Economic and Clinical Burden of Recurrence Among Elderly Patients With Resected Locoregionally Advanced Head and Neck Squamous Cell Carcinoma (LA HNSCC) in the US

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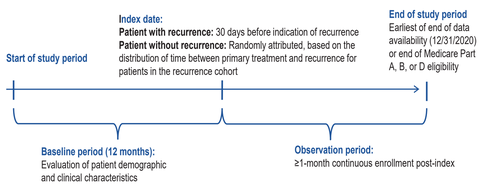
Background and objective

- Around 60% of patients with HNSCC present with locoregionally advanced (LA) disease at diagnosis, ie, stage III to IVB[1]
- For resectable LA HNSCC, the standard treatment approach typically involves surgery followed by radiotherapy (RT) with or without systemic therapy (ST)
- A significant proportion of patients with LA HNSCC develop locoregional or distant recurrence, suffering from poor prognosis, with a median overall survival (OS) of ~ 1 year[2]
- There is limited research addressing the clinical and economic burden of disease recurrence after primary treatment[3]
- This study aimed to estimate the real-world impact of HNSCC recurrence following primary treatments on OS, healthcare resource utilization (HCRU), and costs among elderly patients with resected LA HNSCC in the US

Methods

Study design

- This retrospective, observational study used the Surveillance, Epidemiology, and End Results (SEER)-Medicare database
- Patients with newly diagnosed stage III-IVB LA HNSCC (larynx, hypopharynx, oral cavity, or oropharynx) who underwent primary surgery within 4 months of diagnosis were included (**Figure 1**)
  - Recurrence was indicated by (1) at least two visits with a secondary malignancy diagnosis code, spaced at least 30 days apart, with the first occurring no earlier than 30 days after primary treatment initiation; OR (2) new treatment initiation after primary treatment. Recurrence date was the date of the earliest aforementioned events



Study outcomes

- OS: Time from index date to death
- All-cause and HNSCC-related HCRU
  - HNSCC-related HCRU: Defined by claims for medical services with a diagnosis for HNSCC
  - Summarized as incidence rates (IR) on a per-patient-per-month (PPPM) basis, ie, ratios between total number of events and total person-month during the follow-up period
- Mean monthly all-cause and HNSCC-related healthcare costs per patient
  - All costs in 2023 USD using the Personal Consumption Expenditures medical care component

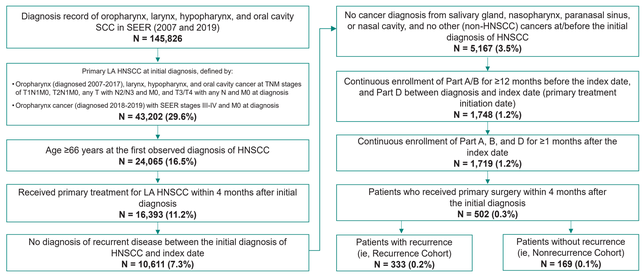
Statistical analysis

- Baseline characteristics were compared between patients with and without recurrence via t tests for continuous variables and Chi square tests for categorical variables
- OS was described using Kaplan-Meier (KM) curves and compared between patients with and without recurrence by a Cox proportional hazards model adjusting for baseline characteristics
- All-cause and HNSCC-related HCRU were compared between patients with recurrence vs without using adjusted generalized linear models with a negative binomial distribution and a log-link function
- Mean monthly all-cause and HNSCC-related healthcare costs per patient were compared between patients with recurrence vs without separately using adjusted generalized linear models with a Tweedie distribution and a log-link function

Results

- **A total of 333 patients with recurrence and 169 patients without recurrence met the selection criteria, with a median follow-up of 17.1 months and 26.6 months, respectively**

Figure 1. Sample selection



LA HNSCC, locally advanced head and neck cancer; SCC, squamous cell carcinoma; SEER, Surveillance, Epidemiology, and End Results; TNM, tumor node metastases.

