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Clinical-Testis cancer

Mean treatment cost of incident cases of penile cancer for privately insured patients in the United States

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Abstract

Purpose: The aims of this study were to estimate the short-term cost of treating newly diagnosed penile cancer and determine the correlates of penile cancer treatment cost in the United States.

Methods: The Truven MarketScan database was used to identify commercially insured patients with penile cancer newly diagnosed during 2011 to 2014. A control group without HPV-related cancer diagnosis was selected by matching to the case group by the propensity score method. Total healthcare costs in the 2 years after the cancer diagnosis index date were measured for each patient. The mean difference between case and control groups was considered the cancer-related cost. For patients without complete 2-year data, a generalized linear regression was performed to predict cost for censored months and identify predictors associated with monthly cost.

Results: A total of 250 patients with newly diagnosed penile cancer and 250 matched controls were included in the study. The adjusted mean differential healthcare cost for penile cancer was $76,404 in the first 2 years. For the penile cancer group, cost peaked in month 1 at $10,202 and dropped substantially each month thereafter until month 7, when the cost was $4,295. After month 7, the monthly cost remained steady at $2,700 to $4,200.

Conclusions: The estimated average cost of penile cancer for insured patients in the United States was about $76,000 in the first 2 years after diagnosis. Monthly cost was directly related to age, length of follow-up, comorbidity score, and prediagnosis cost.

Keywords: Healthcare costs; Health expenditures; Penile cancer; Insurance claims review

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Précis: The estimated average medical cost of penile cancer for insured patients in the United States is about $76,404 in the first 2 years after diagnosis.

Take-away points: Most of the $76,000 first 2-year cost of treating penile cancer occurs during the first 6 months following diagnosis. Monthly costs are directly related to age, length of follow-up, comorbidity score and prediagnosis cost.

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1. Introduction

Penile cancer is a rare, debilitating malignancy that occurs mainly in men 50 to 75 years of age [1]. During 2004 to 2012, the age-related incidence was rising in the United States while the overall incidence remained stable at 0.8 per 100,000 population, with 1,168 new cases per year during 2008 to 2012 [2]. Blacks and Hispanics had higher rates and Asian-Pacific Islanders had lower rates than non-Hispanic whites [2,3]. Estimates range from 20% to 60% of cases being attributable to human papillomavirus (HPV) infection [4,5], and therefore HPV immunization is a potentially viable prevention strategy for this disease.

High-risk HPV strains are associated with development of several different cancers, including penile cancer, whereas the low-risk HPV strains are associated with development of genital warts. During the period 2013 to 2014, among males aged 18 to 59, the prevalence of any genital HPV infection was 45.2% and of high-risk HPV infection, 25.1%. For females aged 18 to 59, the prevalence of any genital HPV infection was 39.9% during the same period and of high-risk HPV infection, 20.4%. The rates were highest among non-Hispanic blacks and lowest among non-Hispanic Asians [6].

The US HPV immunization rate is lower than in other developed countries, where there is more concerted public effort to vaccinate [7]. In a 2015 study, approximately 42% of females and 28% of males aged 13 to 17 years in the United States had completed the HPV vaccination series of 3 doses, while 52% of females and 39% of males had completed 2 doses [8]. With most US states reluctant to require HPV vaccination for schoolchildren, healthcare providers, and public health agencies need to consider the economic and health consequences of expending resources to increase the HPV vaccination rate. The cost associated with cancer treatment provides an important offset to the cost of immunization promotion efforts.

While there are economic models of HPV-related cancers, they are limited by the quality of data on the cost of treating HPV-associated cancers. Economic models have relied on approximations of the cost of penile cancer that were developed by scenario analysis by a US Institute of Medicine committee in 1999 [9]. More recent cost studies were conducted in England and Denmark and are not applicable to the US system, given the differences in cost structure and treatment protocols [10,11]. Therefore, our primary aim was to estimate the current initial and continuing treatment costs associated with incident cases of penile cancer and to examine the demographic, comorbidity, and treatment-modality correlates of these costs.

