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Mean medical costs associated with vaginal and vulvar cancers for commercially insured patients in the United States and Texas

Shuangshuang Fu [a], David R. Lairson [b,*], Wenyaw Chan [c], Chi-Fang Wu [b], Lois Ramondetta [d]

[a] Department of Epidemiology, Human Genetics & Environmental Sciences, School of Public Health, The University of Texas Health Science Center at Houston, 1200 Pressler St, Houston, TX 77030, USA
[b] Department of Management, Policy, and Community Health, School of Public Health, The University of Texas Health Science Center at Houston, 1200 Pressler St, Houston, TX 77030, USA
[c] Department of Biostatistics, School of Public Health, The University of Texas Health Science Center at Houston, 1200 Pressler St, Houston, TX 77030, USA
[d] Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030, USA

HIGHLIGHTS

- Mean first year cost of new vaginal cancer cases in the U.S. was $86,995.
- Mean second year cost of vaginal cancer cases in the U.S. was $51,107.
- Mean first year cost of new vulvar cancer cases in the U.S. was $37,657.
- Mean second year cost of vulvar cancer cases in the U.S. was $19,139.
- Costs were associated with higher co-morbidities and pre-cancer cost.

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ABSTRACT

Objective. To estimate the average medical costs for vaginal and vulvar cancers in a commercially insured population in the U.S. and Texas.

Methods. 2011–2014 U.S. MarketScan databases were used to estimate the average medical costs associated with vaginal and vulvar cancers. Women with newly diagnosed vaginal or vulvar cancer were matched to a comparison group without cancer using propensity score. Year 1 and year 2 costs after index diagnosis date were estimated. A generalized linear model was used to estimate the cost for censored months. The differential costs between groups were defined as the net costs associated with cancer diagnosis and treatment.

Results. The analysis included 355 women with vaginal cancer and 997 with vulvar cancer in the U.S. The year 1 and year 2 costs for vaginal cancer were $86,995 and $51,107, respectively. The year 1 and year 2 costs for vulvar cancer were $37,657 and $19,139, respectively. The major factors associated with higher monthly vaginal and vulvar cancer costs were higher Charlson Comorbidity Index score and higher medical costs prior to cancer diagnosis. Monthly costs for vaginal and vulvar cancers decreased rapidly from month 1 to month 6 after diagnosis and then remained stable.

Conclusions. Seventy to 75% of all vaginal and vulvar cancers are due to HPV infections and mean medical costs associated with these cancers are substantial. These data will serve as key cost parameters in the economic evaluation of HPV vaccination dissemination and estimation of the long-term net economic benefit of promoting HPV vaccination.

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1. Introduction

The U.S. Centers for Disease Control and Prevention estimates that about 5000 cases of vulvar cancer were diagnosed in the U.S. in 2013 and 1000 U.S. women died of the disease in the same year [1]. Vulvar cancer incidence in the U.S. ranges from 1.8 to 2.6 per 100,000 women per year and has not changed much over the past four decades [2]. The incidence is higher among white women, at 2.1 per 100,000, than in other groups, including blacks at 1.5, American Indian/Alaska Natives

* Corresponding author at: Division of Management, Policy, and Community Health, School of Public Health, The University of Texas Health Science Center at Houston, 7000 Fannin, Suite 1200, Houston, TX 77030, USA.
E-mail addresses: Shuangshuang.fu@uth.tmc.edu (S. Fu), David.R.Lairson@uth.tmc.edu (D.R. Lairson), Wenyaw.Chan@uth.tmc.edu (W. Chan), Chi-Fang.Wu@uth.tmc.edu (C.-F. Wu), lramonde@mdanderson.org (L. Ramondetta).

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at 1.1, and Asian/Pacific Islanders at 0.4. The non-Hispanic rate is 2.1, while the Hispanic rate is 1.3. The Texas rate is 1.5, possibly reflecting the relatively large Hispanic population in the State [3].

Human papillomavirus (HPV) strains 16, 18, 31, 33, 45, 52, and 58 are risk factors for vulvar cancer, accounting for an estimated 70% of vulvar cancer cases [3]. Age is another major risk factor for vulvar cancer; less than 20% of cases are diagnosed in women younger than 50 years and over 50% are diagnosed in women older than 70 years. Invasive disease is more likely to be diagnosed in women older than 70, whereas non-invasive disease is more typically diagnosed in women aged about 50 years. Association of vulvar cancer with HPV is more common among younger women than older women [4]. Smoking is an additional risk factor for vulvar cancer, especially in woman infected with a high-risk strain of HPV.