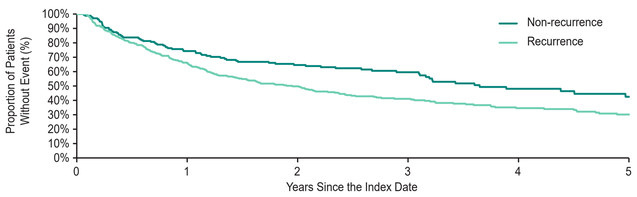
Table 1. Baseline characteristics

Baseline characteristics	Recurrence cohort (N = 333)	Nonrecurrence cohort (N = 169)	*P*-value
Age at index (years), mean ± SD	74.4 ± 6.4	75.5 ± 7.0	0.085
Male, N (%)	199 (59.8)	104 (61.5)	0.700
Race/ethnicity, N (%)			0.686
White	273 (82.0)	141 (83.4)	
Others	60 (18.0)	28 (16.6)	
Region, N (%)			0.160
West	129 (38.7)	53 (31.4)	
South	96 (28.8)	64 (37.9)	
Northeast	60 (18.0)	32 (18.9)	
Midwest	48 (14.4)	20 (11.8)	
Year of initial diagnosis, N (%)			0.223
2007-2010	86 (25.8)	35 (20.7)	
2011-2014	102 (30.6)	48 (28.4)	
2015-2019	145 (43.5)	86 (50.9)	
Tumor stage at diagnosis[a], N (%)			0.380
III	129 (38.7)	70 (41.4)	
IVA	167 (50.2)	86 (50.9)	
IVB	32 (9.6)	N <11 (<6.5)	
IV unspecified	N <11 (<3.3)	N <11 (<6.5)	
Missing stage	N <11 (<3.3)	N <11 (<6.5)	
Tumor site at diagnosis, N (%)			0.170
Oral cavity	139 (41.7)	69 (40.8)	
Larynx	109 (32.7)	66 (39.1)	
Oropharynx	73 (21.9)	N >23 (>13.6)	
Hypopharynx	12 (3.6)	N <11 (<6.5)	
Charlson Comorbidity Index, mean ± SD	1.8 ± 1.9	1.8 ± 1.7	0.847

Notes: Categories with N <11 were not reported per SEER-Medicare data reporting policy.
[a]Tumor stage was from SEER and was based on AJCC 6th TNM staging for diagnosis between 2007 and 2015, AJCC 7th TNM staging for diagnosis between 2010 and 2015, and AJCC 7th/UICC 7th TNM staging for diagnosis between 2016 and 2017, and AJCC 8th TNM staging for diagnosis between 2018 and 2019. SEER used both clinical and pathologic TNM to determine stage.

- **Patients with recurrence had a 63% increased risk of death vs those without (aHR = 1.63; 95% CI: 1.24, 2.15; P<0.001), after adjustment for primary treatment, age at index date, sex, race, region, disease stage, tumor site, and CCI score (Figure 2)**

Figure 2. OS of patients with and without recurrence



	Median (95% CI) OS, months	5-year OS	Log-rank *P*-value
Recurrence cohort	23.8 (17.6, 29.5)	30.2%	0.008
Nonrecurrence cohort	44.4 (37.7, 67.0)	42.5%	

- **PPPM HCRU was substantially higher in patients with than without recurrence**
- **Patients with recurrence had double the rate of all-cause outpatient visits, as well as significantly higher rates of all-cause inpatient admissions and all-cause emergency department visits relative to patients without recurrence, after adjusting for key baseline characteristics**

Table 2. All-cause and HNSCC-related HCRU between patients with and without recurrence

	IR		IRR [recurrence cohort vs nonrecurrence cohort]			
			Unadjusted model[a]		Adjusted model[b]	
	Recurrence cohort (N = 333)	Nonrecurrence cohort (N = 169)	IRR (95% CI)	*P*-value	IRR (95% CI)	*P*-value
All-cause healthcare resource utilization						
Number of visits (events/person-month)						
Inpatient admissions	0.160	0.109	1.47 (1.09, 1.99)	0.011*	1.73 (1.31, 2.29)	<0.001*
Emergency department visits	0.183	0.111	1.65 (1.16, 2.33)	0.005*	2.02 (1.47, 2.77)	<0.001*
Outpatient visits	3.154	1.665	1.89 (1.62, 2.21)	<0.001*	2.00 (1.72, 2.32)	<0.001*
Skilled nursing facility stays	0.109	0.161	0.68 (0.38, 1.21)	0.189	0.77 (0.45, 1.35)	0.366
Inpatient length of stay (days/person-month)						
Inpatient days	2.076	1.563	1.33 (0.91, 1.95)	0.146	1.86 (1.26, 2.75)	0.002*
HNSCC-related healthcare resource utilization						
Number of visits (events/person-month)						
Inpatient admissions	0.106	0.061	1.73 (1.15, 2.62)	0.009*	2.21 (1.47, 3.34)	<0.001*
Emergency department visits	0.051	0.025	2.04 (1.08, 3.84)	0.028*	3.14 (1.64, 6.02)	<0.001*
Outpatient visits	1.237	0.423	2.93 (2.28, 3.76)	<0.001*	3.71 (2.87, 4.79)	<0.001*
Skilled nursing facility stays	0.035	0.034	1.03 (0.49, 2.17)	0.946	1.58 (0.78, 3.19)	0.207
Inpatient length of stay (days/person-month)						
Inpatient days	1.696	1.227	1.38 (0.83, 2.31)	0.215	2.13 (1.20, 3.76)	0.009*