2. Material and methods

2.1. Data source and study population

The Truven MarketScan Commercial Claims and Encounter Database (CCAE) from 2011 to 2014 was the data source. CCAE contains patient-level information on health insurance claims collected from multiple sources, such as employers and health plans. CCAE has proven to be a reliable and comprehensive data set for healthcare cost and utilization studies [12]. At the time this study was funded (September 2015), the latest data available to the University of Texas Data Center was for years 2011 to 2014. The data set contained healthcare claims for 200 million lives covered by private health insurance in the United States. Our previous work on female genital cancers suggested that this data set would be sufficient for estimating the cost of relatively rare cancers [13]. With 4 years of data, we had sufficient follow-up to cover the period of time where most treatment costs were incurred. The study included employees and their dependents younger than 65 years who were covered by private insurance. Costs included healthcare claim payments for inpatient services, outpatient services, and prescription drugs. The database was deidentified and exempt from Institutional Review Board approval.

2.2. Case identification

A penile cancer case was defined by patients with at least 1 inpatient (primary or secondary) or 2 outpatient diagnoses more than 30 days apart (primary or secondary) with an International Classification of Disease ninth revision, Clinical Modification (ICD-9-CM) code of 187.1 (malignant neoplasm of penis and other male genital organs, prepuce), 187.2 (glans penis), 187.3 (body of penis), 187.4 (penis, part unspecified), or 187.8 (other specified sites of male genital organs). The first date on which the diagnosis of penile cancer occurred was defined as the index diagnosis date. Patients were excluded if they either did not have continuous enrollment in the health plan during the 6 months before and 6 months after the index date or had another cancer diagnosed in any site during the 6 months before the index date (ICD-9-CM code of 140–208). Patients who had more than $1,000,000 of healthcare costs after the index date were defined as the outliers and were excluded from the study to avoid overestimating the mean treatment cost.

2.3. Control selection

Controls were selected from the health plan enrollees who had no penile cancer or other HPV-related cancer, including cervical, oropharyngeal, vaginal, vulvar, or anal cancer. An initial control group was selected on the basis of the following matching criteria: (1) index date (identical with cases), (2) age (within 5 years of case age), (3) male, and (4) geographic area. Patients who had not been enrolled in the health plan continuously during the period 6 months before and 6 months after the index date were excluded. The exclusion criterion of 6 months continuous enrollment before the index date allowed identification of patients' Charlson Comorbidity Index score (CCI) [14], psychiatric diagnosis groups (PDGs) [15] and pre-diagnosis cost before the index date. The 6 months after the

index date ensured that patients had at least 6 months of follow-up health insurance claims data. Patients who were diagnosed with any cancer during the 6 months before the index date were excluded. The propensity score was computed for each case and its initially matched controls using logistic regression, with the following covariates: (1) CCI during 6 months before the index date, (2) PDGs during 6 months before the index date, (3) cost observed during the period from 3 months to 6 months prior to the index date (prediagnosis cost), and (4) healthcare insurance plan. We excluded the costs incurred during the 3 months immediately before the index date to avoid the costs associated with cancer diagnosis [16]. For each case, 1 control was selected for matching from those who had a very close propensity score (the Mahalanobis distance within 0.5 standard deviation). Once the control was selected for a given case, that control was removed from the control candidate pool.

2.4. Study outcome and data analysis

The primary outcome in the study was the model-adjusted healthcare costs of penile cancer treatment during the initial 2 years after diagnosis. The observed (no model adjustments) cancer treatment costs were also calculated in total and by cancer stage, approximated from available treatment codes. Six treatment modalities were defined by our clinical experts (CP and KH) for approximating cancer stage (and the treatments associated with that cancer stage) from the health insurance claims data (Supplementary Table 1). Patient's claims for procedure codes (Healthcare

