

Incidence, cost and gender differences of oropharyngeal and noncervical anogenital cancers in South Korea

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Research article

Keywords: Cost, Incidence, Burden of disease, Oropharyngeal cancer, Noncervical anogenital cancer

Posted Date: February 13th, 2020

DOI: <https://doi.org/10.21203/rs.2.23463/v1>

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Version of Record: A version of this preprint was published on June 29th, 2020. See the published version at <https://doi.org/10.1186/s12889-020-09161-y>.

Abstract

Background: Human papillomavirus (HPV) is associated with a significant public health burden, yet few studies have been conducted in Asia, especially on noncervical cancers. We estimated the incidence and cost of oropharyngeal and noncervical anogenital (anal, vulvar, vaginal, penile) cancer in Korea.

Methods: We conducted a retrospective cohort study using Korea's National Health Insurance (NHI) claim database from 2013 to 2016. The main outcome measures were the number of respective cancer incidences during the study period and the annual costs per patient in the first year after diagnosis, which was adjusted by relevant variables based on the regression analysis.

Results : During the study period, 8,022 patients with these cancers were identified, and oropharyngeal cancer comprised 46% of them. The incidence rate for male oropharyngeal cancer was significantly higher than that of females (3.1 vs. 0.7 per 100,000 as of 2016, respectively). Additionally, the incidence of male oropharyngeal cancer increased from 2.7 in 2013 to 3.1 in 2016, whereas that of female and other cancers was stable during the study period. The mean annual incidence-based cost per patient in 2016 was highest for oropharyngeal cancers (21,870 USD), and it was significantly higher in males than in females based on then regression analysis ($p < .001$).

Conclusions: Oropharyngeal cancer comprises the highest number of HPV-associated noncervical cancer incidences in Korea, and the incidence and cost of oropharyngeal cancer was significantly higher among males than females. More aggressive public health policy toward males may decrease gender gap of oropharyngeal cancer.

Introduction

Cancer is a major cause of death in Korea, resulting in 82,155 deaths in 2018 [1]. In Korea, 11.3% of them were caused by Human papillomavirus (HPV), and 6% of them died [2]. Currently, a 2-valent HPV vaccine (Cervarix™), 4-valent vaccine (Gardasil®), and 9-valent vaccine (Gardasil®9) are available in Korea [3], and the National Immunization Program (NIP) has been implemented for 12-year-old girls with 2-valent HPV vaccine and 4-valent vaccine since June 2016 [4]. A previous Korean study using claim data suggested that the number of HPV-associated patients steadily increased between 2002 and 2015 [5]. In addition, in 2015, a total of 124.9 million USD was spent in Korea for healthcare costs for HPV-associated diseases [5]. Previous studies suggested that the prevalence of cervical cancer decreased from 28,027 in 2007 to 22,739 in 2011. However, the prevalence of noncervical HPV-associated cancers, such as anal, vulvar, vaginal, and penile cancers, tended to increase [6].

Most HPV-associated cancer studies in Korea have estimated prevalence-based cost [5, 6], yet studies on incidence-based healthcare costs are scarce. Prevalence-based costs estimate the total cost of a disease during a particular year, including survivors and end-of-life patients [7–9]. Incidence-based costs estimate the cost of treatment for patients first diagnosed in a particular year [7–9]. Since a prevalence-based approach captures the medical expenditure that occurs during a specific period regardless of the pertinence of the specific disease in question, its implication in estimating the burden of disease is limited [10]. However, incidence-based costs include only newly diagnosed patients, so it is possible to estimate health care costs after initial disease diagnosis [11]. Therefore, incidence-based cost estimation results are especially important for cancers, where most cost occur in the first year of the diagnosis [12–16]. The purpose of our study is to estimate the incidence rate and incidence-based healthcare cost of noncervical anogenital cancer and oropharyngeal cancer in Korea using nationally representative data.

Materials And Methods

Database

We used the Health Insurance Review and Assessment (HIRA) database, which contains National Health Insurance (NHI) claims data in South Korea. The HIRA claims data cover almost 50 million patients, nearly 98% of Korea's total population, and include utilization information regarding healthcare services reimbursed by the NHI (such as diagnosis code, cost of treatment, demographic characteristics, and prescription information) [17, 18].

