

Medical Care Cost of Oropharyngeal Cancer among Texas Patients

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Abstract

Background: The incidence of oropharyngeal cancer is rising rapidly, with the majority of cases being attributable to human papillomavirus (HPV). Despite the availability of a vaccine, rates of HPV vaccination among Texas youth are low. The healthcare cost of oropharyngeal cancer in Texas is unknown. The aims of this study were to estimate the first 2-year cost of treating new cases of oropharyngeal cancer and determine the predictors of oropharyngeal cancer treatment cost in Texas.

Methods: This study included a retrospective cohort of 467 Texas patients with commercial insurance claims data with oropharyngeal cancer diagnosed from 2011 to 2014 and a control group of 467 noncancer patients obtained with propensity score matching. Total healthcare cost during the first 2 years after the index date was measured. A generalized linear model was used to identify

predictors of monthly cost during the 2 years after the index date.

Results: The mean differential adjusted healthcare cost for oropharyngeal cancer cases was \$139,749 in the first 2 years. The mean adjusted monthly cost in the first 2 years was \$6,693 for cases and \$870 for controls. Age, comorbidity, mental health, prediagnostic healthcare cost, and time index were significant predictors of monthly cost.

Conclusions: Medical care cost was about \$140,000 in the first 2 years after diagnosis of oropharyngeal cancer among commercially insured patients in Texas.

Impact: The cost estimates provide important parameters for development of decision-analytic models to inform decision makers about the potential value of initiatives for increasing the HPV immunization rate in the state. *Cancer Epidemiol Biomarkers Prev*; 26(9); 1443–9. ©2017 AACR.

Introduction

The incidence of oropharyngeal cancer is rising rapidly in the United States, especially among middle-aged men. Though traditionally thought to be caused by alcohol and tobacco consumption, the proportion of oropharyngeal cancer attributable to human papillomavirus (HPV) is increasing. From 2008 through 2012 in the United States, 11,000 new cases of oropharyngeal cancer were attributed to HPV annually (1). According to the U.S. Centers for Disease Control and Prevention, oropharyngeal cancer is the most common HPV-related cancer (1–3).

The rising incidence of oropharyngeal cancer provides a major public health opportunity for primary prevention, and approxi-

mately 72% are attributable to HPV. The HPV vaccine is highly effective at preventing oncogenic infections and HPV-related premalignancies (4, 5). However, the immunization rate in Texas is low where there is no school-based HPV vaccine requirement. A 2015 survey of adolescents ages 13 to 17 years found approximately 41% of girls and 24% of boys in Texas completed the HPV vaccination series, similar to rates observed in the United States overall (6). Given the cost of increasing the HPV vaccination rate for girls and boys, it is important to consider the potential cost offset of reducing HPV-related cancers in Texas by increasing the vaccine coverage. The primary aims of this study were to estimate the first 2-year cost of treating new cases of oropharyngeal cancer and identify demographic, comorbidity, and treatment-modality predictors of oropharyngeal cancer treatment cost in Texas.

Materials and Methods

Data source

Data were obtained from the 2011–2014 Truven MarketScan Commercial Claims and Encounter Database (CCA). The database contains enrollment and healthcare claims data for active employees, early retirees, Consolidated Omnibus Budget Reconciliation Act continues, and dependents insured by employer-sponsored commercial health insurance plans in the United States. The data are collected from employers and health plans and comprise service-level claims for inpatient, outpatient, and emergency room services and outpatient prescription drugs on 160 to 260 million enrollees each year during the study period. Approximately 92% of patients were insured through commercial plans, and 8% were enrolled in a Medicare Supplement plan. The

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database was fully deidentified, conforming to the Health Insurance Portability and Accountability Act of 1996, and was exempt from institutional review board approval.

