

could be its prognostic limit. Further studies would be needed to assess if a diameter range should be applied to the BDR; although, in general, thin lesions of large diameters correlate with low BDR and thick lesions with a small diameters correlate with high BDRs, lesions with large diameters and focal deep components would suggest a favorable BDR and prognosis but an unfavorable Breslow prognosis.

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Funding sources: Supported by grants from the Ministerio de Economía y Competitividad (co-financing with Fondos FEDER) (SAF2016-77241-R) and the Fundación Séneca, the Región de Murcia (19304/PI/14) to Drs Rodríguez-López, Cabezas-Herrera, and Piñero-Madrona.

Conflicts of interest: None disclosed.

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REFERENCES

1. Gershenwald JE, Scolyer RA, Hess KR, et al. Melanoma of the Skin. In: Edge SB, Greene FL, Schilsky RL, Gaspar LE, Washington MK, Brookland RK, Brierley JD, Balch CM, Compton CC, Hess KR, Gershenwald JE, Jessup JM, Byrd DR, Winchester DP, Madera M, Asare EA, eds. *AJCC Cancer Staging Manual*. 8th Edition. Switzerland: Springer; 2017:563-585.
2. Balch CM, Gershenwald JE, Soong SJ, et al. Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol*. 2009;27(36):6199-6206.
3. Moreno-Ramírez D, Ojeda-Vila T, Ríos-Martín JJ, Nieto-García A, Ferrándiz L. Association between tumor size and Breslow's thickness in malignant melanoma: a cross-sectional, multicenter study. *Melanoma Res*. 2015;25(5):450-452.
4. Crocetti E, Fancelli L, Caldarella A, Buzzoni C. Thickness and diameter in melanoma: is there a relation? *Tumori*. 2015; 102(1):e1-e3.
5. Voss B, Wilop S, Jonas S, et al. Tumor volume as a prognostic factor in resectable malignant melanoma. *Dermatology*. 2014; 228(1):66-70.

<https://doi.org/10.1016/j.jaad.2018.09.034>

Vulvar cancer association with groin hidradenitis suppurativa: A large, urban, midwestern US patient population study



To the Editor: Anogenital cancer risk factors include age, smoking, human papilloma virus, and lichen sclerosus. Recently, 13 cases of secondary anogenital cancer, including vulvar cancer, were described with pre-existing hidradenitis suppurativa (HS).¹ However, association between anogenital cancer and HS has not been assessed to date.

The aims of this study were to determine whether there is an association between HS and anogenital cancer and to compare the incidence of anogenital cancer among adult females with HS with that among the US adult female population.

Existing data from the Northwestern Medicine Enterprise Data Warehouse, a previously described repository of medical record data of more than 5 million patients,² were extracted; the data extracted were from January 2001 to October 2017 for females age 18 to 89 years with dermatologist follow-up of at least 1 year. In these data, HS was indicated by *International Classification of Diseases, Ninth and 10 Revision* (ICD-9/10) codes (705.83 and L73.2). The control population consisted of all adult female dermatology patients without HS. The outcomes of interest were a subsequent diagnosis of anal cancer (ICD-9/10 codes 154.2, 154.3, and C21) or subsequent diagnosis of genital cancer (cancer of the vulva, labia minora/majora, and vagina) (ICD-9/10 codes 184, C51, and C52) recorded at least 2 months after the diagnosis of HS (or first dermatology encounter date for the controls). The data collected included age, race, smoking status, a diagnosis of lichen sclerosus, and duration of follow-up.

Adjusted odds ratios and 95% confidence intervals were estimated by using multivariate logistic regression analysis. In addition, the Surveillance, Epidemiology, and End Results 2000-2014 database was utilized to estimate the nationwide incidence of anogenital cancer.³

Data for a total of 133,936 patients qualified for analysis (Table I and Fig 1). Of these patients, 716 had HS; vulvar cancer was diagnosed in 3 of the 716 (2 African American and 1 white patient age 45-59 years). No other anogenital cancers were detected in patients with HS. All 3 patients with vulvar cancer had groin HS (adjusted odds ratio, 5.56; 95% confidence interval, 1.74-17.76; $P = .004$), and none of the 3 had lichen sclerosus or human papilloma virus. Moreover, the age-adjusted incidence of vulvar cancer among females with HS in this study population (2.8 per 10,000 persons/y) was 8-fold greater than the age-adjusted nationwide