Our study was approved by the Institutional Review Board of Ewha Womans University (IRB File No. 168-10).

Study population

Patients primarily or secondarily diagnosed with [6] oropharyngeal (including base of tongue, tonsil), anal, vulvar, vaginal, and/or penile cancer between January 2011 and December 2017 based on the International Classification of Diseases (ICD) code were identified from the NHI claim database. The ICD 10th codes for each cancer are as follows: oropharynx with base of tongue and tonsil (C01, C09, C10), anus (C21), vulva (C51), vagina (C52), and penis (C60).

The washout period was defined as two years based on the clinicians' advice that each patient could be defined as a new patient if there was no medical use for the same disease in the past two years based on the index date, which is the first diagnosed with corresponding cancers, from 2013 to 2016. The follow-up period was defined as 1 year from the index date to estimate the annual cost per patient. The flow chart for the new patient included in the study through this operational definition is shown in Figure 1. The Charlson comorbidity index (CCI) was used to adjust the comorbidities of patients [19].

Outcomes

We estimated the number of newly diagnosed patients and incidence rates from 2013 until 2016 with 2011 and 2012 being used for the washout period, and analyzed the incidence-based medical cost per patient per year of oropharyngeal (including base of tongue, tonsil) and anogenital cancer (vulvar, vaginal, penile, anal cancer). All costs were adjusted by the medical care component of the Consumer Price Index in 2016 [20]. The cost was converted from Korean Won to US Dollar using the 2013-2016 average exchange rate (1USD = 1,110 KRW) [21].

Statistical analysis

Descriptive statistics were used to examine the overall distribution of the new patients for each cancer. To compare the medical cost differences between groups of independent variables, parametric tests (t-test, ANOVA test) and nonparametric tests (Wilcoxon test, Kruskal-Wallis test) were performed. Regression analysis was used to identify the association of medical costs with the independent variables. Independent variables included sex (female = 0, male = 1), age (under 65 or 65 = 0, 65 over = 1), surgical experience (inexperience = 0, experience = 1), health plan type (healthcare insurance = 0, Medicaid = 1), year and CCI. Because the distribution of medical costs was right-skewed, the log-transformation was considered [22, 23]. However, despite the conversion to the logarithm, Kolmogorov-Smirnov tests for checking normality failed for all cancer types ($p < 0.05$). Therefore, in addition to the linear regression model, generalized linear models (GLMs) were performed when the distribution of medical costs was assumed to be from gamma distribution. Gamma GLM fits a skewed distribution well and is frequently used for dealing with nonnormal data such as healthcare costs [24]. Using GLM, medical costs were analyzed by adjusting the effects of confounding factors such as age, surgical experience, health plan type, year, and CCI. Before adjusting for confounding factors, univariate analyses for each variable were also applied. After the analysis, regression models were compared based on the Akaike information criterion (AIC).

All data collection and statistical analysis were performed using SAS software (version 9.4, SAS Institute Inc., Cary, NC, USA) and RStudio (version 1.1.463, RStudio, Inc., USA). All analyses were conducted using $p < 0.05$ as the level of significance.

Results

The demographic characteristics of newly diagnosed patients for oropharyngeal cancer and anogenital cancers are presented in Table 1. For all five cancers, the mean age was greater than 60, and the CCI score was between 1 and 2. Most patients were covered by the NHI insurance (>90%). There was a large gender gap in oropharyngeal cancer, with male patients comprising 81.2% (811 out of 999 patients) in 2016. During the study period, consistently higher number of male patients were observed in oropharyngeal cancer, with incidence rates per 100,000 for males vs. females being 3.1 vs. 0.7 in 2016 (Table 2). Additionally, the incidence of males increased from 2.7 in 2013 to 3.1 in 2016, but the incidence of females did not change from 0.7 in 2013 to 0.7 in 2016.