HPV-related vulvar cancers start out as vulvar intraepithelial neoplasia (VIN). Most cases of VIN can be treated successfully and do not progress to invasive vulvar cancer. However, it is not now possible to determine which cases will advance, so careful monitoring is required. Additional risk factors include cervical precancer or cervical cancer, HIV infection and smoking. Chronic vulvar itching or burning of the vulva are early signs of vulvar dysplasia [5]. VIN can be treated topically, whereas vulvar cancer is treated, depending on the stage at detection and patient preference, with surgery, radiation therapy, and/or chemotherapy.

Vaginal cancer is relatively rare in the U.S., with 1312 cases diagnosed in 2014 and 430 women dying of the disease during the same period [6]. The age-adjusted incidence was higher among black women, at 0.9 per 100,000, than in other groups, including whites and Hispanics at 0.6 each and Asian/Pacific Islanders at 0.3 [1]. The Texas age-adjusted incidence was 0.7 in the 2010–2014 period [7]. About 75% of vaginal cancer cases are caused by HPV [8,9]. The median age at diagnosis of vaginal cancer is 67 years, with incidence monotonically increasing from near zero at age 35 years and the rate of increase rising slightly at age 65 years [10]. Additional risk factors include a history of pre-cancer of the cervix, HIV and smoking. Vaginal cancer is often asymptomatic in early stages [5]. Depending on the stage at detection and other factors, vaginal cancer may be treated with surgery, radiation therapy, and/or chemotherapy.

Healthcare cost estimates for vulvar and vaginal cancers used in leading HPV economic models, including that in a 2010 study by Elbasha and Dasbach, were taken from research by Hu and Goldie [11]. However, those cost estimates were derived from a survey of the literature and scenario analyses because of the lack of empirical studies on the lifetime costs of these cancers. These treatment cost estimates are not applicable to the current situation in the U.S. since they were based on 2003 US dollars (USD) and were rough approximations of lifetime costs. During 2013–2014, for males aged 18–59 years, prevalence of any genital HPV infection was 45.2% and that of high-risk HPV was 25.1%. During the same period, for females aged 18–59 years, prevalence of any genital HPV was 39.9% and of high-risk HPV was 20.4%. The rates were highest among non-Hispanic blacks and lowest among non-Hispanic Asians [12].

While HPV vaccination is highly effective at preventing HPV-related cancers, the U.S. immunization rate is low compared to other developed countries, where there has been a more concerted public effort to vaccinate [13]. Reagan-Steiner et al. found that, of U.S. adolescents aged 13 to 17 years, approximately 42% of females and 28% of males completed the HPV vaccination series of 3 doses; 52% and 39%, respectively, completed 2 doses [14]. Given the reluctance of most U.S. states 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 immunization rates. The costs associated with treatment of vaginal and vulvar cancer and other HPV-related conditions provide an important offset to immunization promotion efforts. Our purpose, therefore, was to determine the costs associated with a diagnosis of vulvar or vaginal cancer in women with commercial health insurance in the U.S. and Texas.

2. Methods

2.1. Data sources

We used the 2011–2014 U.S. Truven MarketScan Commercial Claims and Encounters (CCAE) databases to estimate the medical costs associated with vaginal and vulvar cancers. Truven MarketScan CCAE databases were part of the MarketScan databases created by Truven Health, which has created the MarketScan data warehouse to offer healthcare data on privately insured Americans. MarketScan claims databases have a very large sample size, with approximately 240 million covered lives since 1995 and 43.6 million covered lives in the most recent full year data, large enough to create a representative sample of people with the employer-provided health insurance. The databases come from approximately 350 private-sector payers each year and cover more than 90 million commercially insured populations across the U.S. in the study period. The databases are a main source for private health insurance cost studies of disease. Demographic, insurance enrollment, inpatient cost, outpatient cost, drug cost, and utilization information is available in the databases. MarketScan databases conform to the U.S. Health Insurance Portability and Accountability Act of 1996, and this study was exempted from submission for Institutional Review Board approval.

