



Incidence and Cost of Non-Cervical Human Papillomavirus (HPV)-Associated Cancer in Korea

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INTRODUCTION

Background

- 4.5% of all cancers worldwide are caused by human papillomavirus (HPV), which is primarily sexually transmitted¹
- According to the IARC(International Agency for Research on Cancer), almost 100% of cervical cancer results from HPV. Moreover, 88% of anal cancer, 78% of vaginal cancer, 50% of penile cancer, 30.8% of oropharyngeal cancer, and 24.9% of vulvar cancer result from HPV¹. This demonstrates that the contribution of HPV on other diseases as well as cervical cancer are high
- Previous HPV-associated disease studies using Korean claims data are primarily prevalence-based studies^{2,3}. Although there is an incidence-based study of cervical cancer, other HPV-related cancers have rarely been incidence-based cost study

Objective

- This study aims to estimate the incidence and cost of non-cervical HPV-associated cancers in Korea and observe the trend

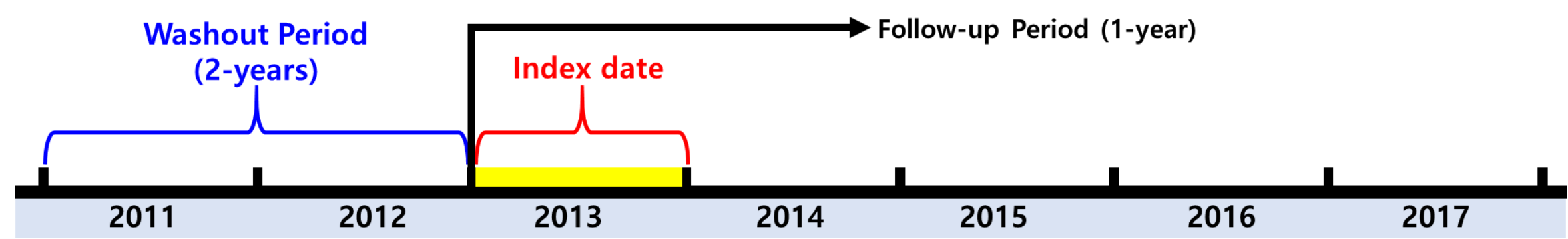
METHODS

Database

- We used the database from the Health Insurance Review and Assessment (HIRA) service, a national health insurance claims data in South Korea
- The HIRA claims data contains the data of the entire population (97% national health insurance, 3% medical aid) and includes all the medical services of patients who have been treated at the hospital (general information such as diagnosis code, cost of treatment, surgical status, age, gender, and in-hospital healthcare services, outpatients prescription)

Study Design

- This population-based, retrospective cohort study used claim database from 2011 to 2017
- We selected relevant cancers, excluding cervical cancer, that are considered to be associated with HPV through medical experts consultation and article review
- The index date corresponded to the first diagnosis of the case. After incorporating 2-year washout period before diagnosis and one-year follow period subsequent to diagnosis, 2013~2016 were used as index periods



* Same study design with each year 2013, 2014, 2015, 2016 as index date

Study Population

- Patients primarily or secondarily diagnosed with oropharyngeal including base of tongue, tonsil and anogenital (vulvar, vaginal, penile, anal) cancer were included in the analysis. The International Classification of Diseases (ICD) 10th code is as follows: base of tongue (C01), tonsil (C09), oropharynx (C10), anus (C21), vulva (C51), vagina (C52), penis (C60)
- If no applicable diseases were identified for the previous 2-years, the patient is defined as a new patient and analyzed
- Patients was defined based on the identification code for cancer patients within the special identification code V(V027, V193, V194). In other words, analysis was performed based on those with both identification V code for cancer patients and the ICD-10 code

Outcome

- For each cancer, we estimated the number of new patients and incidence rates for 2013, 2014, 2015, and 2016, and analyzed the mean annual incidence-based medical cost per patient of oropharyngeal and anogenital cancer