Table 3 and Figure 2 show the incidence-based cost per patient for oropharyngeal cancer and anogenital cancer (anal, vulvar, vaginal, penile cancer). The incidence-based cost per patient was highest in oropharyngeal cancer and lowest in penile cancer. In all five cancers, the incidence-based cost per patient increased between 2013 and 2016. Among them, vaginal cancer showed the steepest increase from USD 12,515 in 2013 to USD 18,636 in 2016, followed by anal cancer, which increased from USD 10,662 in 2013 to USD 15,911 in 2016. The cost of oropharyngeal cancer was consistently higher for males than for females throughout the study period (Table 3, Figure 2B). Specifically, the cost of oropharyngeal cancer per male patient was 23,041 USD whereas that per female being 16,819 USD in 2016. Accordingly, we analyzed cost per patient according to gender in oropharyngeal cancer through t-test and Wilcoxon test. The results demonstrated that the p-value of $< .001$ was significantly higher in male medical cost per patient than in females (Table 4).

Regression analysis was performed on oropharyngeal cancer and anal cancer, which can occur in both females and males. Table 4 shows the distribution of medical costs for each category of independent variable, and the regression analysis results are shown in Table 5. In multivariate regression analysis, the cost of oropharyngeal cancer was significantly higher in males than in females after adjustment for confounding factors such as age, year, surgery, health plan type, and CCI ($p < .001$). Both the linear regression model and generalized linear model showed similar results. Also, the linear regression model showed better suitability as a result of comparing the goodness-of-fit of two multivariate models using the AIC.

Discussion

Our study estimated the incidence and cost of oropharyngeal cancer (including base of tongue, tonsil) and anogenital cancer (anal, vulvar, vaginal, penile cancer) in 2013–2016 using nationally representative sample in Korea.

During the study period, 8,022 new patients were identified, and the total number of patients with five cancers increased from 1,952 in 2013 to 2,101 in 2016. The incidence rate for male oropharyngeal cancer was the highest among the five cancers, and oropharyngeal cancer showed a significant gender gap, with males vs. females being 3.1 vs. 0.7 per 100,000 as of 2016, respectively. A previous Korean study also showed that the number of male patients was higher than that of female patients, which is similar to our study [5]. Additionally, the incidence of male oropharyngeal cancer increased from 2.7 in 2013 to 3.1 in 2016, whereas that of female and other cancers was stable during the study period. The incidence rate of oropharyngeal cancer associated with HPV is increasing in Asian countries such as Singapore, Taiwan and developed countries such as Northern Europe, Australia, and the United States, and the incidence rate is 2–3 times higher in males than in females [25–28], which is consistent with our study.

The total incidence-based medical cost for oropharyngeal and noncervical anogenital cancer in 2013–2016 was 133,964,586 USD, bringing a significant economic burden to Korea, and greatly increased from 27,803,613 USD in 2013 to 38,864,428 USD in 2016. Vaginal cancer and anal cancer demonstrated the steepest increase in medical costs during 2013–2016 (12,515 USD in 2013 to 18,636 USD in 2016 (49%); 10,662 USD in 2013 to 15,911 USD in 2016 (49%), respectively). The cost of oropharyngeal cancer was the highest among the five cancers, which is consistent with a previous study [29]. Oropharyngeal cancer is anatomically complex and difficult to operate compared to other cancers, and reconstruction may be added to restore function [30]. Therefore, the cost of

surgery is expected to be higher than that of other cancers. Additionally, cetuximab has been reimbursed since 2014, which is in line with a sudden increase in expenditure in 2014, whereas only chemical drugs are reimbursed for the rest of the other cancers [31]. Moreover, because the head and neck are the organs that are used for speaking and swallowing food, it is closely related with patients' quality of life, and there is a risk of having a disability even after treatment such as neck resection [32]. Therefore, aggressive prevention of oropharyngeal cancer should be considered to improve health outcomes as well as reduce financial burden. Regression analysis was conducted in oropharyngeal cancer and anal cancer to estimate gender-specific annual cost, since those two cancers can occur in both genders. The cost of oropharyngeal cancer for males was significantly higher than that of females based on the regression analysis ($p < .001$), both in univariate and multivariate analysis. It is not surprising that annual costs were significantly higher as years pass and for the patient who had experienced surgery. Interestingly, our analysis showed that patients under 65 and a lower CCI had significantly higher cost based on the multivariate analysis, using both the GLM and OLS models. Since we defined cancer patients based on primary or secondary diagnosis only, patients who are defined to have respective cancers based on the tertiary or beyond diagnoses codes are not included in our analysis. Since those patients are likely to be older and have higher CCI scores, our study might underestimate the cost of patients with higher CCI or older age; thus, our study should be interpreted with caution.