2.2. Study population

2.2.1. Cancer patient group selection

The study included all women who were newly diagnosed with vaginal or vulvar cancer during 2011 to 2014 who met our eligibility criteria; it also included a selected matched control population without cancer. To be eligible for the study, a patient had to 1) have at least one inpatient claim or two outpatient claims 30 days apart with primary or secondary diagnosis of vaginal or vulvar cancer (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9] diagnosis code: 184.0 for vaginal cancer, 184.1–184.8 for vulvar cancer); 2) have been continuously enrolled in the healthcare plan for 6 months before and 6 months after the index diagnosis date, where the index date was defined as the first date upon which the diagnosis was documented; 3) had no other cancer diagnosis before the index diagnosis date; and 4) be aged 18 years or older on the index diagnosis date. Patients with year 1 costs after the index diagnosis date greater than 1 million USD were deemed outliers and were excluded from the study.

2.2.2. Comparison group selection

The comparison group is important for estimating the cost of treating the cancers since each service component cannot be clearly identified as being utilized for treatment of the cancer. Thus, we measure total cost for the cases (all medical costs incurred during the study period) and total costs for matched controls who do not have a cancer diagnosis. The average difference is the cost attributed to the cancer diagnosis. The matched control population was selected by using a two-step matching process. First, all potential population controls in the database were randomly assigned an index date derived from those of the cancer patients. An initial control was selected if she 1) had the same index date as the cancer patient; 2) had no cancer ICD-9 diagnosis (140.0–208.9) during the 6-month period prior to the index date; 3) was of an age on the index date within 5 years of the age of the case; 4) was female; and 5) lived in the same U.S. census division (e.g., Pacific, Mountain, West North Central, etc.) as the case. Second, after the initial control group was selected, the propensity score matching method with Mahalanobis distance [15,16] was used to select a one-to-one matched control for each cancer patient. The following variables were used to calculate the distance between each cancer case and control: 1) Charlson Comorbidity Index (CCI) score in the 6-month period before the index date [17]; 2) number of psychiatric diagnosis groups in the 6-month period before the index date [18];

3) healthcare costs between 6 months and 3 months prior to the index date; and 4) health plan type.

2.3. Cost measurement and statistical analysis

The primary outcomes were year 1 and year 2 medical costs associated with vaginal and vulvar cancers. Costs were measured from the payer perspective with the amount paid by the insurer and patient for professional and institutional medical care services during the study period. Indirect costs such as lost earning for patient and caregivers were not included. Costs were adjusted for inflation to 2015 USD using the Medical Care component of the U.S. Bureau of Labor Statistics Consumer Index [19]. Case and comparison groups were followed up for 2 years after the index diagnosis date. All costs, including inpatient, outpatient, and drug costs, for year 1 and year 2 after index date were summed for each patient. Differential costs between case and comparison groups were calculated for each of these 2 years. For patients censored before completing the follow-up period, a generalized linear model with gamma distribution and log link was used to predict costs for censored months [20]. Polynomial terms of month were included in the model to address the non-linearity relationship between cost and time and to predict the cost of the censored months. The monthly cost using a combination of the observed and predicted data was plotted for the first 2 years after the index date.

Baseline characteristics of the cancer group and the matched control group were compared. Continuous variables were compared by using the *t*-test, and categorical variables were compared by using the chi-square test. All data analyses were conducted using SAS Enterprise Guide 7.1.

3. Results

3.1. Baseline characteristics

A total of 355 vaginal and 997 vulvar U.S. cancer patients were included and the same numbers of population controls. The average age at cancer diagnosis was 53.98 years for vaginal cancer and 53.21 years for vulvar cancer. All baseline characteristics were similar between cancer and comparison groups (Table 1).

3.2. Two-year costs for vaginal and vulvar cancer patients

The year 1 adjusted overall differential costs after index date for vaginal and vulvar cancers were $86,995 and $37,657, respectively. The year 2 adjusted overall costs for vaginal and vulvar cancers were $51,107and $19,139, respectively. Table 2 presents the overall observed costs broken down by type of services for vaginal and vulvar cancer patients. For vaginal cancer, the year 1 average differential cost for outpatient services was $53,610, followed by inpatient services at $24,880 and drugs at $685. The year 2 cost for vaginal cancer had similar patterns, with the differential cost for outpatient services was $8241, followed by inpatient services at $4982 and drugs at $56. For vulvar cancer, average differential inpatient service costs in year 1 were $22,105, followed by outpatient services costs $12,629 and drugs $566; in year 2, differential outpatient costs were $3824, followed by inpatient service costs $2830 and drugs $128.