Statistical Analysis

- Regression analysis was used to analyze variables related to medical costs. Independent variables include sex (female=0, male=1), age (under 65=0, over 65=1), year, surgical experience (inexperience=0, experience=1), health plan type (healthcare insurance=0, medicaid=1), and CCI
- Medical cost data is usually skewed, so we used gamma generalized linear model(GLM) with log link in our analysis. Thus, two models were used for the regression analysis: linear regression model and generalized linear model
- All data collection and statistical analysis was performed using SAS 9.4 (SAS Institute, Cary, NC, USA)

RESULTS

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

Variable	Oropharynx* (C01,09,10)	Anus (C21)	Vulva (C51)	Vagina (C52)	Penis (C60)
N	3,694	2,981	608	476	263
Age, mean (SD)	61.7 (12.4)	65.1 (13.9)	62.3 (16.0)	61.7 (14.2)	66.3 (14.7)
Gender, n (%)					
Male	2,976 (80.6)	1,593 (53.4)	-	-	263 (100)
Female	718 (19.4)	1,388 (46.6)	608 (100)	476 (100)	-
CCI score, mean (SD)	1.7 (1.2)	1.9 (1.2)	1.2 (1.2)	1.5 (1.2)	1.2 (1.2)
Health plan type, n (%)					
National healthcare insurance	3,458 (93.6)	2,732 (91.7)	569 (93.6)	440 (92.4)	248 (94.3)
Medical aid	227 (6.2)	245 (8.2)	39 (6.4)	36 (7.6)	15 (5.7)
Etc ^a	9 (0.2)	4 (0.1)	-	-	-

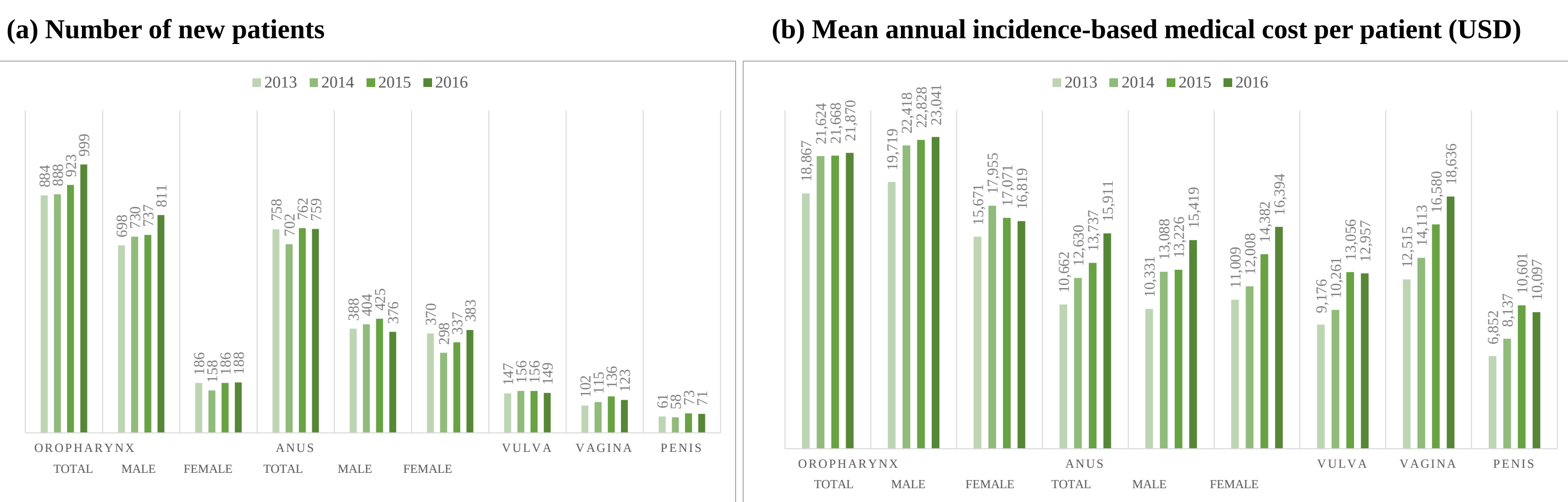
SD, Standard Deviation; CCI, Charlson Comorbidity Index