A previous prevalence-based cost-of-illness study estimated the health care costs of HPV-associated diseases in Korea using claims data in 2015 and suggested that the number of patients for anal, vulvar, vaginal and penile cancer was 2,071, 588, 383, and less than 300, respectively [5]. Since we estimated the new patients of each cancer, our estimates are lower than the prevalence of each cancer, yet the trend observed in their study is consistent with what we have estimated in the number of incidences of each cancer. Since the definitions of diseases included in oropharyngeal cancer in our study and previous study are different, the direct comparison of oropharyngeal cancer was difficult. The prevalence-based healthcare costs per patient in a previous study were estimated at 4,096 USD for oropharyngeal, 3,737 USD for vaginal, 3,370 USD for vulvar, 2,807 USD for anal and 2,169 USD for penile in 2015. The cost of oropharyngeal cancer was the highest, and the cost of penile cancer was the lowest, which is consistent with our study. The prevalence-based cost estimated in a previous study and the incidence-based cost estimated in our study are nearly five times different. This difference appears to be due to the high initial treatment cost of cancer after the first diagnosis [12, 13, 15, 16]. As such, the cost of incidence and prevalence-based cost are quite different and should not be confused.

The HPV associated annual cost per patient in 2016 was estimated to be 14,536 USD for vaginal cancer, 14,002 USD for anal cancer, 6,736 USD for oropharyngeal cancer, 5,049 USD for penile cancer and 3,226 USD for vulvar cancer, respectively, after accounting for the HPV attributable fraction [25]. Overseas countries estimated the incidence of HPV-associated noncervical cancers. A Danish study estimated the annual incidence rate of HPV-associated anogenital cancers (anal, penile, vaginal, vulvar cancer) in Denmark in 2004–2007 and suggested that the incidence rates for anal, penile, vaginal and vulvar cancer were 1.9, 1.7, 0.9 and 3.6 per 100,000 persons, respectively [15], which was higher than what we observed in our study (1.5, 0.3, 0.5, 0.6 for each year 2016, respectively) [15]. According to another Danish study, the incidence of anal cancer in Denmark has been steadily increasing, presumably due to patterns of change in sexual behavior [33]. The sex culture of Korea has changed rapidly in recent years, and the trend of an open sex culture is spreading due to the rapid westernization of social culture, which explains our increasing trend [34]. Therefore, appropriate prevention should be considered to prevent the increase in the incidence rate of HPV-associated disease in Korea. The incidence of oropharyngeal disease was estimated in Singapore, and the incidence per 100,000 persons of oropharyngeal squamous cell carcinoma was 2.66 for males and 0.72 for females in 2008–2012 [27]. In comparison with the results of our study, the incidence per 100,000 persons of oropharyngeal cancer in 2013 was 2.7 for males and 0.7 for females, similar to that of the Singaporean study. The Singaporean study suggested that Singapore has a potential burden of male oropharyngeal cancer and that changing current HPV precautions that focus on cervical cancer may also help prevent male oropharyngeal cancer.

Our study has some limitations. The burden of disease may be underestimated because non-medical costs, such as transportation costs, caregiver costs, and productivity losses are excluded. Second, we defined patients based on the primary or secondary diagnosis, so disease recorded after secondary diagnosis was excluded. Therefore, the result of estimating medical costs may vary according to such operational definition. Although large data sets are used, the CCI used in the regression analysis may depend on these operational definitions. However, our study has the following strengths. The HIRA claim data include almost 98% of Korea's entire population, which is representative of the Korean population. In addition, 99% of HIRA claims data are claimed through electronic data interchange (EDI) [18]. Therefore, it is expected that almost all patients who used medical services for oropharyngeal and anogenital cancer (anal, vulvar, vaginal, penile cancer) during 2013–2016 would be included [35]. To our knowledge, our study is the first to estimate the incidence-based medical cost for oropharyngeal (including base of tongue, tonsil) and anogenital cancer (anal, vulvar, vaginal, penile cancer) in Asia. It is also the first to show that the incidence-based medical costs of oropharyngeal and anal, vulvar, vaginal, and penile cancers are increasing in Korea. The incidence-based medical cost estimation results in our study are particularly useful when considering disease prevention and can be useful as a basis for providing estimates of the potential costs [36, 37].