3.3. Two-year costs for vaginal and vulvar cancer patients in Texas

Among all vaginal and vulvar cancer patients included in the study, 27 (7.6%) vaginal cancer patients and 57 (5.7%) vulvar cancer patients were from Texas (Table 3). In Texas, the year 1 and year 2 incremental costs associated with vaginal cancer were $92,680 and $14,460, respectively. The year 1 and year 2 incremental costs associated with vulvar cancer were $29,563 and $3569, respectively.

3.4. Monthly costs for vaginal and vulvar cancer patients in the U.S.

The associations between the cost and the independent variables generated from the generalized linear model are presented in Table 4. Only coefficients for CCI score and 3-month cost prior to the index diagnosis date were statistically significant for both vaginal and vulvar cancers. Monthly costs for vaginal and vulvar cancers showed the same trend during the 2-year follow-up period (Fig. 1). Cancer patients had higher costs in the first 6 months after index diagnosis date with a decreasing trend, with month 1 costs being the highest and month 6 costs being the lowest. After month 6, the cost remained stable until the end of the 2-year follow-up period. Average monthly cost for vaginal cancer was estimated to be $3300 higher than that for vulvar cancer. The costs for comparison groups were lower than those for the cancer groups and stayed level during the entire 2-year period.

4. Discussion

This study examined the medical costs associated with vaginal and vulvar cancers in commercially insured women in the U.S. and Texas. We found that the highest costs associated with cancer treatment were incurred in the first year and specifically the first 6 months after diagnosis. For vaginal cancer patients in the U.S. overall, the year 1 differential costs were 6 times higher than those of year 2, while for vulvar cancer, the year 1 costs were 5 times higher than those of year 2. Our previous study on cervical cancer costs in a similar population found year 1 and year 2 costs of $50,846 and $27,656, respectively [21]. Therefore, the medical cost associated with vaginal cancer was the highest among all three HPV-related gynecological cancers, and the cost associated with vulvar cancer was the lowest. To understand why vaginal cancer costs were much higher than vulvar cancer costs, we examined the services used by the two groups and found that the type of services used by vaginal and vulvar cancer groups was similar. However, vaginal cancer patients had more utilization of services compared to vulvar cancer patients. Vaginal cancer patients had an average 256 procedures per patient in the two year follow-up period after cancer diagnosis, while the vulvar cancer patients had an average 148 procedures per patient. This result was consistent with the findings of Insinga et al., whereby the cost of vaginal cancer was about 2 times higher than that of vulvar cancer. We also examined the frequency of the major 3 types of treatments (chemotherapy, surgery, and radiation) received by vaginal and vulvar cancer patients. On a per person month coverage basis, vaginal cancer patients experienced an average of 0.24 chemotherapy, 0.01 surgery, and 0.81 radiation claims, respectively; while vulvar cancer patients used an average of 0.07 chemotherapy, 0.11 surgery, and 0.32 radiation claims, respectively.

Only a few studies on vaginal and vulvar cancer costs have been published, and the majority are now out of date. Insinga et al. estimated the costs associated with 621 vulvar cancer cases and 254 vaginal cancer cases from insurance claims data for a large U.S. health plan during the 4-year period 1998–2003 [22]. They utilized initial one-to-one matching on index date, no cancer in 12 months prior to index date, age, and region to identify a control group, refined by propensity score matching on co-morbidity score and healthcare costs prior to the index diagnosis date. They estimated a year 1 cumulative incremental cost of $4073 and a 4-year cost of $8236 for vulvar cancer and a year 1 cumulative incremental cost of $9160 for vaginal cancer, with a 3-year cost of $13,835. (There were too few cases available for a 4-year estimate). For each cancer, the cost for patients who died during follow-up was about double the cost for those who survived the follow-up period. Hu et al. computed the lifetime costs for vaginal and vulvar cancers using data from a cost-effectiveness study and a mathematical model in 2003 USD; they estimated the lifetime cost for vaginal cancer to be $31,141 and vulvar cancer to be $27,142 (2015 USD) [11]. The costs estimated in our study are higher than those estimated in these two studies. Since the population of these two studies were different from ours,

Table 1
Baseline characteristics of vaginal and vulvar cancer patients (case group) and matched population controls (comparison group)[a].