*Oropharynx(C10) including base of tongue(C01) and tonsil(C09)

^a war veteran

- The mean age of the five HPV-associated cancers was mainly in their 60s, and the Charlson Comorbidity Index(CCI) score was mainly between 1 and 2. In addition, the patient was primarily a national healthcare insurance patient

Figure 1. Number of new patients and mean annual incidence-based medical cost per patient of oropharyngeal and anogenital cancers



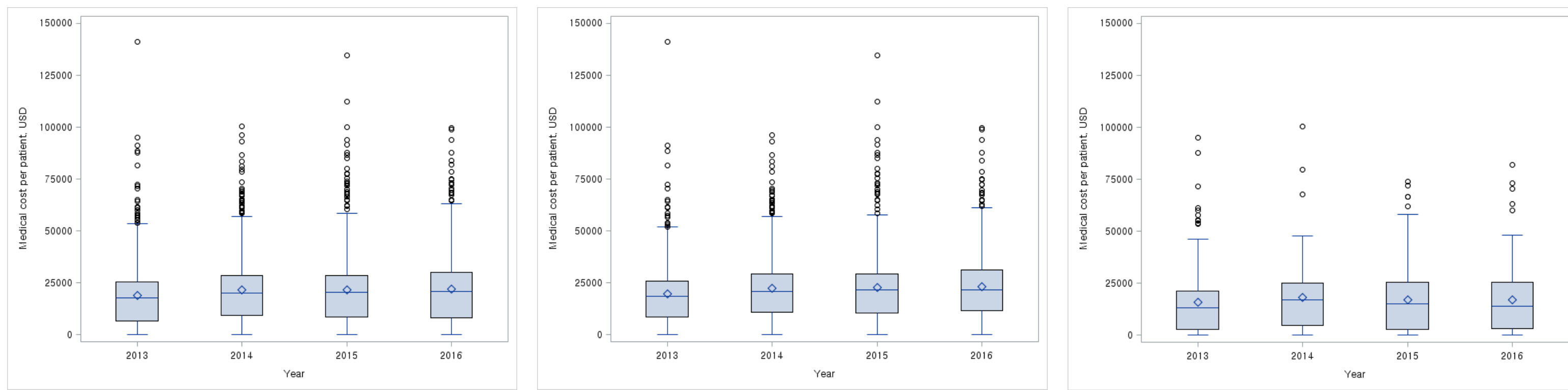
Unit: USD, United States Dollar

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

* Oropharynx(C10) including base of tongue(C01) and tonsil(C09)

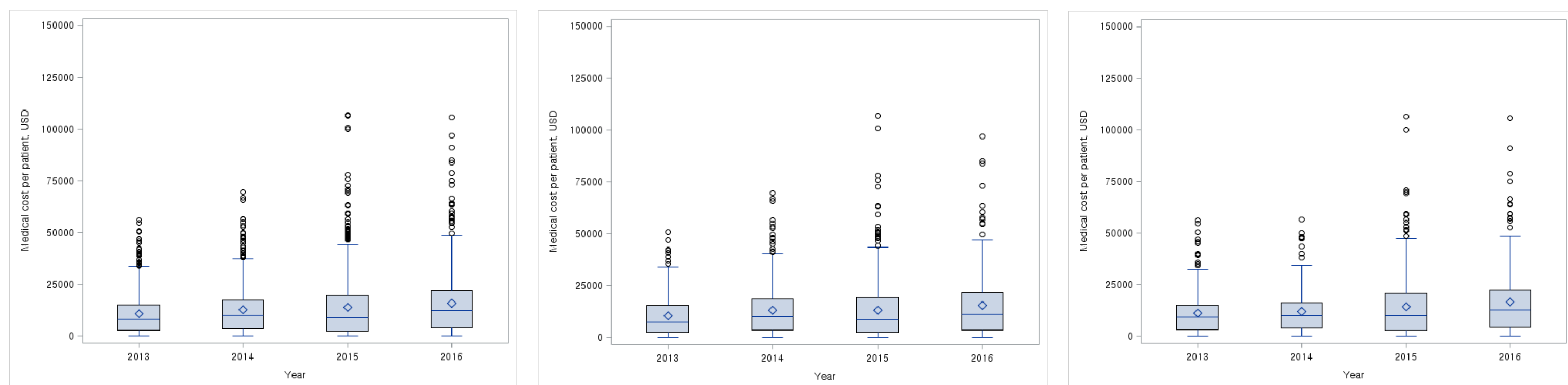
Figure 2. Mean annual incidence-based medical cost per patient in Boxplot