Identification of cases

All patients at least 18 years of age living in Texas and diagnosed with oropharyngeal cancer during the years 2011–2014 were selected. Patients were considered diagnosed with oropharyngeal cancer if they had a primary or secondary diagnosis of cancer at one of the following sites indicated by the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) code: base of tongue and lingual tonsil (codes 141.0 and 141.6), soft palate and uvula (145.3–145.4), oropharynx (146.0–146.9), pharynx otherwise unspecified, and Waldeyer's ring (149.0–149.1). Specific attention was given to ensure HPV-related subsites in the oropharynx were included. Patients had at least 1 inpatient service claim or 2 outpatient service claims at least 30 days apart. This requirement of at least two outpatient service claims increased the likelihood that only oropharyngeal cancer patients with active disease would be selected. The first oropharyngeal cancer service date was defined as the index date. Patients had to be continuously enrolled for 6 months before and after the index date. This enrollment requirement allowed assessment of whether any oropharyngeal cancer disease code was entered in the database during the 6 months before the index date and assessment of the patient's total healthcare utilization during the first 6 months after the index date. Cases with total first-year cost above \$1,000,000 were excluded.

Selection of controls

The CCAE was searched to identify potential noncancer controls. Potential controls had to: (1) live in Texas during the study period, (2) be continuously enrolled for 6 months before and after the index date, (3) have no ICD-9-CM code for cancer at any site (140.0–208.9) during the 6 months before the index date, (4) have no diagnosis of recurrent respiratory papillomatosis (ICD-9-CM code 212.1), which is associated with HPV infection, and (5) have age within 5 years of age of case. An index date identical to the case index date was randomly assigned to each subject in this initial pool of controls to represent a hypothetical diagnosis date for measuring the cost expected without oropharyngeal cancer.

The propensity score was computed from the following covariates: (1) Modified Charlson comorbidity index (CCI) in the 6 months prior to the index date. The modified CCI excluded possible risk factors for oropharyngeal cancer, including malignancy, metastatic solid tumor, and chronic pulmonary disease (7). (2) Psychiatric diagnosis groups (PDG) in the 6 months prior to the index date. PDGs account for subjects' mental health status and include 12 major psychiatric diagnostic groupings (8). (3) Prediagnosis healthcare cost for the period from 6 months prior to diagnosis to 3 months prior to diagnosis. Costs in the 3 months immediately prior to diagnosis were excluded to avoid including the cost of treating symptoms of an undiagnosed cancer. Therefore, if a patient was diagnosed with oropharyngeal cancer on January 7, 2011, the prediagnosis-phase cost was defined as the cost from July 7, 2010, through October 6, 2010. (4) Health insurance plan type, and (5) region of Texas (northeast, southeast, or west) categorized using a three-digit zip code (Supplementary Table S1). These regions mainly reflected the populations in and around Dallas (northeast), Houston (southeast), and El Paso (west). CCI and PDG served as indicators of the prediagnosis

health status for cases and controls. One control was matched to each case using nearest neighbor matching (9). Once individuals were selected as controls for given cases, they were removed from the pool of candidate controls. Matched sets of cases and controls were created with similar demographic, health plan, location, and preindex-date health status and healthcare cost.

Analysis of healthcare cost

The primary outcome measure was the mean differential healthcare cost for cases in the first 2 years after the index date with model adjustments. Healthcare cost was defined as the total gross payments for all inpatient services, outpatient services, and outpatient prescription drugs. The payments included copayments, coinsurance, deductibles, and coordination of benefits and other savings. All dollars were adjusted to year 2015 values using the Consumer Price Index from the U.S. Bureau of Labor Statistics (10). Means and SDs were presented to describe the cost distribution. The Student *t* test was used to identify significant differences between cases and controls. We further analyzed the costs for the treatments relevant to oropharyngeal cancer during the first 2 years after the index date. The oropharyngeal cancer treatments were categorized into three modalities: surgery, radiation therapy (XRT) including intensity-modulated radiotherapy (IMRT), and chemotherapy, and were identified by each patient's claims for specific procedure codes (Supplementary Table S2).

