The Incidence and Survival of HPV-Positive and HPV-Negative Malignant Head and Neck Squamous Cell Carcinoma (HNSCC) in the United States: A Surveillance, Epidemiology, and End Results (SEER) 2000-2022 Database Analysis

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Introduction

- According to the GLOBOCAN estimates from 2020, head and neck squamous cell carcinoma (HNSCC) was the seventh most common cancer worldwide. HNSCC accounted for around 4.5% of all cancer diagnoses and around 4.6% of all cancer-related deaths.[1]
- Approximately 25% of HNSCC patients reported a significant economic burden, which was strongly linked to worse physical, mental, and functional outcomes. Financial burden primarily depended on disease progression and treatment costs.[2,3] One of the primary predictors of prognosis and management in HNSCC is the human papillomavirus (HPV) status.[4]

Objective

- The primary study aim was to compare the patient characteristics and disease burden of malignant HPV-positive (HPV+) and HPV-negative (HPV-) HNSCC in the US by analyzing the updated Surveillance, Epidemiology, and End Results (SEER) database released in April 2025.

Methods

- The SEER database consists of multiple local cancer registries across the US and covers about half of the US population. It contains patient characteristics and cancer management data from cancer diagnostic and treatment institutions.[5]
- This retrospective study analyzed the updated SEER database with fully available data from 17 US cancer registries (2000 - 2022). SEER*Stat analytical software was used for data analysis.
- Selection of patients with malignant HNSCC is shown on the scheme below.

Cancer site, recoded (ICD-O-3* 2023 revision) = 'Head and Neck'

↓

Malignant cancer behavior flag = 'ON'

↓

ICD-O-3* histology/behavior = 8085/3 (squamous cell, HPV-positive)

ICD-O-3* histology/behavior = 8086/3 (squamous cell, HPV-negative)

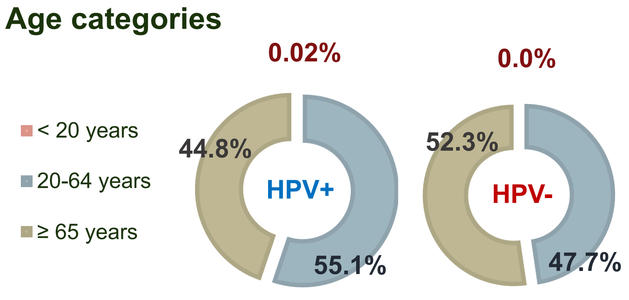
**ICD-O-3 - The International Classification of Diseases for Oncology, third edition*

- The outcomes were crude incidence rates (per 100,000 population) and survival rates (1-year and 4-year).
- For survival estimation, only patients with known age were included.
- Results were reported by demographic population subgroups to show the effects of social determinants on study outcomes.

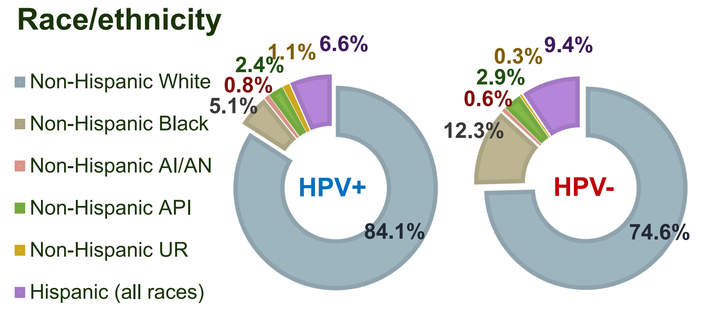
Results

- The final study sample consisted of 4,912 HNSCC patients with known HPV status. There were 4,220 HPV+ (85.9%) and 692 HPV- patients (14.1%). The most common site of HNSCC in both cohorts was the oropharynx (99.1% in HPV+ and 96.5% in HPV-).