(a) Oropharyngeal cancer[†] (Total, Male, Female)

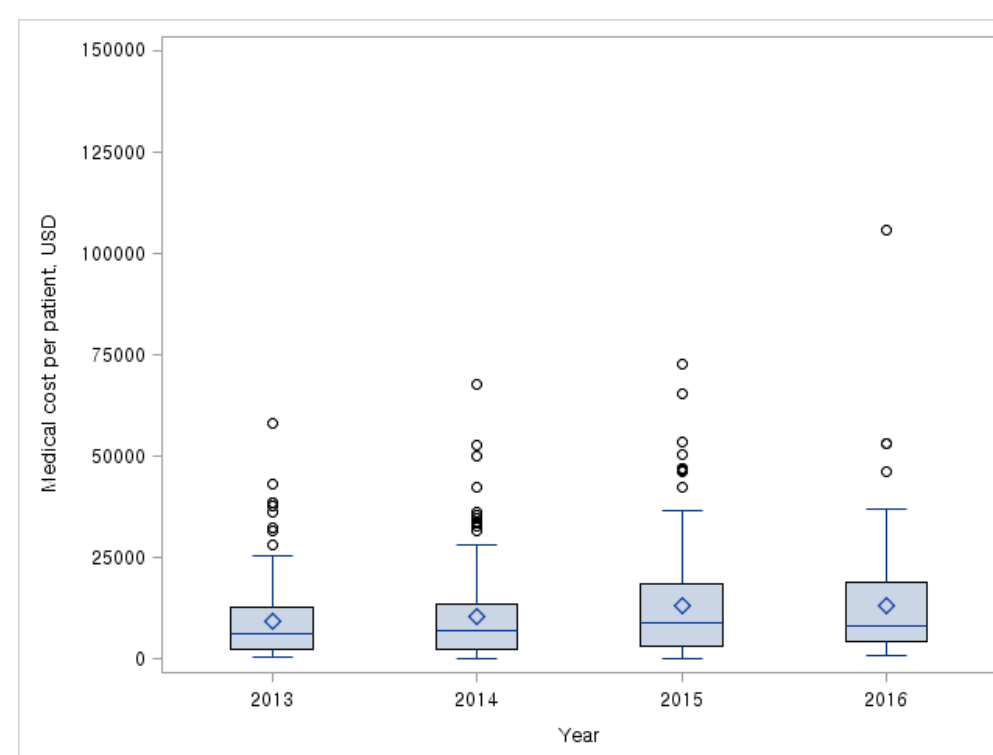


[†]Oropharynx(C10) including base of tongue(C01) and tonsil(C09)

