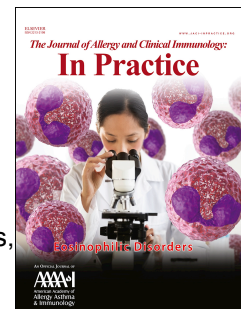


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Prevalence of Prurigo Nodularis in the United States

Katherine A. Whang, BS¹, Varun Mahadevan¹, Pegah R. Bakhshi, BS¹, Kyle A. Williams, BS¹, Sylvie Gabriel, MD, MBA², Rajeev Chavda, MD², Shawn G. Kwatra, MD^{1,3}

Affiliations: ¹Department of Dermatology, Johns Hopkins University School of Medicine, Baltimore, MD, ²Galderma SA, Prescription GBU, Switzerland, and ³Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

Address correspondence to:

Shawn G. Kwatra, MD
Cancer Research Building II, Johns Hopkins University School of Medicine, Suite 206
1550 Orleans Street
Baltimore, MD 21231, USA
Tel: 410-955-8662
Email: skwatra1@jhmi.edu

Clinical Implications Statement: Prurigo nodularis is an underrecognized inflammatory skin condition characterized by intensely itchy nodules that may accompany atopic dermatitis and accounts for 125,000 [95% confidence interval 84,758-165,893] ambulatory visits per year in the United States.

Keywords: prurigo nodularis; itch; ambulatory; disease burden

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Conflict of Interest: Dr. Shawn G. Kwatra is an advisory board member for Menlo and Trevi Therapeutics and has received grant funding from Kiniksa Pharmaceuticals. Dr. Sylvie Gabriel and Dr. Rajeev Chavda are employed by Galderma SA. Galderma is conducting clinical trials of nemolizumab for treatment of pruritus in prurigo nodularis.

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Prurigo nodularis (PN) is an underrecognized inflammatory skin disease that presents with intensely itchy nodules on the extensor surfaces of the limbs and trunk¹. PN is frequently associated with a personal history of atopy and can present concurrently with atopic dermatitis, but represents a distinct dermatologic diagnosis that requires diagnostic evaluation and specific treatment strategies¹. Associated systemic comorbidities include chronic kidney disease, human immunodeficiency virus, and Type 2 diabetes mellitus²⁻⁴. Little is known about the etiology of PN, although current studies describe the role of pro-inflammatory cytokines and neuropeptides in altering nerve density in lesional skin^{1,5}. Despite PN's debilitating psychosocial burden and significant comorbidities, there is a severe lack of epidemiological data on PN^{2,4,6}. One reason for limited available data is that PN has not previously had a dedicated diagnosis code in the widely used diagnostic classification system, International Classification of Diseases, Ninth Revision (ICD-9)⁷. In the current study, we assess the distribution and epidemiology of PN in the United States (US).

We analyzed data from the National Ambulatory Medical Care Survey, a nationally representative survey conducted by the Centers for Disease Control and Prevention. The survey takes a stratified sample of visits from physician offices nationally. We compiled data from 2011 to 2015 and searched for visits with a diagnosis of lichenification (ICD-9 code 698.3), which encompasses both lichen simplex chronicus (LSC) and PN. Survey analysis was performed in STATA 15 to determine nationally representative estimates using published sample weights, clusters, and strata to account for multi-level sample design. We also analyzed data from Johns Hopkins Health System (JHHS) to determine the frequency of the individual diagnoses of PN relative to LSC. Using the electronic medical record system Epic, we searched for the total number of patients diagnosed with each of LSC and PN from 2013-2017, employing similar

methodology to prior studies^{3,6,8}. Based on the proportions of each diagnosis amongst the JHHS patient population adjusted for race, we extrapolated the estimated number of visits for each diagnosis from the NAMCS dataset.

Out of 4.7 billion total weighted ambulatory visits, there were an estimated 1.9 million ambulatory visits (95% confidence interval (CI): 1.3-2.5 million) from 2011-2015 with a diagnosis of 'lichenification' (ICD-9 code 698.3) within the United States with an average of 378,000 visits (95% CI: 256,000-500,000) each year. The leading reasons for visit amongst patients with this diagnosis in the NAMCS dataset included skin rash (13.5%) and skin lesion (10%). These patients were primarily seen by dermatologists (83.2%), while only a minority were seen by primary care providers (11.8%). NAMCS patients with a 'lichenification' diagnosis were 79% white, 8.8% black or African American, and 8.6% of unknown race. At JHHS during the past five years, 958 patients were diagnosed with PN, and 1,732 patients with LSC, representing 35.6% and 64.4% of the patient population with lichenification-related diagnoses, respectively (**Table 1**). When adjusted for race, we estimate that there are 125,322 ambulatory visits per year (95% CI: 84,758-165,893) for PN nationally, or 13 visits (95% CI: 9-18) per 100,000 outpatient visits per year. For lichen simplex chronicus, we estimate 252,504 visits per year (95% CI: 170,769-334,241), or 27 visits (95% CI: 18-35) per 100,000 ambulatory visits per year.

Here, we report a nationally representative estimate of the PN population within the United States. These results are likely to be an underestimation of the overall PN ambulatory burden as well because there is a lack of disease awareness among non-dermatologic physicians. A limitation of our study is that our national dataset captures visits rather than unique patients. Overall, our cross-sectional study of US ambulatory care visits demonstrates that prurigo

nodularis accounts for over 100,000 ambulatory visits each year nationally. Despite the patient burden of PN, there remain limited effective therapies for these patients⁹. Future efforts are needed to better understand disease pathogenesis and investigate treatment options.

Katherine A. Whang, BS¹, Varun Mahadevan¹, Pegah R. Bakhshi, BS¹, Kyle A. Williams, BS¹, Sylvie Gabriel, MD, MBA², Rajeev Chavda, MD², Shawn G. Kwatra, MD^{1,3}

From the ¹Department of Dermatology, Johns Hopkins University School of Medicine, Baltimore, MD, ²Galderma SA, Prescription GBU, Switzerland, and ³Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

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122 **Table 1.** Baseline demographics for prurigo nodularis and lichen simplex chronicus patients at
 123 Johns Hopkins Health System and lichenification patients in the National Ambulatory Medical
 124 Care Survey dataset
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	PRURIGO NODULARIS (n = 958)	LICHEN SIMPLEX CHRONICUS (n = 1732)	LICHENIFICATION (n = 1,889,134)
	JHHS	JHHS	NAMCS
	Freq (%)	Freq (%)	Weighted Freq (%)
GENDER			
Female	501 (52)	1061 (61)	943253 (50)
Male	457 (48)	671 (39)	945882 (50)
RACE			
White	391 (41)	782 (45)	1497129 (79)
Black	476 (50)	700 (40)	166465 (9)
Other	91 (9)	250 (14)	225539 (12)
AGE (years)			
Under 15	31 (3)	68 (4)	73151 (4)
15-24	38 (4)	77 (4)	205561 (10)
25-44	153 (16)	395 (23)	322716 (17)
45-64	483 (50)	710 (41)	584862 (31)
65-74	162 (17)	301 (17)	357295 (19)
75 and older	91 (10)	181 (11)	345551 (18)

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