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Prevalence and risk factors for high-frequency basal cell carcinoma in the United States

To the Editor: Rare genetic diseases such as basal cell nevus syndrome (BCNS) or Gorlin syndrome are known to predispose patients to early-onset, high-frequency basal cell carcinoma (HF-BCC).[1] However, there are patients who develop unusually frequent BCCs but who do not harbor germline mutations in *PTCH1* or *SUFU* or meet the clinical phenotypes of known genetic syndromes. A retrospective study of patients with BCC at Stanford evaluated with genetic testing and pathology found that among patients with nonsyndromic BCC monitored for 5 to 10 years, 3% of patients developed 9 or more BCCs.[2] Patients with HF-BCC were also noted to have a 4-fold higher risk for other malignancies such as lymphoma, leukemia, and breast and colon cancer.[3] A retrospective cohort study of the Danish health national registries, which include all country inhabitants, found that the prevalence of patients with nonsyndromic HF-BCC, defined as 9 or more BCCs during any 3-year period from 1999 to 2013, was 49.39 per 100,000.[4] Patients with nonsyndromic HF-BCC have not been well characterized in the United States.

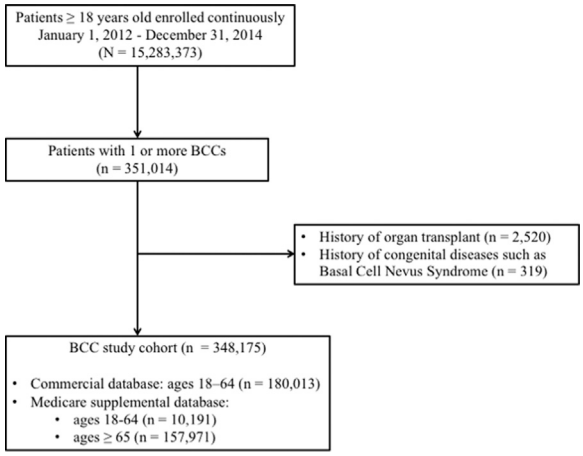

Fig 1. Consolidated Standards of Reporting Trials (CONSORT) diagram of enrollees included in this study. BCC was identified in patients with International Classification of Diseases, Ninth Revision—Clinical Modification diagnosis code for BCC associated with a Current Procedural Terminology code for malignant destruction, excision, or Mohs micrographic surgery. *BCC*, Basal cell carcinoma.

We conducted a national retrospective cohort study using insurance claims data from 15,283,373 patients ages 18 years and older in the IBM MarketScan Commercial and Medicare Supplemental databases from January 1, 2012, through December 31, 2014. We defined HF-BCC as 9 or more BCCs during 3 years, approximately more than 3 standard deviations above the mean, which translates to a clinically significant tumor burden of 3 per year. Fig 1 summarizes the study methodology. A Stanford University institutional review board waiver of informed consent was obtained.

Table I summarizes the demographics of patients with 1 or more and 9 or more BCCs during 2012 to 2014. The multiplicity coefficient in this study, defined as the total BCC tumor burden compared to single BCC tumor burden, was 1.8, which is higher than estimates of studies in Europe, which found multiplicity coefficients of 1.5 in male and 1.2 in female patients.[5] The mean number ± standard deviation of BCCs on the face for patients with HF-BCC was 3.2 ± 3.6. We found that having 9 or more BCCs versus only 1 BCC during the 3 years was associated with male sex (odds ratio [OR], 2.02; 95% CI, 1.90-2.14; $P < .001$), history of squamous cell carcinoma (OR,

Table I. Study demographics and US BCC prevalence estimates

Characteristic	Study population, N*	Patients in study with ≥1 BCC, n	Patients in United States with ≥1 BCC, n	Prevalence of ≥1 BCC per 100,000	Patients in study with HF-BCC, n†	Patients in United States with HF-BCC, n†	Prevalence of HF-BCC per 100,000†
Total patients	15,283,373	348,175			6141		
Age group, y							
18-19	601,935	23	324	0.1	0	0	0.0
20-24	973,936	243	5621	2.3	0	0	0.0
25-29	796,774	674	18,341	7.5	<11	163	0.1
30-34	1,150,076	2593	48,067	19.7	16	297	0.1
35-39	1,344,944	5835	85,719	35.2	44	646	0.3
40-44	1,629,666	12,976	163,007	66.9	132	1658	0.7
45-49	1,817,620	23,266	266,402	109.3	268	3069	1.3
50-54	1,991,275	38,890	439,975	180.4	517	5849	2.4
55-59	1,924,559	52,988	591,480	242.6	688	7680	3.1
60-64	1,162,653	52,716	841,040	344.9	650	10,370	4.3
65-69	630,431	34,102	828,409	339.8	635	15,425	6.3
70-74	457,676	35,072	848,347	347.9	751	18,166	7.5
75-79	351,822	33,319	750,070	307.6	881	19,833	8.1
80-84	259,917	29,717	658,269	270.0	896	19,848	8.1
≥85	190,089	25,761	834,049	342.1	657	21,271	8.7
Age adjusted			6,379,120	2616.3		124,275	51.0
Sex							
Male	7,195,830	193,474	3,177,922	1303.4	4529	74,391	30.5
Female	8,087,543	154,701	2,403,099	985.6	1612	25,041	10.3
Sex adjusted			5,581,021	2288.9		99,432	40.8
Region							
Northeast	3,103,576	67,184	956,309	392.2	1350	19,216	7.9
North Central	3,556,529	78,859	1,150,792	472.0	1371	20,007	8.2
South	5,492,613	129,885	2,150,518	882.0	2053	33,992	13.9
West	2,817,612	64,580	1,302,025	534.0	1250	25,202	10.3
Unknown	313,043	7667	N/A	N/A	117	N/A	N/A
Region adjusted			5,559,644	2280.2		98,417	40.4

BCC, Basal cell carcinoma; *HF-BCC*, high-frequency basal cell carcinoma; *N/A*, not applicable.
*Eligible participants within the IBM MarketScan Databases at least 18 years old in 2012 and enrolled continuously within the study period from January 1, 2012, to December 31, 2014.
†HF-BCC is defined as 9 or more BCCs in 3 years.

4.66; 95% CI, 4.41-4.92; $P < .001$), and melanoma (OR, 2.47; 95% CI, 2.29-2.66; $P < .001$). Based on age-adjusted census data, an estimated prevalence of 51 per 100,000 persons ages 18 years and older (an estimated 124,275 patients) in the United States had HF-BCCs in 2012 to 2014. In basal cell nevus syndrome, the most common genetic syndrome associated with frequent BCC, the highest documented prevalence is 1:31,000, or 3.24 per 100,000 persons, which extrapolates to approximately 10,000 patients in the United States in 2014.[1] Further research of patients with nonsyndromic HF-BCC may lead to oncogenic markers for risk-stratifying patients at highest risk for developing subsequent BCCs and internal malignancies.

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this study, and all data complied with the Health Insurance Portability and Accountability Act.

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