Characteristics	Vaginal cancer			Vulvar cancer		
	Case group	Comparison group	*P*-value	Case group	Comparison group	P-value
Total number of patients	355	355		997	997	
Age, years, mean (SD)	53.98 (8.46)	53.70 (8.34)	0.658	53.21 (8.50)	52.93 (8.58)	0.464
Follow-up time, years, mean (SD)	1.67 (0.86)	1.84 (0.93)	0.014	1.78 (0.85)	1.81 (0.89)	0.455
Follow-up time			0.420			0.655
More than 1 year	270 (76.06)	279 (78.59)		801 (80.34)	793 (79.54)	
Less than 1 year	85 (23.94)	76 (21.41)		196 (19.66)	204 (20.46)	
Employee classification			0.795			0.327
Salary nonunion	34 (9.58)	38 (10.70)		95 (9.53)	99 (9.93)	
Salary union	5 (1.41)	4 (1.13)		7 (0.70)	11 (1.10)	
Salary other	6 (1.69)	10 (2.82)		17 (1.71)	15 (1.50)	
Hourly nonunion	21 (5.92)	27 (7.61)		71 (7.12)	60 (6.02)	
Hourly union	28 (7.89)	35 (9.86)		102 (10.23)	94 (9.43)	
Hourly other	6 (1.69)	7 (1.97)		13 (1.30)	24 (2.41)	
Nonunion	36 (10.14)	31 (8.73)		77 (7.72)	99 (9.93)	
Union	9 (2.54)	12 (3.38)		23 (2.31)	27 (2.71)	
Unknown	210 (59.15)	191 (53.80)		592 (59.38)	568 (56.97)	
Employment status			0.312			0.474
Active full time	128 (36.06)	155 (43.66)		393 (39.42)	428 (42.93)	
Active part time or seasonal	1 (0.28)	0 (0.00)		5 (0.50)	11 (1.10)	
Early retiree	42 (11.83)	33 (9.30)		89 (8.93)	95 (9.53)	
Medicare eligible retiree	4 (1.13)	5 (1.41)		15 (1.50)	9 (0.90)	
Retiree (status unknown)	3 (0.85)	5 (1.41)		17 (1.71)	14 (1.40)	
COBRA continuee	0 (0.00)	0 (0.00)		2 (0.20)	1 (0.10)	
Long-term disability	1 (0.28)	0 (0.00)		1 (0.10)	1 (0.10)	
Surviving spouse/depend	1 (0.28)	0 (0.00)		9 (0.90)	9 (0.90)	
Other/unknown	175 (49.30)	157 (44.23)		466 (46.74)	429 (43.03)	
Health plan type			0.925			0.882
Comprehensive	16 (4.51)	12 (3.38)		36 (3.61)	33 (3.31)	
EPO/unknown	15 (4.23)	14 (3.94)		44 (4.41)	37 (3.71)	
HMO/POS with capitation/POS	81 (22.82)	79 (22.25)		210 (21.06)	219 (21.97)	
PPO	218 (61.41)	227 (63.94)		632 (63.39)	627 (62.89)	
CDHP/HDHP	25 (7.04)	23 (6.48)		75 (7.52)	81 (8.12)	
Division			1			1
Unknown	12 (3.38)	12 (3.38)		39 (3.91)	39 (3.91)	
New England	19 (5.35)	19 (5.35)		53 (5.32)	53 (5.32)	
Middle Atlantic	42 (11.83)	42 (11.83)		137 (13.74)	137 (13.74)	
East North Central	72 (20.28)	72 (20.28)		222 (22.27)	222 (22.27)	
West North Central	14 (3.94)	14 (3.94)		49 (4.91)	49 (4.91)	
South Atlantic	63 (17.75)	63 (17.75)		189 (18.96)	189 (18.96)	
East South Central	18 (5.07)	18 (5.07)		89 (8.93)	89 (8.93)	
West South Central	50 (14.08)	50 (14.08)		81 (8.12)	81 (8.12)	
Mountain	18 (5.07)	18 (5.07)		46 (4.61)	46 (4.61)	
Pacific	47 (13.24)	47 (13.24)		92 (9.23)	92 (9.23)	
Charlson Comorbidity Index score, mean (SD)[b]	0.81 (1.20)	0.81 (1.20)	1	0.74 (1.11)	0.74 (1.11)	1
No. of psychiatric diagnosis groups, mean (SD)[b]	0.15 (0.50)	0.11 (0.37)	0.198	0.15 (0.46)	0.13 (0.42)	0.334
Costs between 6 months and 3 months prior to diagnosis, mean (SD), $[c]	5725 (11068)	3840 (5608)	0.175	4195 (6844)	3464 (6843)	0.132