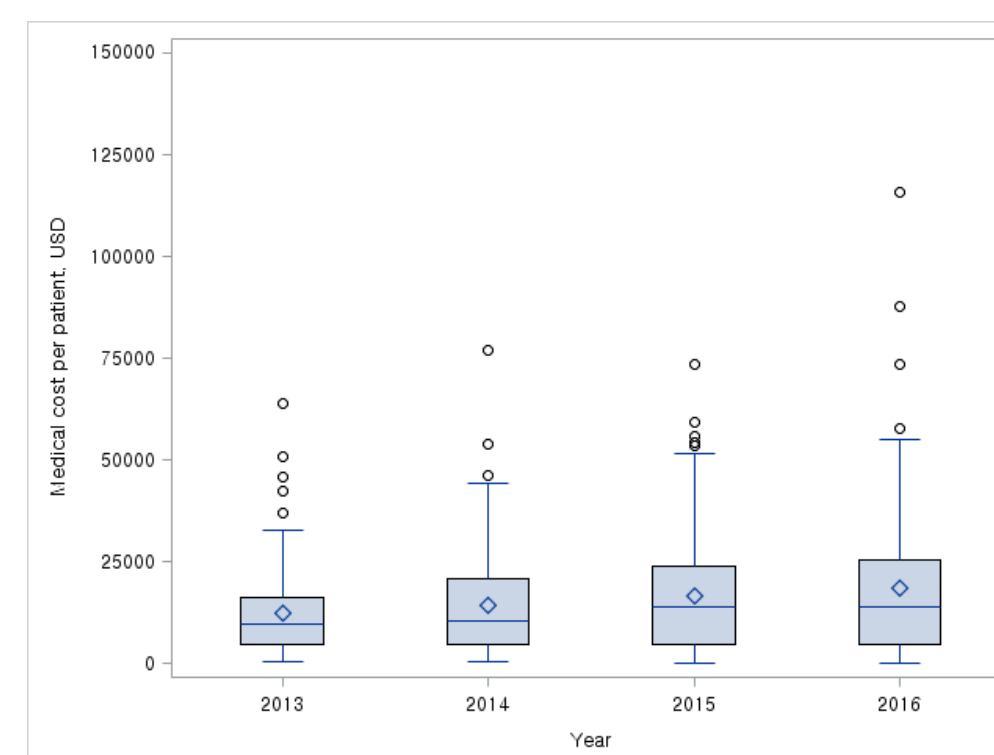
(b) Anal cancer (Total, Male, Female)