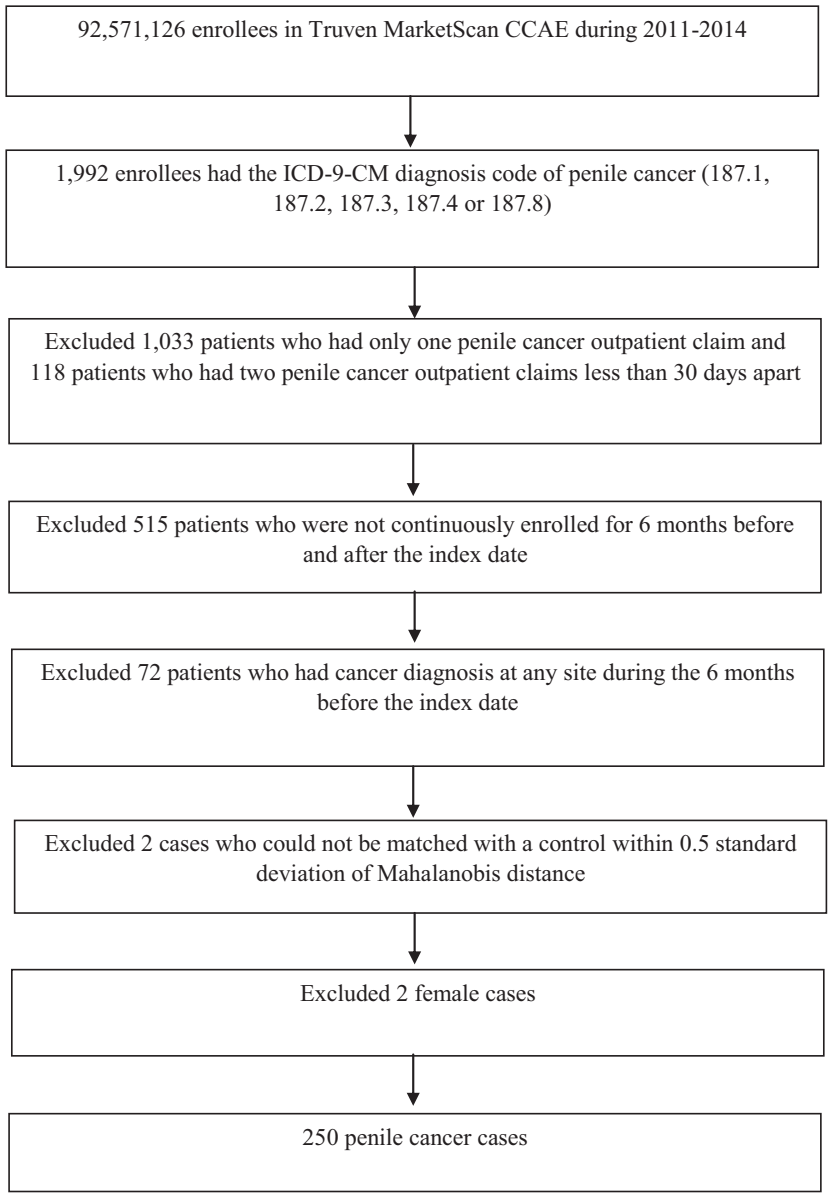


Fig. 1. Flow chart of penile cancer case selections.

Table 1
Characteristics of penile cancer cases and matched controls.