Abbreviations: CDHP, consumer-driven health plan; COBRA, Consolidated Omnibus Budget Reconciliation Act; EPO, exclusive provider organization; HDHP, high-deductible health plan; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization; SD, standard deviation.
[a] Values are expressed as number of patients (percentage) unless otherwise indicated.
[b] Measured during 6-month period prior to the index date.
[c] Costs incurred during the 3 months immediately prior to the index date were excluded to avoid including the costs of treating symptoms or diagnosing cancer.

cost comparisons are only approximate. Insinga et al. study included not only commercially insured population but also Medicare beneficiaries [22]. The cost estimations were affected by including patients with different insurance coverages. In Hu et al. Study, the cost estimates were drawn from Medicare reimbursement data and included only diagnosis and initial treatment costs, which may represent the lower bound of cost estimates [11]. Treatment costs are higher for commercially insured populations compared to public insurance. For example, Jacobson et al.

Table 2
Observed costs in U.S. dollars for year 1 and year 2 after the index date for vaginal and vulvar cancer patients in the U.S. and matched population controls.

Year	Group	Vaginal cancer ($N = 355$)				Vulvar cancer ($N = 997$)			
		Cancer case group	Comparison group	Difference	*P*-value	Cancer case group	Comparison group	Difference	*P*-value
Year 1	All costs	88,581 (99353)	9406 (18226)	79,174 (71425)	<0.0001	45,432 (66083)	10,132 (33023)	35,300 (52238)	<0.0001
	Inpatient services	26,864 (62554)	1983 (9046)	24,880 (44693)	<0.0001	15,367 (35808)	2737 (26473)	12,629 (31488)	<0.0001
	Outpatient services	58,646 (63064)	5036 (10533)	53,610 (45211)	<0.0001	27,518 (41444)	5413 (11131)	22,105 (30344)	<0.0001
	Drugs	3072 (9593)	2387 (6174)	685 (8067)	<0.0001	2548 (8097)	1983 (5413)	566 (6887)	0.067
Year 2	All costs	18,964 (54723)	5685 (14402)	13,279 (40013)	<0.0001	12,532 (37030)	5750 (20601)	6782 (29963)	<0.0001
	Inpatient services	5871 (27159)	889 (6637)	4982 (19769)	0.0009	4309 (26899)	1479 (17086)	2830 (22533)	0.005
	Outpatient services	11,668 (39807)	3427 (8749)	8241 (28819)	0.0002	6779 (17488)	2955 (7277)	3824 (13394)	<0.0001
	Drugs	1425 (5299)	1369 (3808)	56 (4614)	0.871	1445 (6011)	1316 (4422)	128 (5277)	0.587

Table 3
Observed costs in U.S. dollars for year 1 and year 2 after the index date for vaginal and vulvar cancer patients in Texas and matched population controls.

Cancer group	Year	Cancer case group	Comparison group	Difference	*P*-value
Vaginal ($N = 27$)	Year 1	101,633 (110270)	8953 (21065)	92,680 (79383)	0.0002
	Year 2	18,998 (41814)	4538 (8513)	14,460 (30173)	0.089
Vulvar ($N = 57$)	Year 1	39,290 (78714)	9727 (13885)	29,563 (56519)	0.007
	Year 2	8047 (18926)	4478 (7013)	3569 (14272)	0.186

estimated the cost of oral pharyngeal cancer patients and found that cost was highest for patients with commercial insurance, followed by Medicaid and Medicare [23]. Another study conducted in Denmark estimated the year 1 and year 2 hospital costs for patients with vaginal or vulvar cancer diagnosed from 2004 to 2007 [24]. They estimated the year 1 hospital costs to be $24,829 for vaginal cancers and $17,882 for vulvar cancers. The year 2 hospital costs were $10,443 for vaginal cancers and $5854 for vulvar cancers. The hospital costs estimated for the Denmark vaginal and vulvar cancer patients were comparable to the inpatient cost estimates for the U.S. patients in the present study.