Analysis of monthly spending patterns

Adjusted mean monthly payments in the first 2 years after the index date were estimated for cases and controls. Patients who disenrolled during the follow-up period were right censored. Their costs were adjusted for right censoring and skewness by applying a generalized linear model with log link function (11). The log of arithmetic mean monthly cost was modeled (i.e., $\ln(E(y/x)=X\beta)$) during 2 years, resulting in 24 partitioned monthly cost estimators for each patient. The covariates included sex, age, CCI, PDGs, health insurance plan type, Texas region, prediagnosis healthcare cost, case versus control status, cancer versus no cancer before diagnosis, and censored versus noncensored. Subjects' employment classifications were excluded as more than 50% of data were missing. Each patient had 24-month index partitions and the polynomials up to fifth degree of 24 months (e.g., $\text{month}^1 = 1, 2, 3$, up to 24; $\text{month}^2 = 1, 4, 9$, up to 576; continued up to month^5). The model with the smallest Akaike information criterion was selected for cost estimation (12). The significant interaction term for 24-month index and case/control was added using forward selection to adjust for different slopes of cost over time between cases and controls. Line graphs were plotted to show the monthly healthcare spending during the first 2 years after the index date for cases and controls. All analyses were performed using SAS for Windows, version 9.4 (SAS Inc.).

Results

Characteristics of the cases and controls are summarized in Table 1. A total of 467 Texas patients were identified who had a primary or secondary diagnosis of oropharyngeal cancer during the study period (Supplementary Fig. S1). One of the patients in the case group had payments exceeding \$1,000,000 and was excluded. The propensity score was not significantly different between cases (0.00218 ± 0.00124) and controls (0.00237 ± 0.00172 ; *P* value = 0.05). Supplementary Fig. S2 shows the

Table 1. Characteristics of oropharyngeal cancer patients and matched controls

Characteristic	Cases	Controls	P
Number of patients	467	467	
Age, mean (SD), years	54.62 (7.38)	54.26 (7.47)	0.459
Sex, N (%)			
Male	382 (81.80)	382 (81.80)	Matched
Female	85 (18.20)	85 (18.20)	
Follow-up, mean (SD), years	1.51 (0.80)	1.73 (0.91)	<0.001
Employee classification, N (%)			
Salary	78 (16.70)	125 (26.77)	<0.001
Hourly	97 (20.77)	113 (24.2)	
Other	29 (6.21)	38 (8.14)	
Missing/unknown	263 (56.32)	191 (40.9)	
Union/nonunion, N (%)			
Union	39 (8.35)	52 (11.13)	<0.001
Nonunion	138 (29.55)	171 (36.62)	
Other	27 (5.78)	53 (11.35)	
Missing/unknown	263 (56.32)	191 (40.9)	
Employment status, N (%)			<0.001
Active full time	177 (37.90)	267 (57.17)	
Active part time or seasonal	3 (0.64)	5 (1.07)	
Retired	39 (8.35)	42 (8.99)	
COBRA(continue)/long-term disability/surviving spouse/dependent	6 (1.28)	1 (0.21)	
Other/unknown	242 (51.82)	152 (32.55)	
Plan type, N (%)			0.571
Comprehensive	9 (1.93)	13 (2.78)	
EPO/missing	22 (4.71)	15 (3.21)	
HMO/POS/POS with capitation	68 (14.56)	78 (16.70)	
PPO	338 (72.38)	329 (70.45)	
CDHP/HDHP	30 (6.42)	32 (6.85)	
Region, N (%)			0.481
Southeast	219 (46.90)	230 (49.25)	
Northeast	201 (43.04)	200 (42.83)	
West	47 (10.06)	37 (7.92)	
CCI, mean (SD) ^a	0.49 (1.00)	0.45 (0.96)	0.594
PDGs, mean (SD) ^{a,b}	0.09 (0.30)	0.07 (0.28)	0.373
Healthcare cost for 3 months before OPC diagnosis, mean (SD), USD ^c	3,205 (9,748)	2,220 (10,254)	0.133

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; OPC, oropharyngeal cancer; POS, point of service plan; PPO, preferred provider organization; USD, United States dollars.