Characteristics	Case group	Comparison group	*P* value
Age, years, mean (SD)	53.08 (9.89)	52.68 (9.89)	0.66
Enrollment duration, months, mean (SD)	19.98 (10.42)	21.22 (10.53)	0.19
Complete 1-year follow-up, *n* (%)			0.37
Less than 1 year	75 (30.00%)	66 (26.40%)	
More than 1 year	175 (70.00%)	184 (73.60%)	
Employment status, *n* (%)			0.35
Active full time	105 (42.00%)	110 (44.00%)	
Active part time or seasonal	1 (0.40%)	3 (1.20%)	
Retired	34 (13.60%)	23 (9.20%)	
Other[a]/Unknown	110 (44%)	114 (45.60%)	
Health insurance plan, *n*(%)			0.96
Comprehensive	14 (5.60%)	17 (6.80%)	
EPO/Unknown	13 (5.20%)	13 (5.20%)	
HMO/POS with capitation/POS	53 (21.20%)	55 (22.00%)	
PPO	143 (57.20%)	142 (56.80%)	
CDHP/HDHP	27 (10.80%)	23 (9.20%)	
Geographic area, *n* (%)			Matched
New England division	9 (3.60%)	9 (3.60%)	
Middle Atlantic division	42 (16.80%)	42 (16.80%)	
East North Central division	47 (18.80%)	47 (18.80%)	
West North Central division	13 (5.20%)	13 (5.20%)	
South Atlantic division	47 (18.80%)	47 (18.80%)	
East South Central division	23 (9.20%)	23 (9.20%)	
West South Central division	29 (11.60%)	29 (11.60%)	
Mountain division	9 (3.60%)	9 (3.60%)	
Pacific division/Unknown	31 (12.4%)	31 (12.4%)	
Charlson Comorbidity Index score, mean (SD)	1.06 (1.57)	1.04 (1.55)	0.91
Psychiatric diagnostic groups, mean (SD)	0.07 (0.27)	0.06 (0.25)	0.73
Prediagnosis 3-mo costs, mean (SD), USD	3,079 (14,916)	1,954 (5,043)	−0.009[b]

[a] Included Consolidated Omnibus Budget Reconciliation Act (continue)/ Long-term disability/ Surviving spouse/Depend/ Other.
[b] Applied the standardized difference method for comparison. Imbalance was defined as the absolute value was greater than 0.2.
Abbreviations: CDHP = consumer-driven health plan; EPO = exclusive provider organization; HDHP = high-deductible health plan; HMO = health maintenance organization; PPO = preferred provider organization; POS = point of service plan; SD = standard deviation; USD, US dollars.

Common Procedure Coding System, Current Procedural Terminology-4, and ICD-9-CM) were assessed to identify their treatment modalities after the diagnosis date (Supplementary Table 2). Proxy cancer stage was classified into 4 levels of increasing disease burden: low-risk primary tumor, high-risk primary tumor, low-risk metastatic, and high-risk metastatic disease. The corresponding treatments for the 4 above levels were (1) minimally invasive surgery alone (Mohs microsurgery, laser surgery, cryosurgery, and surgical excision), or (2) if penectomy (partial and full penectomy), or brachytherapy utilized alone (3) if nodal surgery performed, and (4) if radiation (external beam radiation and intensity-modulated radiotherapy) or chemotherapy utilized with/without other surgical procedures (See Supplementary Table 1)

Costs of copayment, coinsurance, deductibles, and co-ordination of benefits, and other savings were included. Because of skewness of the monthly cost, a generalized linear model with gamma distribution and log link function was applied to estimate the total healthcare costs during the 2 years after the index date. Covariates in the model were age, health insurance coverage plan, geographic area, completion of a 1-year follow-up period, case or control, CCI score, PDGs, prediagnosis cost, proxy cancer stage, first-order month index from months 1 to 24, squared month index from 1 to 576, and interaction terms of (1) case/control and first-order month index and (2) case/control and squared month index. The dependent variable for the model was the patients' 24-partition mean monthly healthcare cost for the 2-year period after the index date. Prediagnosis cost was included to adjust for each subject's healthcare spending. Monthly costs were estimated with the model when patients disenrolled and their cost data were missing. Akaike information criteria were applied to determine the final model on choice of degree of polynomial for month. Due to the nonlinear trend of cost over time, a polynomial of month was chosen to describe the change in cost over time. All the costs were adjusted to year 2015 using the Consumer Price Index from the US Bureau of Labor Statistics [17]. The analysis was performed with SAS for Windows, version 9.4 (SAS Inc.)

3. Results

We identified 250 men with newly diagnosed penile cancer in the CCAE during 2011 to 2014 (Fig. 1). Baseline

Table 2
Observed and model adjusted healthcare costs in cases and controls and differences in costs in the first 2 years after the index date.