This study provides up-to-date medical costs associated with vaginal and vulvar cancers in the U.S. Given that important public health decisions are made at the state level, we also conducted a subgroup cost analysis for Texas. Texas vaginal cancer costs appear to be about 17% higher than national costs for year 1 and about the same for year 2, whereas vulvar cancer treatment costs are lower than the national average. These estimates will be coupled with end of life cost estimates and estimates of the cost of other HPV related conditions to estimate the cost-effectiveness of increasing the relatively low levels of immunization to higher levels in the U.S. and Texas.

Approximately 75% of vaginal cancers and 70% of vulvar cancers are caused by HPV infection [25], and HPV infection from 9 viral subtypes (a large percentage of the types that cause gynecological cancers) can be prevented by completing HPV vaccination at an early age. The cost estimates from this study show that the financial burden of treating vaginal and vulvar cancers is substantial. The cost of investments to increase HPV vaccination rates can therefore be partially offset by the expected savings associated with prevention of future cases. The study provides valuable cost parameters for modeling the full impact of HPV immunization.

This study has several limitations. With 4 years of data, the study encompassed a relatively short follow-up period, and costs were measured for only 2 years after cancer diagnosis. This study only estimated the cost after cancer diagnosis, but doesn't account for the sometimes long term vulvar intraepithelial neoplasia (VIN) treatments before vulvar cancer occurs in a percentage of patients. Therefore, costs may

Table 4
Association between costs and selected covariates using generalized linear model.

Covariates	Vaginal cancer		Vulvar cancer	
	Estimated coefficients (SE)	*P*-value	Estimated coefficients (SE)	*P*-value
Age	−0.001 (0.009)	0.938	0.013 (0.004)	0.003**
Charlson Comorbidity Index score[a]	0.12 (0.046)	0.008**	0.164 (0.054)	0.003**
No. of psychiatric diagnosis groups[a]	0.168 (0.136)	0.216	0.061 (0.066)	0.359
Health plan type				
EPO/unknown	−0.153 (0.382)	0.690	−0.23 (0.283)	0.415
HMO/POS with capitation/POS	−0.15 (0.338)	0.657	0.019 (0.216)	0.929
PPO	−0.005 (0.319)	0.988	0.085 (0.201)	0.672
CDHP/HDHP	0.138 (0.326)	0.672	−0.133 (0.266)	0.618
Comprehensive	Ref			
Division				
Middle Atlantic	−0.301 (0.281)	0.284	0.369 (0.182)	0.043*
East North Central	0.089 (0.281)	0.751	0.362 (0.144)	0.012*
West North Central	−0.489 (0.343)	0.154	0.087 (0.206)	0.673
South Atlantic	−0.296 (0.275)	0.281	0.205 (0.139)	0.140
East South Central	−0.451 (0.409)	0.270	0.399 (0.215)	0.063
West South Central	−0.135 (0.285)	0.635	0.282 (0.161)	0.080
Mountain	−0.435 (0.311)	0.162	0.419 (0.196)	0.032*
Pacific	−0.21 (0.275)	0.446	0.343 (0.17)	0.043*
Unknown	−0.2 (0.399)	0.618	0.084 (0.224)	0.707
New England	Ref			
Case/control status				
Case	1.798 (0.121)	<0.0001**,***	1.179 (0.081)	<0.0001**,***
Control	Ref			
Costs between 6 months and 3 months prior to diagnosis[b]	0.000039 (0.000005)	<0.0001**,***	0.000048 (0.000004)	<0.0001**,***
Censor status				
Censored	0.241 (0.116)	0.037*	0.251 (0.08)	0.002**
Non-censored	Ref			
Month index				
Month	−0.027 (0.152)	0.862	−0.416 (0.115)	0.0003**,***
Month^2	−0.044 (0.043)	0.303	0.049 (0.033)	0.141
Month^3	0.006 (0.005)	0.234	−0.003 (0.004)	0.440
Month^4	−0.0003 (0.0002)	0.257	0.0001 (0.0002)	0.610
Month^5	0.000004 (0.000004)	0.298	−0.000001 (0.000003)	0.674

Abbreviations: CDHP, consumer-driven health plan; EPO, exclusive provider organization; HDHP, high-deductible health plan; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization; Ref, reference.