Conclusion

The incidence-based cost per patient of oropharyngeal cancer (including the base of tongue, tonsil) and anogenital cancer (anal, vulvar, vaginal, penile cancer) increased from 2013 to 2016. Specifically, the incidence of oropharyngeal cancer was significantly higher in men, and costs were significantly higher in men than in women. More aggressive public health policy toward males may decrease the gender gap of oropharyngeal cancer.

Declarations

- Ethics approval and consent to participate

Our study was approved by the Institutional Review Board of Ewha Womans University (IRB File No. 168-10).

- **Consent for publication**

Not applicable

- **Availability of data and materials**

The data that support the findings of this study are available from [Health Insurance Review and Assessment Service] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [Health Insurance Review and Assessment Service].

- **Competing interests**

Authors were financially supported by MSD Korea.

- **Funding**

This work was financially supported by Merck Sharp & Dohme, Seoul, South Korea [grant number M20197901]. The funding body has not been involved with the study design nor the conduct of the study.

- **Authors' contributions**

IC conducted the data collection, statistical analysis and interpretation. IC and SB designed the analysis and generated the manuscript. SB, DL and KB interpreted and supervised the statistical analysis of the data. All authors critically edited the manuscript and approved the final version.

- **Acknowledgements**

Not applicable

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Tables

Table 1. Demographic characteristics of new patients for oropharyngeal and anogenital cancer, 2013-2016.

Variable	2013	2014	2015	2016
Oropharynx (C01, C09, C10) ^a				
N	884	888	923	999
Gender, n (%)				
Male	698 (79.0)	730 (82.2)	737 (79.8)	811 (81.2)
Female	186 (21.0)	158 (17.8)	186 (20.2)	188 (18.8)
Age, mean (SD)	61.2 (12.2)	61.6 (12.5)	62.0 (12.5)	61.9 (12.5)
CCI score, mean (SD)	1.7 (1.3)	1.7 (1.2)	1.7 (1.2)	1.8 (1.2)
Health plan type, n (%)				
Healthcare insurance	824 (93.2)	839 (94.5)	868 (94.0)	927 (92.8)
Medicaid, etc ^b	60 (6.8)	49 (5.5)	55 (6.0)	72 (7.2)
Anus (C21)				
N	758	702	762	759
Gender, n (%)				
Male	388 (51.2)	404 (57.5)	425 (55.8)	376 (49.5)
Female	370 (48.8)	298 (42.5)	337 (44.2)	383 (50.5)
Age, mean (SD)	65.0 (12.9)	64.3 (13.5)	65.0 (13.8)	66.1 (13.3)
CCI score, mean (SD)	2.0 (1.1)	1.9 (1.2)	2.0 (1.2)	1.9 (1.2)
Health plan type, n (%)				
Healthcare insurance	704 (92.9)	652 (92.9)	688 (90.3)	688 (90.7)
Medicaid, etc ^b	54 (7.1)	50 (7.1)	74 (9.7)	71 (9.3)
Vulva (C51)				
N	147	156	156	149
Age, mean (SD)	62.0 (17.0)	58.7 (16.0)	64.3 (16.0)	64.0 (15.0)
CCI score, mean (SD)	1.2 (1.2)	1.2 (1.2)	1.1 (1.2)	1.3 (1.2)
Health plan type, n (%)				
Healthcare insurance	143 (97.3)	150 (96.2)	142 (91.0)	134 (90.0)
Medicaid, etc ^b	4 (2.7)	6 (3.8)	14 (9.0)	15 (10.0)
Vagina (C52)				
N	102	115	136	123
Age, mean (SD)	62.9 (13.5)	60.7 (14.3)	61.5 (14.3)	61.8 (14.6)
CCI score, mean (SD)	1.5 (1.2)	1.7 (1.2)	1.4 (1.2)	1.5 (1.3)
Health plan type, n (%)				
Healthcare insurance	96 (94.1)	105 (91.3)	127 (93.4)	112 (91.1)
Medicaid, etc ^b	6 (5.9)	10 (8.7)	9 (6.6)	11 (8.9)
Penis (C60)				
N	61	58	73	71
Age, mean (SD)	63.7 (16.0)	65.5 (15.4)	68.5 (12.6)	66.7 (14.8)
CCI score, mean (SD)	1.3 (1.2)	1.1 (1.2)	1.4 (1.1)	1.1 (1.1)
Health plan type, n (%)				
Healthcare insurance	58 (95.1)	56 (96.5)	70 (95.9)	64 (90.1)
Medicaid, etc ^b	3 (4.9)	2 (3.5)	3 (4.1)	7 (9.9)

CCI, Charlson Comorbidity Index; SD, standard deviation.