	Case group (Median follow-up was 17.5 mo)		Comparison group (Median follow-up was 20 mo)			
Cost estimations	Mean (SD)	Median	Mean (SD)	Median	Difference in means (SD)	*P* value
Year 1 (observed costs)						
All costs	49,591 (83,240)	17,884	7,214 (13,453)	2,432	42,378 (5,333)	<0.01
Inpatient services	23,533 (61,784)	0	877 (4,456)	0	22,656 (3,918)	<0.01
Outpatient services	22,798 (33,191)	11,222	4,380 (10,865)	1,310	18,418 (2,209)	<0.01
Prescription drugs	3,260 (6,886)	670	1,957 (4,422)	209	1,304 (518)	0.01
Years 1 and 2 (observed costs)						
All costs	60,275 (91,192)	23,848	10,952 (22,357)	3,714	49,323 (5,938)	<0.01
Inpatient services	25,948 (64,089)	0	1,629 (8,965)	0	24,319 (4,093)	<0.01
Outpatient services	29,007 (40,174)	15,331	6,457 (14,657)	2,279	22,550 (2,704)	<0.01
Prescription drugs	5,321 (11,421)	1,137	2,866 (6,349)	337	2,455 (823)	0.01
Years 1 and 2 (model adjusted costs which included costs for subjects who were lost in follow-up)						
All costs	91,936 (167,513)	39,043	15,533 (26,265)	7,666	76,404 (119,897)	<0.01

characteristics of the cases and controls are presented in Table 1. The mean age for cases was 53.08 years and for controls, 52.68 years. The median follow-up was 17.5 and 20 months for cases and controls, respectively. About 70% of both populations were monitored for more than 1 year. More than half of patients were covered by a preferred provider organization. There were no significant differences among the cases and controls on demographic or health plan characteristics. There were 1,992 patients with at least 1 penile cancer diagnosis and 1,742 patients were excluded due to not meeting the inclusion criteria. No patients experienced a 2-year healthcare cost of more than $1,000,000. The baseline characteristic and 2 years healthcare cost comparisons between the selected and non-selected penile cancer cases are presented in Supplementary Tables 3 and 4, respectively.

The 2-year observed total healthcare costs for penile cancer without model adjustments were $49,323 (Table 2). The highest cost was incurred for inpatient services, followed by outpatient services and drugs. Only 3.5% of services were paid on a capitated basis. For the proxy cancer stage, 19.6% of patients were defined with low-risk primary tumors and 12.8% for both high-risk primary and high-risk metastatic disease (Supplementary Table 5). Around 50% of patients did not have any treatment modalities in our defined cancer stage classification system. High-risk metastatic patients had the highest mean 2-year healthcare cost ($196,988), followed by high-risk primary ($64,229) and low-risk primary patients ($37,304; Supplementary Table 5). For the generalized linear model, age, having more than 1-year follow-up, case/control, CCI score, prediagnosis costs, interaction term of month index times case/control, and interaction term of squared month index times case/control were significantly associated with cost (Table 3). On average, the 2-year healthcare cost for the cases was 36 times that for the controls ($e^{3.59}$). After adjusting the covariates and censored data, the 2-year total healthcare cost for penile cancer was $76,404 (Table 2). Fig. 2 shows the monthly changes in cost during the 2 years for both cases and controls. Penile cancer patients incurred an average monthly cost of $5,547 during the first 6 months after the index date, compared with $3,259 per month for the remainder of the 2-year period. Note that the predicted 2-year healthcare cost includes costs for subjects who were lost to follow-up whereas the observed costs do not include these missing value estimates.