^aMeasured 6 months before the index date.

^bThe score indicated the average number of mental psychiatric diagnostic disease groupings among our case and control group.

^cThe cost incurred during the 3 months immediately prior to the index diagnosis date was excluded to avoid including the cost of treating symptoms of an undiagnosed cancer.

propensity score distributions. The mean age of the oropharyngeal cancer patients was 54.62 years. Most patients were located in southeast Texas ($n = 219$; 46.90%). Approximately half were covered by a preferred provider organization health insurance plan. Baseline characteristics were not significantly different between cases and controls except for follow-up duration and employment classification.

Expenditures for oropharyngeal cancer patients and controls are summarized in Table 2. The unadjusted observed mean total

healthcare expenditures during the first 2 years for cases and controls were \$134,454 and \$13,693, respectively ($P < 0.001$). Supplementary Fig. S3 shows the unadjusted costs for the pre- and postindex date periods between cases and controls. On average, the unadjusted out-of-pocket payments for cases and controls were \$2,825 and \$1,192 ($P < 0.001$). For oropharyngeal cancer patients, mean unadjusted cost in the first 2 years was \$106,604 for outpatient service, \$24,341 for inpatient services, and \$3,550 for outpatient prescription drugs. There were 7 deaths among the

Table 2. Unadjusted^a and adjusted cost during the first 2 years after the index date for oropharyngeal cancer patients and matched controls

Type of cost	Mean expenditure in 2015 U.S. dollars (SD)			P
	Cases	Controls	Difference	
First 2 years (unadjusted)				
Total	134,454 (108,635)	13,693 (38,306)	120,802 (81,472)	<0.001
Inpatient services	24,341 (48,972)	5,031 (29,550)	19,310 (40,444)	<0.001
Outpatient services	106,604 (82,821)	5,738 (12,293)	100,866 (59,275)	<0.001
Outpatient prescription drugs	3,550 (5,183)	2,924 (6,661)	626 (5,968)	0.11
First 2 years (adjusted)				
Total	160,639 (114,893)	20,890 (53,543)	139,749 (89,631)	<0.001

^aUnadjusted is the observed cost with no regression model estimate of cost for months not enrolled.

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Table 3. The 2-year mean cost after index date by treatment

Treatment	N (%)	Mean cost in 2015 U.S. dollars per person (SD)
Surgery	233 (50%)	8,320 (15,111)
Inpatient	90 (19%)	17,440 (19,030)
Outpatient	190 (41%)	1,942 (2,641)
Radiation-XRT (including IMRT)	341 (73%)	50,362 (28,928)
Inpatient	14 (3%)	1,305 (1,369)
Outpatient	341 (73%)	50,308 (28,938)
Chemotherapy	284 (61%)	3,277 (2,822)
Inpatient	0 (0%)	NA
Outpatient	284 (61%)	3,277 (2,822)