Age categories

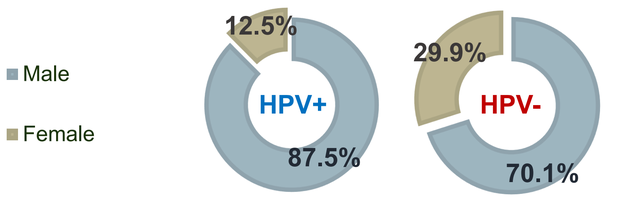


Race/ethnicity

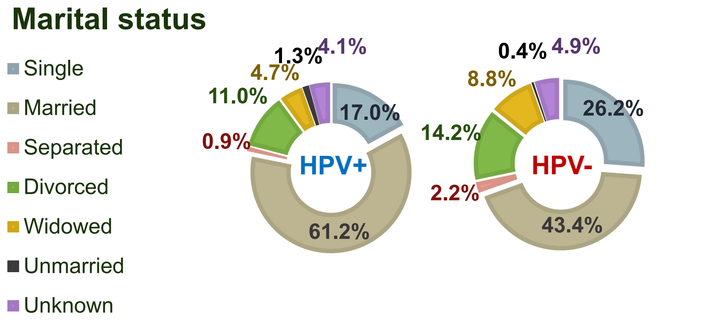


AI/AN – American Indian/Alaska Native; API – Asian or Pacific Islander; UR – Unknown

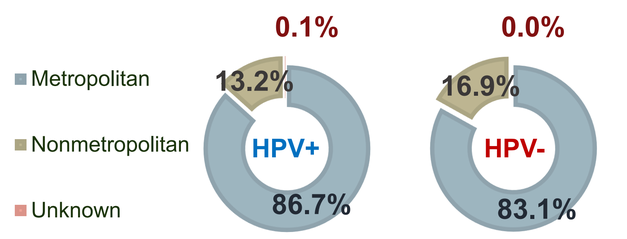
Sex at birth



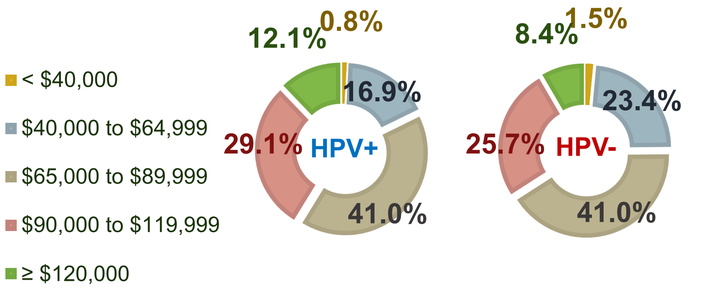
Marital status



Residing Area

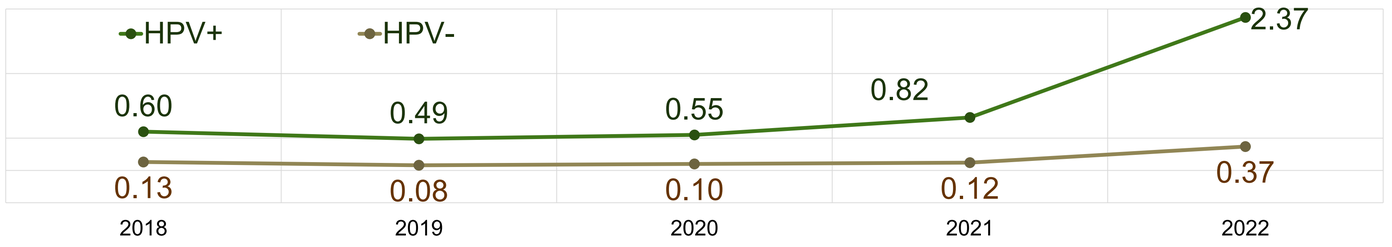


Annual household income (AI



- HPV+ was more common than HPV- (0.22 and 0.04 per 100,000 population). Trends showed increasing rates for both subtypes. Per AHI, HPV+ was most frequent in $120,000+ group (0.43), while HPV- predominantly occurred in the <$40,000 group (0.07).

Incidence rate trends (per 100,000 population)