4. Discussion

We estimated the mean healthcare costs for penile cancer in commercially insured men. A total of 250 penile cancer patients were identified, with the mean age at diagnosis of 53 years. Although a review of penile cancer reported a mean age at diagnosis of 60, with increasing age-specific incidence [18], our population was younger. Of the 1,992 patients with at least 1 healthcare contact with a diagnostic code for penile cancer, 1,033 were excluded because they had only 1 claim for penile cancer in the outpatient service setting. This requirement increased the likelihood that only penile cancer patients with active disease would be selected. Another 515 patients were excluded due to incomplete healthcare insurance enrollment before or after the index date in ensuring that each patient have sufficient follow-up duration in estimating their healthcare costs. We compared the characteristics and 2 years healthcare cost between study cases and patients who did not fully meet the inclusion criterion (Supplementary Tables 3 and 4). Patients who did not meet the full selection criteria were younger and had higher CCI scores, compared with selected cases. There were no significant differences between

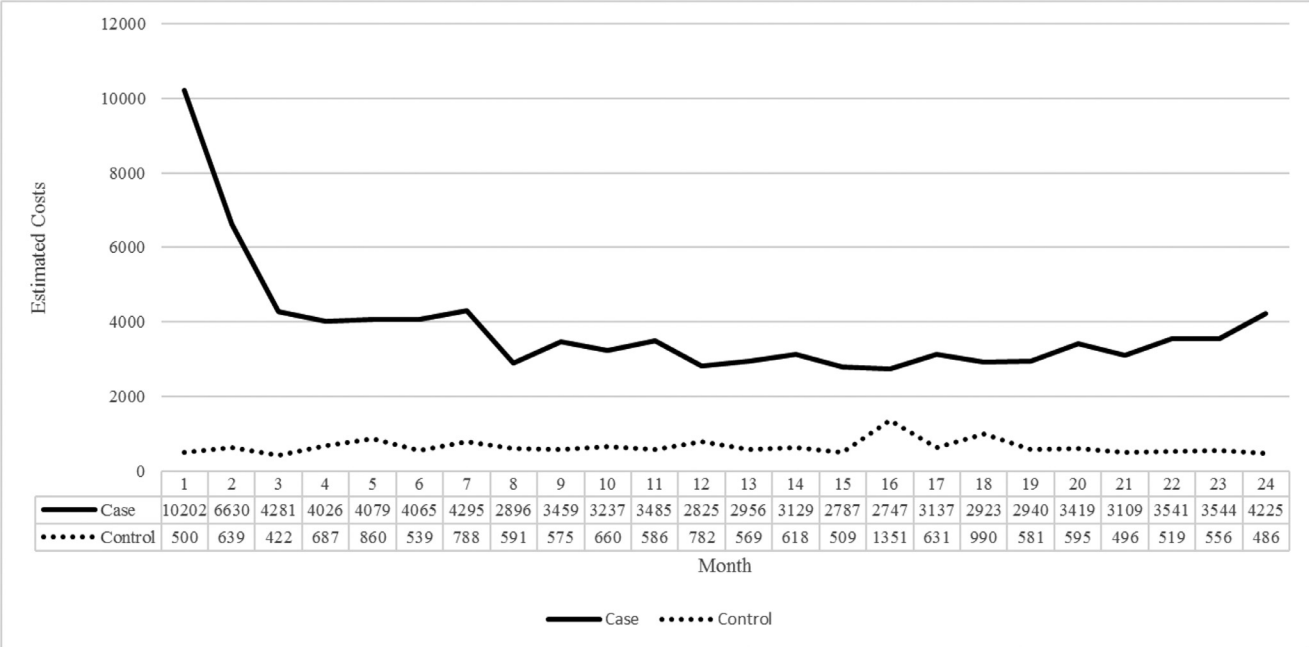
Table 3
Generalized linear model for estimating healthcare costs.