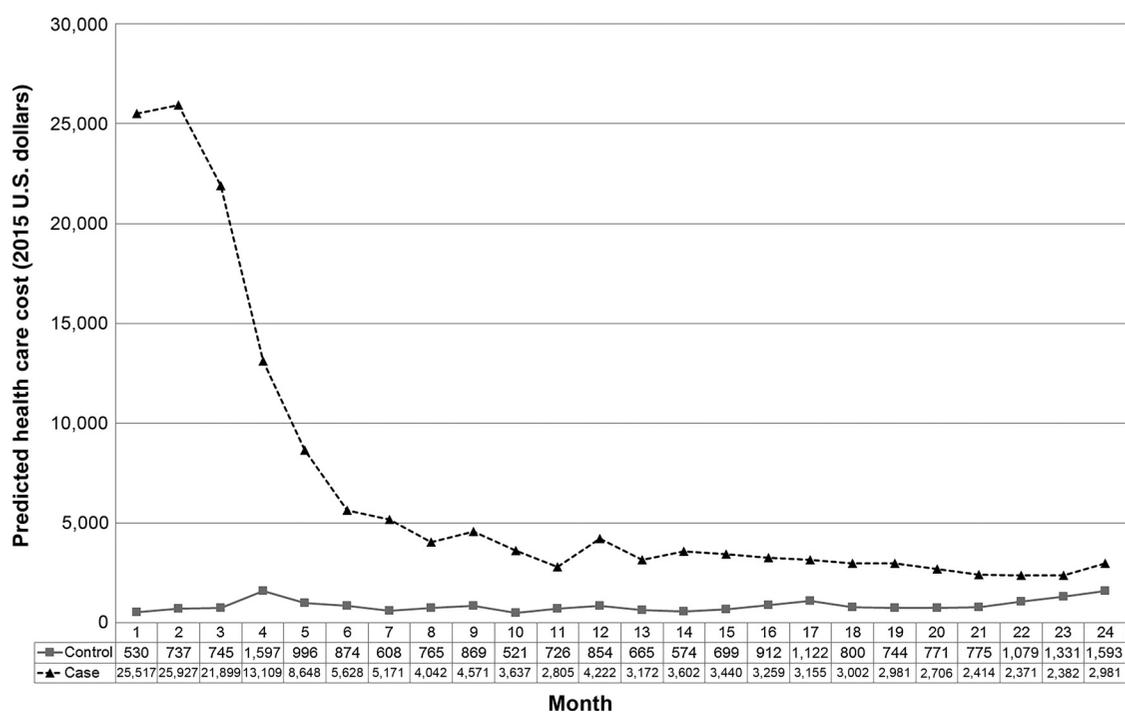
cases and 1 death among the controls reported in the healthcare claims data. Deaths not reported in the claims data were unavailable. Table 3 shows the mean cost of specific services for oropharyngeal cancer patients who received them during the first 2 years following the index diagnosis date. Seventy-three percent of patients were treated with XRT, costing an average of \$50,362. Of this 73% of patients, 96% received IMRT. Mean cost was \$8,320 for the 50% of patients treated with surgery and \$3,277 for the 61% of patients treated with chemotherapy. Supplementary Table S3 shows the number of days from the index date to the initiation of the first modality of therapy. The significant predictors of monthly cost over the first 2 years were age, CCI, PDGs, prediagnosis healthcare cost, case versus control status, polynomial of fifth degree of months since index date, and the interaction term of 24-month index and case/control (Supplementary Table S4). The adjusted mean total healthcare costs in the first 2 years for cases and controls were \$160,639 and \$20,890, respectively (mean differential cost, \$139,749; $P < 0.001$; Table 2). The adjusted monthly costs during the first 2 years for the cases and

controls were \$6,693 and \$870 (Fig. 1). Supplementary Figs. S4 and S5 show histograms of the adjusted 1-year cost and 2-year cost distributions, respectively.

Discussion

Management of oropharyngeal cancer resulted in a mean differential healthcare cost of \$139,749 in 2015 U.S. dollars in the first 2 years after diagnosis. To our knowledge, this is the first population-based estimate of oropharyngeal cancer-specific healthcare cost in Texas. It provides information for state-level modeling and policy analysis of public decisions regarding investment in HPV-related cancer prevention.