^a Oropharyngeal cancer, including the base of tongue and tonsil.

^b War veteran.

Table 2. Incidence rate of oropharyngeal and anogenital cancer.

Cancer	2013		2014		2015		2016	
	Male	Female	Male	Female	Male	Female	Male	Female
Oropharynx (C01, 09, 10) ^a	2.7	0.7	2.9	0.6	2.9	0.7	3.1	0.7
Anus (C21)	1.5	1.5	1.6	1.2	1.7	1.3	1.5	1.5
Vulva (C51)	-	0.6	-	0.6	-	0.6	-	0.6
Vagina (C52)	-	0.4	-	0.4	-	0.5	-	0.5
Penis (C60)	0.2	-	0.2	-	0.3	-	0.3	-

The incidence rate is calculated per 100,000 persons.

^a Oropharyngeal cancer, including the base of tongue and tonsil.

Table 3. Incidence-based medical cost per patient of oropharyngeal and anogenital cancer in South Korea, 2013-2016.

Cancer	2013		2014		2015		2016	
	Mean (USD)	Median (USD)						
Oropharynx (C01, 09, 10) ^a	18,867	17,874	21,624	20,111	21,668	20,408	21,870	20,759
Male	19,719	18,445	22,418	20,635	22,828	21,492	23,041	21,606
Female	15,671	13,294	17,955	17,075	17,071	15,116	16,819	13,857
Anus (C21)	10,662	8,195	12,630	10,105	13,737	9,025	15,911	12,230
Male	10,331	7,301	13,088	10,105	13,226	8,645	15,419	11,042
Female	11,009	9,379	12,008	10,115	14,382	9,864	16,394	12,880
Vulva (C51)	9,176	6,188	10,261	7,075	13,056	8,869	12,957	8,032
Vagina (C52)	12,515	9,835	14,113	10,608	16,580	13,758	18,636	13,954
Penis (C60)	6,852	3,409	8,137	4,114	10,601	4,961	10,097	5,512

Unit: US dollar

Adjusted by the medical care component of the Consumer Price Index in 2016.

^a Oropharyngeal cancer, including the base of tongue and tonsil.

Table 4. Distribution of medical costs of independent variables.

Variable	Oropharynx (C01, 09, 10) ^a				Anus (C21)			
	Mean	p*	Median	p*	Mean	p*	Median	p*
Sex								
Female	16,837	<.001 ^c	15,422	<.001 ^d	13,528	0.295 ^c	10,387	0.045 ^d
Male	22,056		20,475		13,003		9,196	
Age								
≤65	22,195	<.001 ^c	20,644	<.001 ^d	14,933	<.001 ^c	10,978	<.001 ^d
>65	19,192		17,087		11,654		8,710	
Year								
2013	18,867	0.001 ^e	17,874	<.001 ^f	10,662	<.001 ^e	8,195	<.001 ^f
2014	21,624		20,111		12,630		10,105	
2015	21,668		20,408		13,737		9,025	
2016	21,870		20,759		15,911		12,230	
Surgery								
Inexperience	12,243	<.001 ^c	10,840	<.001 ^d	7,490	<.001 ^c	3,735	<.001 ^d
Experience	24,011		22,210		16,216		12,744	
Health plan type								
Healthcare insurance	21,045	0.960 ^c	19,762	0.348 ^d	13,120	0.131 ^c	9,777	0.222 ^d
Medicaid, etc ^b	20,990		18,106		14,655		10,399	
CCI								
0	22,718	<.001 ^e	21,535	<.001 ^f	15,040	<.001 ^e	12,418	<.001 ^f
1	23,993		22,091		15,101		12,154	
2	18,567		16,604		11,303		7,729	
3	20,095		18,470		13,158		8,781	

Unit: US dollar

CCI, Charlson Comorbidity Index

* p<0.05

^a Oropharyngeal cancer, including the base of tongue and tonsil.

