outcome was the frequency of encounters with at least one prescription for an off-label medication. Secondary analyses

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included the percentage of medications which were off-label for a given diagnosis. Statistical analyses were performed using Stata 15 (StataCorp).

The frequency of off-label prescribing ranged from 0.9% for herpes zoster to 58% for systemic lupus erythematosus (Table 1). Notably, since some common treatments such as topical and systemic steroids have broad labelled indications, our results may 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, although this difference was not statistically significant ($p=0.11$, χ^2).

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 may be related to treatments such as spironolactone.⁵ 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 for coverage determinations identified that many off-label treatments for skin disease were not included.³ 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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Table 1.

Data from National Ambulatory Medical Care Survey 2006–2015.

ICD-9	Diagnosis	All				Dermatology			Non-Dermatology		
		% with at least one off-label prescription (95% CI)	% of medications that are off-label	Estimated number of visits, millions	% with at least one off-label prescription (95% CI)	% of medications that are off-label	Estimated number of visits, millions	% with at least one off-label prescription (95% CI)	% of medications that are off-label	Estimated number of visits, 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)*	0.7 (0.2 – 1.2)	35	0.3 (0.0 – 0.7)	0.1 (0.0 – 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 (0.0 – 2.1)	0.4 (0.0 – 1.1)	7.2	0 (0 – 0)	0 (0 – 0)	0.5	0.9 (0.0 – 2.3)	0.5 (0.0 – 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 (0.0 – 12.5)	1.0	16 (0 – 37)	12 (0 – 30)	0.3	16 (0 – 37)	3.0 (0.0 – 6.2)	0.6	
443.0	Raynaud Disease	29 (2 – 56)	25 (1 – 48)	0.8	N/A	N/A	N/A	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	N/A	N/A	N/A	

[†] and other eczemas of unspecified cause

* p<0.05, compared to Non-Dermatology using Chi2 test