An estimated 72% of oropharyngeal cancer cases are attributable to HPV (3). There is currently no screening paradigm for oropharyngeal cancer, and with few symptoms in early stages, the disease often presents at an advanced stage (13). The latency of HPV-induced oropharyngeal cancer is long and is often diagnosed in the fifth or sixth decade of life (13). Given these characteristics, immunization against HPV is an effective strategy to reduce the morbidity and economic cost of oropharyngeal cancer. The U.S. Centers for Disease Control and Prevention recommend routine HPV vaccination for girls and boys (14). The quadrivalent HPV vaccine is covered under the Affordable Care Act for boys and girls in the recommended age range, and most plans are expected to cover the 9-valent vaccine in 2017 (15, 16). Despite federal program and policy support, states like Texas have low immunization rates and may benefit from investment in initiatives to promote HPV immunization (6). To guide such decision making, the potential economic and health benefits of these investments need to be estimated at the state level.

**Figure 1.**

Predicted monthly cost for the 2 years between case and control.

Ours is not the first economic analysis of the potential benefits of HPV immunization, but we believe it is the first analysis to provide information specifically about oropharyngeal cancer in Texas. The leading economic decision analytic models of HPV immunization rely on dated cost estimates for oropharyngeal cancer. In these studies, a variety of methods were applied to identify the cases, estimate the index diagnosis date, and adjust for noncancer costs, nonnormal cost distribution, and censoring. The Elbasha and Dasbach (17) model utilized cost estimates by Hu and Goldie (18) that were rough estimates based on a synthesis of the literature, secondary data, and scenario analysis. The model developed by Brisson and colleagues (19) also applied cost-per-case data for oropharyngeal cancer from work by Hu and Goldie (18). More recent studies have applied SEER-Medicare, state Medicaid, and commercial insurance claims data but considered oral cavity cancer (which is unrelated to HPV) and pharyngeal cancers (which include both HPV-related and non-HPV-related cancers) together (20–22). Etiology and presentation of oropharyngeal cancer differ widely from oral cavity cancer, resulting in major differences in treatment and long-term outcomes (23, 24). HPV is estimated to be causally involved in 72% of oropharyngeal cancers compared with fewer than 10% of oral cavity cancers in North America (3, 25–27). Currently, there is no distinction in HPV-status available in diagnostic codes. Therefore, our study attempted to estimate cost of HPV-related oropharyngeal cancer through careful selection of HPV-related oropharyngeal cancer sites. Prior studies have tended to underestimate the population-attributable fraction of HPV for oropharyngeal cancer. The majority of oropharyngeal cancers present at late stages, requiring extensive treatment; the healthcare cost of oropharyngeal cancer may be underestimated when oropharyngeal cancer is combined with oral cavity cancer (13, 28).

The mean differential 2-year healthcare cost of oropharyngeal cancer in our study, \$139,749, is higher than in previous studies. The differential cost estimate for 1-year after diagnosis was \$115,350 (Supplementary Table S5). Much of this cost can be attributed to outpatient treatment with radiotherapy. We found that more than 70% of patients received radiotherapy, and most of them were treated in outpatient settings. With the introduction of IMRT, its application in the head and neck has grown from 1% in 2000 to 46% in 2005, and was found to be 70% in our study (29). Rafzar and colleagues (30) found that mean cost of patients undergoing treatment with IMRT was \$101,099, significantly higher compared with patients undergoing traditional radiotherapy. This change in treatment paradigm may explain the differences in the high outpatient costs found in our study. Many prior estimates of cost pre-date or occur during this treatment transition (18, 20, 21). Additionally, previous estimates may vary depending on inclusion of non-oropharyngeal cancer types and study population. Using 1995–2003 Medi-Cal data, Epstein and colleagues (21) found a median cost of oral cavity and pharyngeal cancer of \$33,358 (2015 USD) in the first year after diagnosis. Hollenbeak and colleagues (20) used inverse probability weighting to adjust for censoring in SEER-Medicare data and found a 5-year cumulative cost of pharyngeal cancer of \$48,544 (2015 USD). Hu and Goldie (18) used SEER registry and Medicare data to identify the mean cost per oropharyngeal cancer case as \$42,534 (2015 USD). However, HPV-associated oropharyngeal cancer has been found to represent 72% of all oropharyngeal cancers rather than 11%, the proportion used in their estimates