Table I. Baseline characteristics of adult females seen in the Northwestern University dermatology clinic from January 2001 to October 2017

Characteristic	No HS (n = 133,220)	HS (n = 716)	P value
Age, y			
Mean ± SD	42 ± 15.5	39 ± 12.4	<.0001
Duration of follow-up, mo			
Median (interquartile range)	57.0 (31.0-93.0)	47.5 (27.0-73.0)	<.0001
Race			
White	83,016	285	<.0001
African American	12,883	228	
Other	37,321	203	
Smoking status			
Smoker/former smoker	6453	30	.0164
Never-smoker	19,948	54	
Lichen sclerosus			
No	132,401	714	.2514
Yes	819	2	

Two-sample *t* tests were used for continuous variables, and chi-square tests of association were used for categorical variables; all were included as covariates in multivariate logistic regression. Boldface indicates statistical significance. HS, Hidradenitis suppurativa; SD, standard deviation.

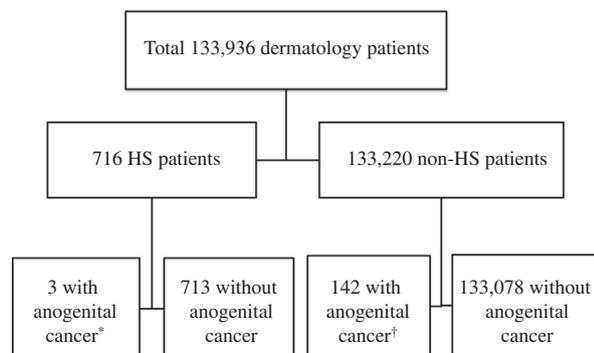


Fig 1. Results of retrospective data collection (January 2001 to October 2017). *All 3 patients with hidradenitis suppurativa (HS) and anogenital cancer had vulvar cancer and groin HS. The incidence of vulvar cancer in patients with HS in this study population was 2.6 per 10,000 persons per year. †The incidence of anogenital cancer in patients without HS was 0.7 per 10,000 persons per year. Specifically, the incidence of vulvar cancer in patients without HS was 0.3 per 10,000 persons per year.

incidence of vulvar cancer among adult females per the Surveillance, Epidemiology, and End Results database (0.3 per 10,000 persons/y).

We report an association between groin HS and vulvar cancer, which is consistent with previously reported cases.⁴ Although the mechanism underlying the association between groin HS and anogenital cancer (specifically, vulvar cancer) is not fully

understood, it seems that chronic local inflammation may be expected to lead to local mutations and cancer, as reported in other inflammatory disorders.⁵ Limitations of this study include the inherent difficulty of verifying diagnostic codes in the medical record and the fact that despite the study's large cohort, 3 cases of HS with vulvar cancer did not allow further stratification. The study's strengths include multiyear follow-up and a large HS population. Because cutaneous malignancies may behave aggressively with HS, increased clinical suspicion for secondary anogenital malignancy may serve to minimize delays in diagnosis and reduce morbidity and mortality. Further exploration of HS as a possible risk factor for vulvar cancer is warranted.

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Acknowledgment: The Northwestern Medicine Enterprise Data Warehouse is supported by Northwestern University Clinical and Transitional Science Institute grant UL1TR0001422.

Conflicts of interest: None disclosed.

Reprints not available from the authors.

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REFERENCES

- Makris GM, Poulakaki N, Papanota AM, et al. Vulvar, perianal, and perineal cancer after hidradenitis suppurativa: a systematic review and pooled analysis. *Dermatol Surg.* 2017; 43(1):107-115.
- Orrell KA, Cices AD, Guido N, et al. Malignant melanoma associated with chronic once daily aspirin exposure in males: a large, single-center, urban, U.S. patient population cohort study from the Research on Adverse Drug Events and Reports (RADAR) project. *J Am Acad Dermatol.* 2018;79:762-764.
- National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Research data (1973-2015), National Cancer Institute, DCCPS, surveillance research program. Cancer stat facts: vulvar cancer. Available at: www.seer.cancer.gov. Accessed October 2, 2018.
- Jourabchi N, Fischer AH, Cimino-Mathews A, et al. Squamous cell carcinoma complicating a chronic lesion of hidradenitis

suppurativa: a case report and review of the literature. *Int Wound J*. 2017;4(2):435-438.