Covariate	Estimated coefficients	Standard error	95% Confidence interval		*P* value
Intercept	5.09	0.77	3.58	6.59	<0.001
Age	0.02	0.01	0.01	0.03	0.005
Health insurance coverage plan					
EPO/Unknown	0.67	0.39	−0.09	1.44	0.083
HMO/POS with capitation/POS	0.07	0.29	−0.50	0.65	0.801
PPO	0.30	0.28	−0.24	0.84	0.284
CDHP/HDHP	0.57	0.50	−0.41	1.54	0.257
Comprehensive	Reference				
Geographic area					
Middle Atlantic division	−0.59	0.40	−1.37	0.20	0.144
East North Central division	−0.25	0.41	−1.05	0.55	0.536
West North Central division	−0.46	0.45	−1.34	0.43	0.313
South Atlantic division	−0.33	0.41	−1.14	0.48	0.426
East South Central division	−0.29	0.43	−1.13	0.56	0.507
West South Central division	−0.29	0.41	−1.08	0.51	0.482
Mountain division	−0.41	0.49	−1.37	0.54	0.399
Pacific division	−0.27	0.43	−1.11	0.56	0.522
New England division	Reference				
Complete 1-year follow-up					
More than 1 year	−0.59	0.18	−0.94	−0.24	0.001
Less than 1 year	Reference				
Case/control					
Case	3.59	0.57	2.47	4.71	<0.001
Control	Reference				
Charlson Comorbidity Index	0.17	0.04	0.08	0.25	<0.001
Psychiatric diagnostic groups	0.36	0.29	−0.21	0.93	0.215
Prediagnosis 3-mo costs	0.00003	0.000005	0	0.0001	<0.001
Stage					
No treatment	−1.00	0.53	−2.04	0.05	0.061
Low-risk primary	−0.74	0.56	−1.85	0.36	0.188
High-risk primary	−0.71	0.54	−1.77	0.35	0.191
High-risk metastatic	0.92	0.53	−0.12	1.96	0.083
Stage combination	Reference				
Month index	0.06	0.04	−0.01	0.13	0.117
Month index^2	0.00	0.00	0.00	0.00	0.105
Interaction term of month index × case/control					
Month index × case	−0.27	0.05	−0.37	−0.16	<0.001
Month index × control	Reference				
Interaction term of month index^2 × case/control					
Month index^2 × case	0.01	0.00	0.01	0.01	<0.001
Month index^2 × control	Reference				

Abbreviations: CDHP = consumer-driven health plan; EPO = exclusive provider organization; HDHP = high-deductible health plan; HMO = health maintenance organization; PPO = preferred provider organization; POS = point of service plan; SD = standard deviation.

selected and nonselected cases on geographic area and prediagnosis costs. The observed first 2-year costs of selected cases were significantly higher than the costs incurred by the nonselected cases. There were slight differences in baseline characteristics and healthcare costs between selected and nonselected patients who had at least 1 diagnosis code for penile cancer.

The mean first 2 years total healthcare cost for penile cancer was $76,404. Age, having more than 1 year of follow-up, CCI score, prediagnosis costs, and interaction term of time and case/control were significantly associated with cost. The available information on the treatment cost for penile cancer is limited. Two articles estimated the cost of treating HPV-related disease by synthesizing published data [19,20]. Hu and Goldie derived a treatment cost estimate of $20,000 per case (adjusting to 2015 prices) from a 1999 Institute of Medicine study on the cost of HPV vaccination [9]. The Institute of Medicine study was based on expert defined clinical scenario analysis to judge resource utilization and cost. Chesson et al. applied the Hu and Goldie cost results updated with current epidemiology of penile cancer to estimate the annual cost burden of penile cancer. Our study used population-based and actual health insurance claims data to estimate the cost, adjusted for covariates and censoring. Total cost for each individual was estimated based on a generalized linear model.



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Case	10202	6630	4281	4026	4079	4065	4295	2896	3459	3237	3485	2825	2956	3129	2787	2747	3137	2923	2940	3419	3109	3541	3544	4225
Control	500	639	422	687	860	539	788	591	575	660	586	782	569	618	509	1351	631	990	581	595	496	519	556	486

Fig. 2. Monthly change of healthcare costs for cases and controls.
Cost estimates shown in US dollars. Months represents month after index date.