^b War veteran.

^c p-value estimated by t-test.

^d p-value estimated by Wilcoxon test.

^e p-value estimated by ANOVA test.

^f p-value estimated by Kruskal-Wallis test.

Table 5. Linear regression model and generalized linear model for incidence-based medical cost.

Model	Variable	Univariate				Multivariate				
		Anal		Oropharynx ^a		Anal		Oropharynx ^a		
		β	p*	β	p*	β	p*	β	p*	
Linear Regression Model	Sex (ref = female)	-0.104	0.024	0.483	<.001	-0.150	0.004	0.422	<.001	
	Age (ref = ≤65)	-0.180	<.001	-0.255	<.001	-0.136	0.001	-0.185	<.001	
	Year	0.102	<.001	0.053	0.002	0.101	<.001	0.046	0.003	
	Surgery (ref = inexperience)	1.040	<.001	1.001	<.001	1.037	<.001	0.956	<.001	
	Health plan type (ref = healthcare insurance)	0.113	0.174	-0.118	0.131	0.115	0.131	-0.121	0.091	
	CCI	-0.065	0.001	-0.079	<.001	0.003	0.987	-0.045	0.002	
	AIC					95,597	12,2571			
Generalized Linear Model	Sex (ref = female)	-0.040	0.286	0.270	<.001	-0.088	0.012	0.249	<.001	
	Age (ref = ≤65)	-0.248	<.001	-0.145	<.001	-0.120	<.001	-0.118	<.001	
	Year	0.129	<.001	0.043	0.001	0.130	<.001	0.038	0.002	
	Surgery (ref = inexperience)	0.773	<.001	0.674	<.001	0.759	<.001	0.657	<.001	
	Health plan type (ref = healthcare insurance)	0.111	0.098	-0.003	0.965	0.129	0.040	0.013	0.823	
	CCI	-0.050	0.001	-0.052	<.001	-0.009	0.534	-0.034	0.003	
	AIC					103,891	132,144			

AIC, Akaike Information Criterion; CCI, Charlson Comorbidity Index.