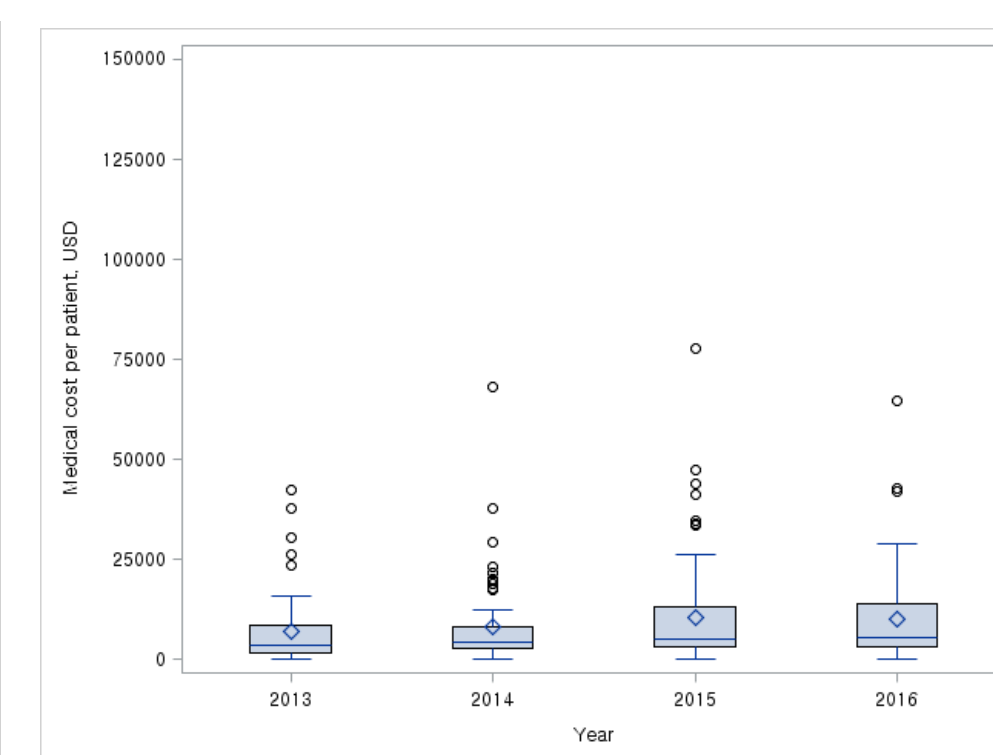
(c) Vulvar cancer



(d) Vaginal cancer



(e) Penile cancer



- For the first year after diagnosis, the mean incidence-based cost per patient was highest in oropharyngeal cancer and lowest in penile cancer. The number of new patients also showed the same trend
- 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

Table 2. Incidence rate of oropharyngeal and anogenital cancer in South Korea, 2013-2016

Cancer	2013		2014		2015		2016	
	Male	Female	Male	Female	Male	Female	Male	Female
Oropharynx [†] (C01, 09, 10)	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	-

[†]Incidence rate is calculated per 100,000 persons

[†]Oropharynx(C10) including base of tongue(C01) and tonsil(C09)

- Higher incidence rates were observed among males compared with females, with incidence rates per 100,000 for males vs. females being 3.1 vs. 0.7 for oropharyngeal cancer in 2016
- In oropharyngeal cancer, the incidence of male increased from 2.7 in 2013 to 3.1 in 2016, but the incidence of female did not change from 0.7 in 2013 to 0.7 in 2016

Table 3. Linear regression model and generalized linear model for incidence-based medical cost

Variable	Linear Regression Model				Generalized Linear Model			
	Anus (C21)		Oropharynx [†] (C01,09,10)		Anus (C21)		Oropharynx [†] (C01,09,10)	
	β	p	β	p	β	p	β	p
Sex (ref = female)	-0.150	0.0004	0.422	<.0001	-0.088	0.012	0.249	<.0001
Age (ref = ≤ 65)	-0.136	0.001	-0.185	<.0001	-0.120	<.0001	-0.118	<.0001
Year	0.101	<.0001	0.046	0.003	0.130	<.0001	0.038	0.002
Surgery (ref = inexperience)	1.037	<.0001	0.956	<.0001	0.759	<.0001	0.657	<.0001
Health plan type (ref = healthcare insurance)	0.115	0.131	-0.121	0.091	0.129	0.040	0.013	0.823
CCI	0.00003	0.987	-0.045	0.002	-0.009	0.534	-0.034	0.003

*p<0.05

[†]Oropharynx(C10) including base of tongue(C01) and tonsil(C09)

- In multivariate regression analysis, the medical cost of oropharyngeal cancer was significantly higher in men than in women after adjustment of confounding factors such as age, year, surgery and health plan type(p <.0001)
- In anal cancer, women showed a higher cost than men, However, the difference was not large when the β value was confirmed
- Both linear regression model and generalized linear model showed similar results

LIMITATIONS

- This study used claims data, patients who did not use medical institutions were excluded from the analysis. In addition, the burden of disease may be underestimated because indirect costs such as transportation costs, caregiver costs, and productivity losses are excluded
- Since we defined patients based on the primary or secondary diagnosis, patients who have the disease yet diagnosed other than primary or secondary diagnosis might be excluded, which may explain lower incidence for the elderly
- However, the HIRA claims data contains the data of the entire population, representing the Korean population. The incidence-based medical cost estimates in this study are useful in considering disease prevention

DISCUSSIONS & CONCLUSIONS

- The total incidence-based cost of oropharyngeal and anogenital cancers associated with HPV increased from 27,803,613 USD in 2013 (in 2016 USD) to 38,864,428 USD in 2016
- In Korea, the direct medical costs of those cancers are a significant burden. The incidence of oropharynx including tonsil and base of tongue cancer was significantly higher in men, and medical costs were statistically significant higher in men than in women. More aggressive public health policy toward males may decrease gender gap of oropharyngeal and anogenital cancers

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