5. Rekawek P, Mehta S, Andikyan V, et al. Squamous cell carcinoma of the vulva arising in the setting of chronic hidradenitis suppurativa: a case report. *Gynecol Oncol Rep*. 2016;16:28-30.

<https://doi.org/10.1016/j.jaad.2018.10.008>

The cost of an itch: A nationally representative retrospective cohort study of pruritus-associated health care expenditure in the United States



To the Editor: Pruritus arises from many common diseases and is reported as a symptom in >7 million outpatient visits annually in the United States.¹ The impact of pruritus on quality of life is substantial and comparable with that of chronic pain.² Although there are limited studies regarding its epidemiology, pruritus has an estimated lifetime prevalence of 25.5% and most commonly affects patients who are female, elderly, and of lower socioeconomic status.¹⁻³ Despite the significant health and biopsychosocial burden posed by pruritus, limited information exists regarding its economic burden. As such, the goal of this study was to provide nationally representative estimates of the incremental health care burden of pruritus controlling for sociodemographic characteristics and comorbidities.

In this study, we used 9 years of data from the Medical Expenditure Panel Survey (MEPS; 2007-2015), a nationally representative survey assessing patterns of utilization of outpatient care in the United States. The methods of administration for MEPS are detailed elsewhere.⁴ All analyses were done in *R* accounting for the complex survey design of MEPS to provide nationally representative samples.

We compared sociodemographic characteristics of patients with pruritus (International Classification of Disease Ninth Revision, Clinical Modification code 698) to those without pruritus using Rao-Scott chi-squared tests. To determine the adjusted incremental inflation-adjusted expenditure (in USD) of pruritus controlling for all other factors, we constructed a 2-part linear regression model to account for the high concentration of zero expenditures in the data. Our 2-part model consists of logistic regression to predict the likelihood of nonzero expenditures and a generalized linear model to predict conditional nonzero expenditures. A generalized linear model with a gamma distribution and log-link function was used to address the positive skewness of the

expenditure data. Our model was used to estimate expenditure ratios, which represented the adjusted multiplicative effect of a variable compared with the reference class. For example, an expenditure ratio of 2 would indicate that patients with pruritus had twice the health care expenditure of patients without pruritus, controlling for other factors. The advantages of this validated 2-part model have been previously described.⁵

In total, our sample included 637 patients with pruritus and 288,061 patients without pruritus. Women, older adults, nonwhite patients, Medicaid and Medicare patients, patients with less education, and patients with more comorbidities were all more likely to have pruritus ($P < .001$ for all, [Table I](#)). Controlling for Charlson Comorbidity Index and all sociodemographic factors, the cost of care for patients with pruritus is 1.64 times as high as patients without pruritus ($P < .001$, [Table II](#)). Although emergency room and home health service expenditures due to pruritus have increased over time, expenditures due to pruritus in both the outpatient and inpatient setting have decreased.

Pruritus is a significant burden to both medical and financial health. Patients with pruritus are estimated to face \$4,843.68 (adjusted for inflation) more in annual health care expenditures than patients without pruritus, even after controlling for comorbidities and sociodemographic factors. When accounting for even the most conservative national estimates of chronic pruritus (6.1%), our data suggests that pruritus is associated with >\$90 billion per year in population-level expenditures in the United States.^{3,6}

Strengths of this study include analysis of a large, nationally representative data set to provide cost estimates.⁴ A limitation is that unmeasured confounders might have overestimated the incremental cost, given the demographic differences between the pruritus and nonpruritus patient population found in this study.

Elucidating the health care costs due to pruritus is vital, considering its association with numerous chronic diseases. Although the incremental cost associated with pruritus has remained steady, expenditures due to pruritus seem to be shifting from outpatient and inpatient settings to the emergency room and home health services. As overall health care costs continue to rise, it is critical to identify effective strategies to improve the control and management of pruritus.

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