

Introduction

- Prurigo nodularis (PN) is a chronic inflammatory, pruritic skin disorder characterized by raised papules and hyperkeratotic nodules
- PN has been linked to malignancy, though **cancer types** and mechanisms remain **unclear**
- Prior studies are limited by **geographic scope**, sample size, or lack of demographic diversity.
- We utilized the **All of Us Research Program**:
 - A **nationally representative**, U.S.-based electronic health record and genomic database
 - Includes **over 1 million diverse participants**

Aims

- Quantify the risk of specific skin cancers in individuals with PN compared to matched controls
- Use a diverse, population-based dataset to enhance generalizability of findings across racial and ethnic groups in the U.S.

Methods

Study Design:

- Retrospective analysis of **869 individuals** with PN using concept ID 4272156 and propensity matched them to two controls (n = 1738) based on age, sex, race, and ethnicity.
- Curated Datasets of
 - Diagnoses of basal cell carcinoma (BCC), cutaneous squamous cell carcinoma (cSCC), and melanoma
 - demographic and clinical variables, smoking status, insurance, income, family skin cancer history, and healthcare use (none, low, or high) (Table 1).

Primary Outcome: PN cases had a higher prevalence of any skin cancers compared to controls

Analysis:

- Univariate associations were tested with χ^2 or Fisher's exact t-test
- Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated
- Multivariable logistic regression models were adjusted for age, race, ethnicity, sex, income, insurance, smoking status, family history of skin cancer, and healthcare utilization.
- P-values were corrected using the Benjamini-Hochberg procedure.

Results

Table 1: Demographics and prevalence of skin cancers in PN patients vs. matched controls

Characteristic	PN group (n = 869)	Controls group (n = 1738)	P-value	Adjusted P-value
Age, years; mean (SD)	66.92 (12.70)	66.90 (12.69)	0.981	
Female	482 (55.5)	964 (55.5)	>0.99	
Race			>0.99	
Asian	<20	28 (1.6)		
Black or African American	212 (24.4)	422 (24.3)		
White	519 (59.7)	1038 (59.7)		
Ethnicity			0.988	
Hispanic	77 (8.9)	152 (8.7)		
Not Hispanic	751 (86.4)	1502 (86.4)		
Ever smoked	428 (49.3)	841 (48.4)	0.071	0.115
Insurance			< 0.001	< 0.001
No	<20	79 (4.5)		
Yes	836 (96.2)	1529 (88.0)		
Income			0.056	0.100
≤ \$50 k	357 (41.1)	784 (45.1)		
> \$50 k	512 (58.9)	954 (54.9)		
Family history of skin cancer			0.001	0.00166
No	52 (6.0)	69 (4.0)		
Yes	268 (30.8)	450 (25.9)		
Missing	549 (63.2)	1219 (70.1)		
Health-care utilization			0.114	0.186
No visits	21 (2.4)	56 (3.2)		
Low utilization	268 (30.8)	496 (28.5)		
High utilization	97 (11.2)	159 (9.1)		
Missing	483 (55.6)	1027 (59.1)		