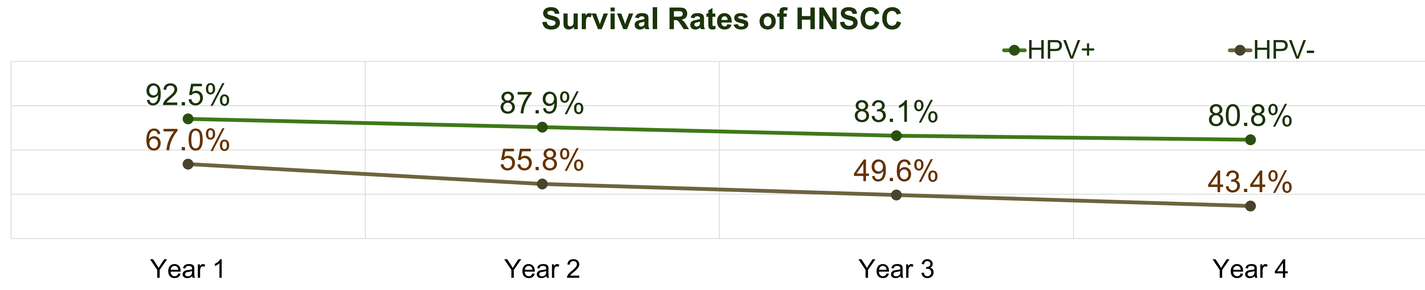
Incidence Rates (per 100,000 population)*		
Demographic Subgroups	HPV+	HPV-
< 20 years old	0.00	0.00
20 – 64 years old	0.20	0.03
≥ 65 years old	**0.77**	**0.15**
Male	**0.39**	**0.05**
Female	0.05	0.02
Metropolitan Area	0.22	0.03
Non-Metropolitan Area	**0.29**	**0.06**

Incidence Rates (per 100,000 population)*		
Race/Ethnicity	HPV+	HPV-
Non-Hispanic White	**0.34**	**0.05**
Non-Hispanic Black	0.10	0.04
Non-Hispanic AI/AN**	0.20	0.02
Non-Hispanic API***	0.05	0.01
Hispanic (all races)	0.06	0.01

**The highest values in each demographic subgroup are bolded*
***AI/AN – American Indian/Alaska Native*
****API – Asian or Pacific Islander*

- HPV+ HNSCC had higher survival rates than the HPV- subtype at all endpoints. Across AHI groups, the lowest 4-year survival rates were observed in the $50,000-55,000 group for HPV+ (71.9%) and the $95,000-100,000 group for HPV- HNSCC (28.2%). Older patients had lower survival rates at all endpoints in both HPV+ and HPV- HNSCC cohorts.

Survival Rates of HNSCC



Survival Rates (4-year endpoint)*		
Demographic Subgroups	HPV+	HPV-
Male	**80.0%**	**42.5%**
Female	86.2%	46.7%
Metropolitan Area	81.7%	44.4%
Non-Metropolitan Area	**75.6%**	**38.7%**

**The lowest values in each demographic subgroup are bolded*
***AI/AN – American Indian/Alaska Native*
****API – Asian or Pacific Islander*

Survival Rates (4-year endpoint)*		
Race/Ethnicity	HPV+	HPV-
Non-Hispanic White	81.3%	45.2%
Non-Hispanic Black	72.9%	37.1%
Non-Hispanic AI/AN**	**63.3%**	NR[#]
Non-Hispanic API***	76.3%	NR[#]
Hispanic (all races)	84.0%	**29.3%**

[#] NR – Survival endpoint not reached due to small sample size

Conclusion

- This analysis reported demographic profiles of HPV+ and HPV- HNSCC in the US.
- Most demographic characteristics were similar between the cohorts, except for age. HPV+ patients were predominantly younger (20-64 years old) than the HPV- (65+ years old).
- HPV+ HNSCC was ~5.5 times more frequent than the HPV- subtype.
- Trend analysis showed an increasing incidence of both HPV+ and HPV- HNSCC in recent years.
- Although more common, HPV+ HNSCC had a better prognosis at all study endpoints in the survival analysis.
- The results of the updated SEER data analysis showed differences between demographic population subgroups on HNSCC incidence and survival regardless of HPV subtype.
- The increasing incidence in the US is concerning, underscoring the need for novel, effective, and affordable therapy for HNSCC.

Limitations

1. **Coding and reporting variability** – local registries have collected SEER data without central review, which may have resulted in potential coding inconsistencies
2. **No continuous patient follow-up** – loss to follow-up bias may have occurred, as the patients could have received cancer-related services outside the institutions covered by the SEER program
3. **Generalizability of findings** – although the SEER database is one of the most comprehensive cancer registry databases in the US, the study conclusions may not apply to states outside the SEER-covered areas
4. **HPV status data availability** – incidence may be underestimated as the HPV status codes were included in SEER since 2018

References

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2. Lenze et al. (2021). Association of self-reported financial burden with quality of life and oncologic outcomes in head and neck cancer. DOI: 10.1002/hed.26934
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4. Zhou et al. (2021). Survival Outcomes and Treatment Decision by Human Papillomavirus Status Among Patients With Stage IVC Head and Neck Squamous Cell Carcinoma. DOI: 10.3389/fonc.2021.668066
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