[a] Measured 6 months prior to the index date.

[b] Costs incurred during the 3 months immediately prior to the index date were excluded to avoid including the costs of treating symptoms or testing of an undiagnosed cancer.

* Statistically significant at $\alpha = 0.05$.

** Statistically significant at $\alpha = 0.01$.

*** Statistically significant at $\alpha = 0.001$.

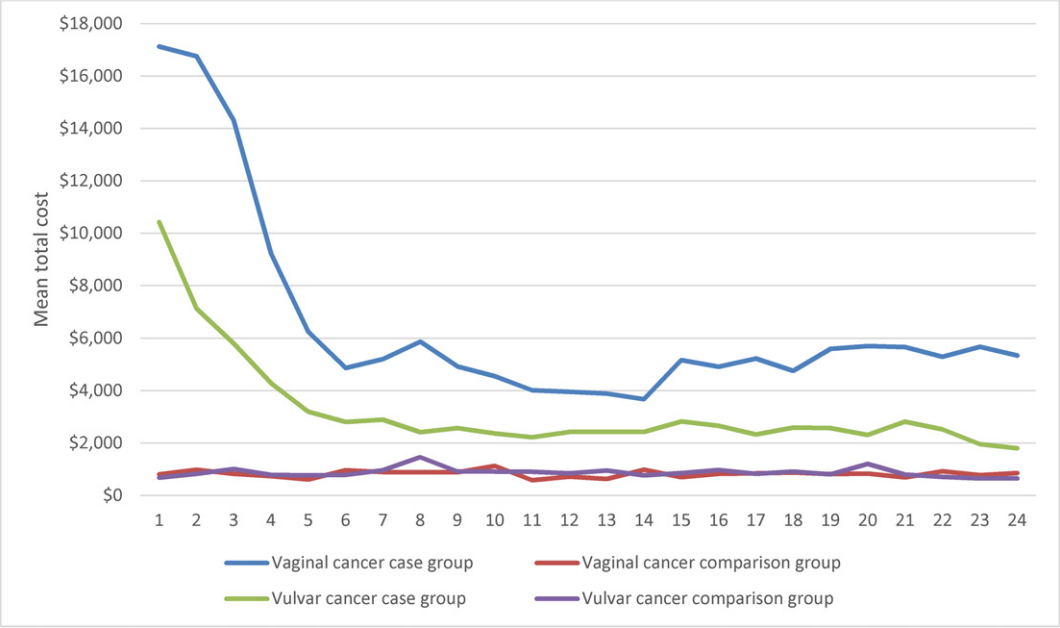

Fig. 1. Mean total medical costs by month during the first 2 years after index diagnosis date in the U.S.

be under-estimated. Disease stage information was not available in claims data, so stratified analyses by tumor stage was not possible. The goal of this study was to determine the overall cost for the entire vaginal and vulvar cancer population, future study by tumor stage is warranted if stage-specific cost or metastatic disease cost is of interest. While the cases and controls were well matched, propensity score matching can only account for the observed differences in the groups. Finally, the Texas cost subgroup mean estimates may be unstable because of the limited numbers of cases and controls.

5. Conclusion

In the commercially insured population in the U.S., the year 1 and year 2 mean medical costs associated with vaginal cancer were $86,995 and $51,107, and those associated with vulvar cancer were $37,657 and $19,139.

Conflict of interest

The authors declare that there are no conflicts of interest.

Author contributions

SF: Data analysis and interpretation; manuscript drafting and revision

DRL: Study concept and design; data collection, analysis, and interpretation; manuscript drafting and revision.

WC: Study concept and design; data interpretation; manuscript drafting and revision.

CFW: Data interpretation; manuscript drafting and revision.

LR: Study concept; data interpretation; manuscript drafting and revision.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2017.12.019.

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