Figure 1: Prevalence of Skin Cancers in PN vs. Control Groups

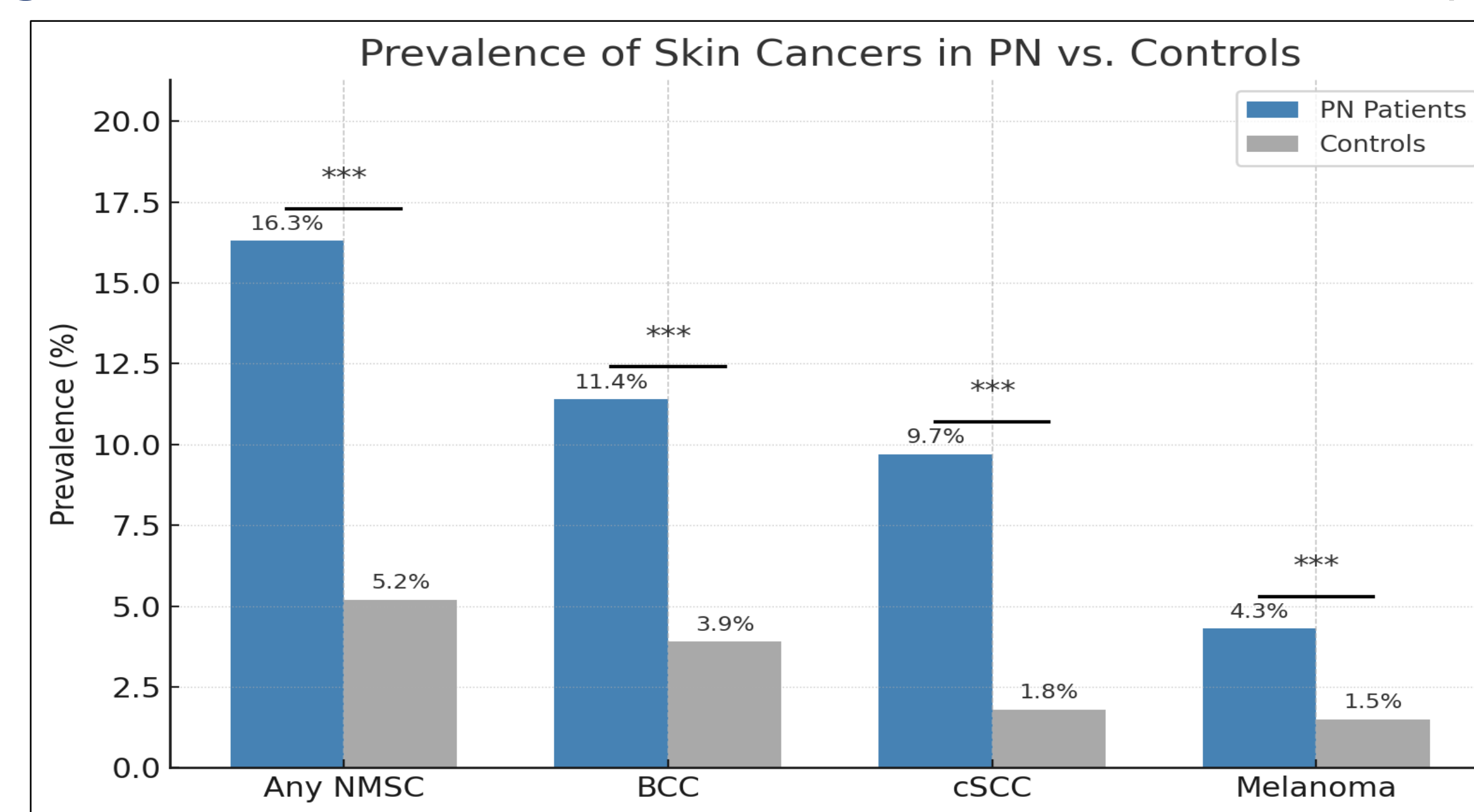


Table 2: Association of PN with melanoma, BCC, and cSCC in univariate and multivariate analyses

Malignancy	Univariable OR (95% CI)	P-value	Multivariable OR (95% CI)	P-value
BCC	3.16 (2.29 - 4.35)	< 0.001	3.31 (2.33 - 4.69)	< 0.001
cSCC	5.89 (3.87 - 8.91)	< 0.001	6.09 (3.89 - 9.53)	< 0.001
Melanoma	2.93 (1.76 - 4.87)	< 0.001	3.01 (1.77 - 5.13)	< 0.001

Conclusions

- This large, matched case-control study found that patients with PN have significantly higher odds of developing basal cell carcinoma, squamous cell carcinoma, and melanoma, independent of demographics, socioeconomic status, and healthcare utilization.
- Several biologic mechanisms may underlie this association:
 - Chronic inflammation and skin trauma** from persistent scratching may promote carcinogenesis through barrier disruption and tissue remodeling.
 - PN is associated with a **Th2-skewed cytokine profile** (elevated IL-4, IL-13), which may impair antitumor immunity and foster a pro-oncogenic microenvironment.
 - Long-term **use of immunosuppressive agents**, common in refractory PN, may further contribute to cancer susceptibility.
- These findings underscore the need for heightened **oncologic vigilance** in patients with PN, particularly those with extensive or long-standing disease.
- Future studies should explore whether treatment with **IL-4/IL-13 inhibitors** (e.g., dupilumab) alters long-term cancer risk in PN, offering insight into the immunologic links between chronic pruritus and tumorigenesis.
- Strengths:** Large, diverse cohort; robust matching and multivariable adjustment.
- Limitations:** Residual confounding, potential surveillance bias, missing data (e.g., family history, utilization rates).

References

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