*Denotes *P*-value <0.05.
CI, confidence interval; HCRU, healthcare resource utilization; IR, incidence rate; IRR, incidence rate ratio; HNSCC, locally advanced head and neck cancer.
[a]Unadjusted incidence rate ratios and *P*-values were estimated using univariable generalized linear models with a negative binomial distribution and a log-link function.
[b]The adjusted models controlled for age at index date, sex, race, region, CCI, disease stage at diagnosis, cancer site, primary treatment, corresponding HCRU during the baseline period.

- **Patients with recurrence incurred substantially more mean monthly healthcare costs than patients without recurrence**
- **After adjusting for key baseline characteristics, the incremental mean monthly all-cause total healthcare costs associated with recurrence was $3,831**

Table 3. All-cause and HNSCC-related healthcare costs between patients with and without recurrence

	Mean monthly cost		Monthly cost difference [recurrence cohort - non-recurrence cohort]			
	Recurrence cohort (N = 333)	Non-recurrence cohort (N = 169)	Unadjusted[a]	*P*-value	Adjusted[b]	*P*-value
All-cause healthcare costs (2023 USD)						
Total costs	8,442	5,095	3,346	<0.001*	3,831	<0.001*
Medical costs	8,113	4,854	3,259	<0.001*	3,732	<0.001*
Inpatient costs	4,444	2,977	1,467	0.047*	1,756	<0.001*
Emergency department costs	216	96	121	0.006*	121	<0.001*
Outpatient costs	2,107	556	1,551	<0.001*	1,607	<0.001*
Skilled nursing facility costs	670	587	83	0.687	57	<0.001*
Other costs[c]	676	639	37	0.732	85	<0.001*
Part D pharmacy costs	329	241	88	0.148	92	<0.001*
HNSCC-related healthcare costs (2023 USD)						
Total costs	3,626	2,022	1,604	0.007*	1,820	<0.001*
Medical costs	3,616	2,022	1,594	0.007*	1,809	<0.001*
Inpatient costs	2,237	1,434	803	0.123	955	<0.001*
Emergency department costs	78	13	66	0.004*	61	<0.001*
Outpatient costs	816	118	698	<0.001*	708	<0.001*
Skilled nursing facility costs	255	199	56	0.613	118	<0.001*
Other costs[c]	229	258	-29	0.680	-12	<0.001*
HNSCC-related Part D pharmacy costs	10	0.0	10	<0.001*	5	<0.001*

*Denotes *P*-value <0.05.
HNSCC, locally advanced head and neck cancer; USD, US dollars.
[a]Unadjusted mean costs, incremental cost differences, and *P*-values were estimated using univariable generalized linear models with a Tweedie distribution (a compound Poisson-gamma distribution) and log-link function.
[b]The adjusted models controlled for age at index date, sex, race, region, CCI, disease stage at diagnosis, cancer site, primary treatment, corresponding costs during the baseline period.
[c]The "other costs" category includes hospice care, home health agency, and durable medical equipment costs.

Limitations

- The study included elderly Medicare patients only, so the results may not be generalizable to a younger patient population, those with another form of insurance, or the uninsured
- Recurrence of HNSCC was determined using procedure codes, diagnosis codes, and drug codes, which could introduce misclassification bias or inaccuracies due to coding errors
- Key risk factors, including HPV status and smoking history, were not captured in the database. Future research leveraging datasets that include these variables may be needed

Conclusions

- Among elderly patients with resected LA HNSCC in the US, those with recurrence had significantly shorter OS, higher subsequent HCRU rate, and higher subsequent monthly healthcare costs than patients without recurrence
- These findings highlight the need for more effective therapies that both prevent or delay recurrence and prolong survival for patients with resectable LA HNSCC

References

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3. Wissinger E, et al. *Pharmacoeconomics.* 2014;32(9):865-882.

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