We believe that the latter method is more precise and accurate than the former estimates. With the different data sources and cost estimation methods, it is difficult to make comparisons between our findings and the other published results.

We found that the healthcare cost of penile cancer was highest in the first 6 months after the diagnosis. Findings for initial treatment and continuing care costs are consistent with the results in our prior cost studies of HPV-related disease [21–23]. Future studies are planned to estimate the terminal phase cost and thereby generate an estimate of lifetime cost of penile cancer.

Cancer disease extent at diagnosis is important for estimating the healthcare costs of cancer treatment. Given the limited clinical detail in insurance claims data, we used procedure codes and an original classification system designed by clinical experts to approximate cancer stage at diagnosis. However, about 50% of the cancer patients ($N = 129$) did not have procedure combinations defined in our proxy cancer stage classification system. Their 3 most common inpatient procedure codes for the unclassified group were 88332 (frozen section block), 99232 (physicians' evaluation and management of a patient on an inpatient basis), and 11045 (debridement procedure on the skin). As the unclassified group's healthcare cost was not significantly different to low-risk primary patients (P value = 0.70), we suspect that they were also low-risk primary cases. Of note no patient was identified in the low-risk metastatic stage (nodal surgery but no chemotherapy and no external beam radiation). Three patients underwent nodal surgery but all of them also had either chemotherapy or radiation. The classification issues highlight the difficulties in using procedure codes to approximate cancer stage at diagnosis. Nonetheless, Table 5 in the Supplementary Material illustrates the large differences in cost per patient by the proxy classification. For example, low-risk primary patients incurred a cost per patient of $37,000 in the first 2 years compared with $64,000 for high-risk primary patients and $197,000 for high-risk metastatic patients. The cost distribution illustrates how a relatively rare condition can be very costly to treat depending on the stage at diagnosis and the particular set of treatments employed.

This study has limitations. The MarketScan CCAE database comprised individuals aged 64 years or younger who were privately insured. Therefore, our study results cannot be generalized to the penile cancer populations covered by Medicaid or Medicare, or the uninsured. A Centers for Disease Control and Prevention survey found that adolescents covered by private insurance were more likely to be fully vaccinated for HPV (78.4%) compared with those covered by Medicaid (66.1%) and the uninsured (50.3%) [24]. Thus, our estimates of cost savings are particularly pertinent to the privately insured population who are more likely to be vaccinated compared with other groups. Stage at diagnosis was approximated by expert judgment of the relationship between initial treatment and cancer stage. Initial treatment was determined from the insurance claims data but research has shown errors in concordance between clinical registry and administrative claims data [25]. Similarly, about 50% of our cases could not be classified and therefore our cost by disease stage estimates need further validation and should be used with caution. A similar caution was

highlighted by the presence of 2 female cases in the administrative data, which were likely coding errors and therefore omitted from the study. We used propensity score matching to reduce the observed difference between cases and controls, but unobserved risk factors were not accounted for, such as smoking status or sexual behavior. Information on death outside the hospital was not available in the MarketScan database, which limited our analysis of long-term cost. Patients with only 1 outpatient visit with a penile cancer diagnosis code were excluded from the study. If they had penile cancer but were untreated or treated outside of the insurance payment system, our estimates of mean cost may be biased upward. Information on nonmedical costs such as lost productivity or time spent by unpaid caregivers was not available, precluding a full societal cost estimate.

To our knowledge, this is the first US population-based estimate of the mean healthcare costs of penile cancer. The strengths of the study were use of real-world and up-to-date health claims data with a longitudinal follow-up period adjusting for censoring and non-normal cost distribution to estimate the cost and to understand the cost pattern among the patient population. MarketScan is a large-scale database which allowed cost analysis for a relatively rare condition.

5. Conclusions

The adjusted average medical cost for insured penile cancer patients was $76,404 in the first 2 years after diagnosis. This estimate represents one of the potential offsets to the cost of HPV vaccination initiatives in the United States.

Conflicts of interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.urolonc.2019.01.004.

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