(3, 18). The conclusions derived from Medicare cannot be generalized to the overall population. Furthermore, those estimates were derived from public payment rates paid by state and federal governments, which may underestimate the economic burden of disease (31). Jacobsen and colleagues (22) found that for patients with commercial insurance, the mean cost estimates for oropharyngeal cancer were \$87,445 (2015 USD), double that of the cost in Medicare cases. This study also included patients with salivary gland and oral cavity cancer, which may have lowered mean cost.

In our study, the healthcare cost of oropharyngeal cancer was highest in the first 6 months, and outpatient services accounted for the bulk of the cost. A previous study also showed that most of the cost for oropharyngeal cancer was incurred in the first year following the diagnosis (22). Furthermore, previous studies showed that outpatient services accounted for the greatest portion of utilization and cost (22, 32). This cost pattern is consistent with the National Comprehensive Cancer Network practice guidelines for head and neck cancer, which recommend a history and physical examination every 1 to 3 months in the first year after the initial treatment (33). Future studies are needed to define and quantify the long-term posttreatment management of oropharyngeal cancer to better understand the lifetime cost of this disease.

Our finding that patients' prediagnosis comorbidities were significantly associated with 2-year cost of oropharyngeal cancer treatment is consistent with findings of previous studies (20, 21). The mean CCI of our case population was lower than that in previous studies (21, 22). We excluded other cancer and chronic pulmonary diseases from the oropharyngeal cancer risk factors when calculating the CCI score. This exclusion allowed us to identify a general population for the control group that was used to estimate the counter-factual of cost incurred without oropharyngeal cancer.

Use of retrospective administrative claims data over a 4-year period for one state limits the generalizability of our findings. Costs associated with lost earnings due to morbidity and premature mortality were not available, precluding a full societal cost estimate. Propensity score matching reduces observable differences between cases and controls but does not correct for unobservable differences that may affect costs. Whether people were salaried, in a union, or working full time were significantly different between cases and controls in Table 1, but most of these variables had nearly 50% missing data. Cases experienced statistically significant shorter follow-up time compared with controls, 1.51 years compared with 1.73 years. This difference did not affect the predicted stable cost trend in both groups following the initial 6-month treatment for the cases. Data were not available for the stage at diagnosis, deaths outside the hospital, and other covariates, which precluded analysis of the variation in cost based on provider characteristics and patients' socioeconomic status, race, ethnicity, specific geographic location, and vital status. Previous authors have used patients' five-digit zip code to link to census data as a proxy for socioeconomic status (22). This information was not available based on our agreement with Truven. Laboratory results to identify HPV-related cancer were not available in the claims data (34). However, epidemiologic studies demonstrate that approximately 72% of oropharyngeal cancer is HPV-related (3).

Strengths of the study include use of comprehensive longitudinal up-to-date healthcare claims data along with methods to

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measure the differential cost due to oropharyngeal cancer, while adjusting for the cost of unrelated health care, right censoring, and nonnormally distributed cost data. Careful selection of oropharyngeal cancer-specific ICD-9-CM codes ensured that patients with head and neck cancers from other sites were excluded from the analysis. We included only cancer sites in the oropharynx that are known to be HPV-related, in contrast to other studies that included oral cavity sites, which may have resulted in underestimation of cost associated with treating HPV-related cancer (16, 18–20, 31).

Conclusion

Medical care cost was about \$140,000 in the first 2 years after diagnosis of oropharyngeal cancer among commercially insured patients in Texas. The cost estimates provide important parameters for development of decision-analytic models to inform decision makers about the potential value of alternative strategies for increasing the HPV immunization rate in the State.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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