* p<0.05

^a Oropharyngeal cancer, including the base of tongue and tonsil

Figures

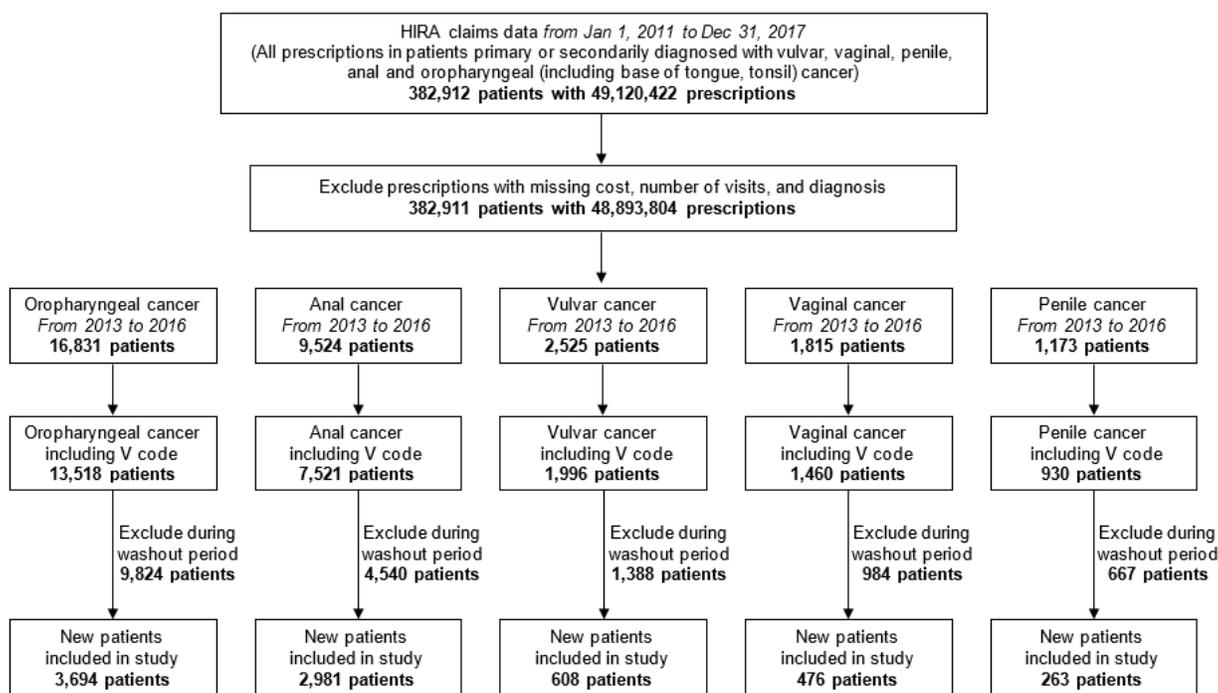


Figure 1
Flow chart of new patients included in the study through operational definition. Flow chart of extracting new patients from 2013-2016 through operational definition using HIRA claims data from patients diagnosed primary or secondary with vulvar, vaginal, penile, anal and oropharyngeal (including base of tongue, tonsil) cancer from Jan 1, 2011 to Dec 31, 2017.

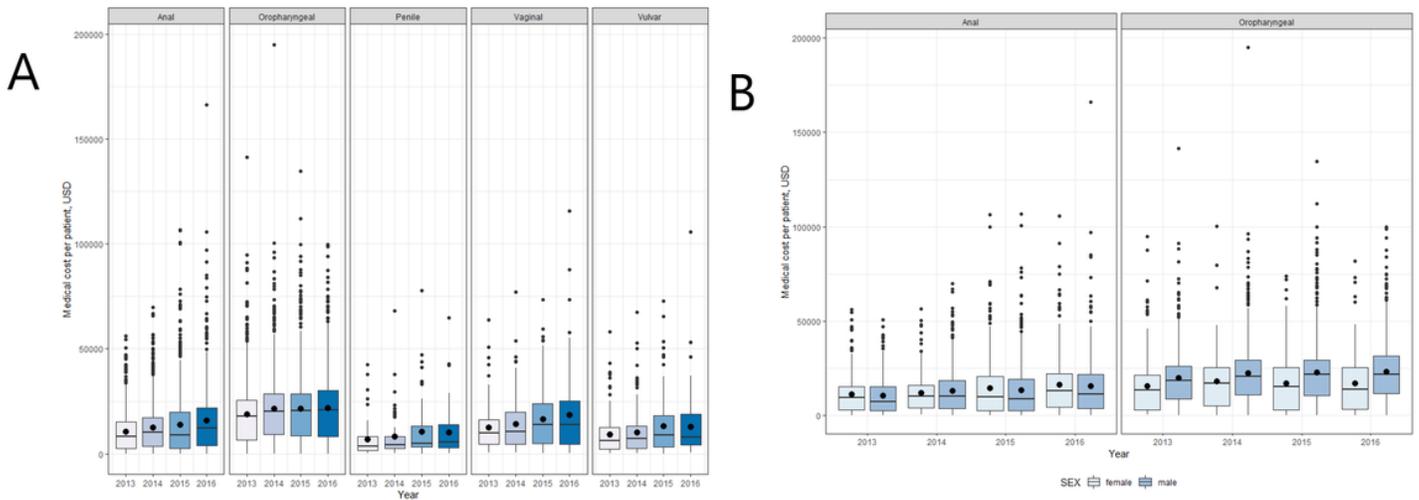


Figure 2

Incidence-based medical cost per patient, 2013-2016. (a) Anal, oropharyngeal, penile, vaginal and vulvar cancer Incidence-based medical cost per patient in 2013-2016 of anal, oropharyngeal (including base of tongue, tonsil), penile, vaginal and vulvar cancer. All costs were adjusted by the medical care component of the Consumer Price Index in 2016. For the first year after diagnosis, the incidence-based cost per patient was highest in oropharyngeal cancer and lowest in penile cancer. In all five cancers, the incidence-based cost per patient increased between 2013 and 2016. (b) Anal and oropharyngeal cancer by gender Differences in incidence-based medical cost per patient of anal cancer and oropharyngeal cancer according to gender. Oropharyngeal cancer demonstrated consistently higher results for males than for females during 2013-2016 for medical cost per patient. Anal cancer did not differ significantly between genders.