

Healthcare Disparities in SCCHN

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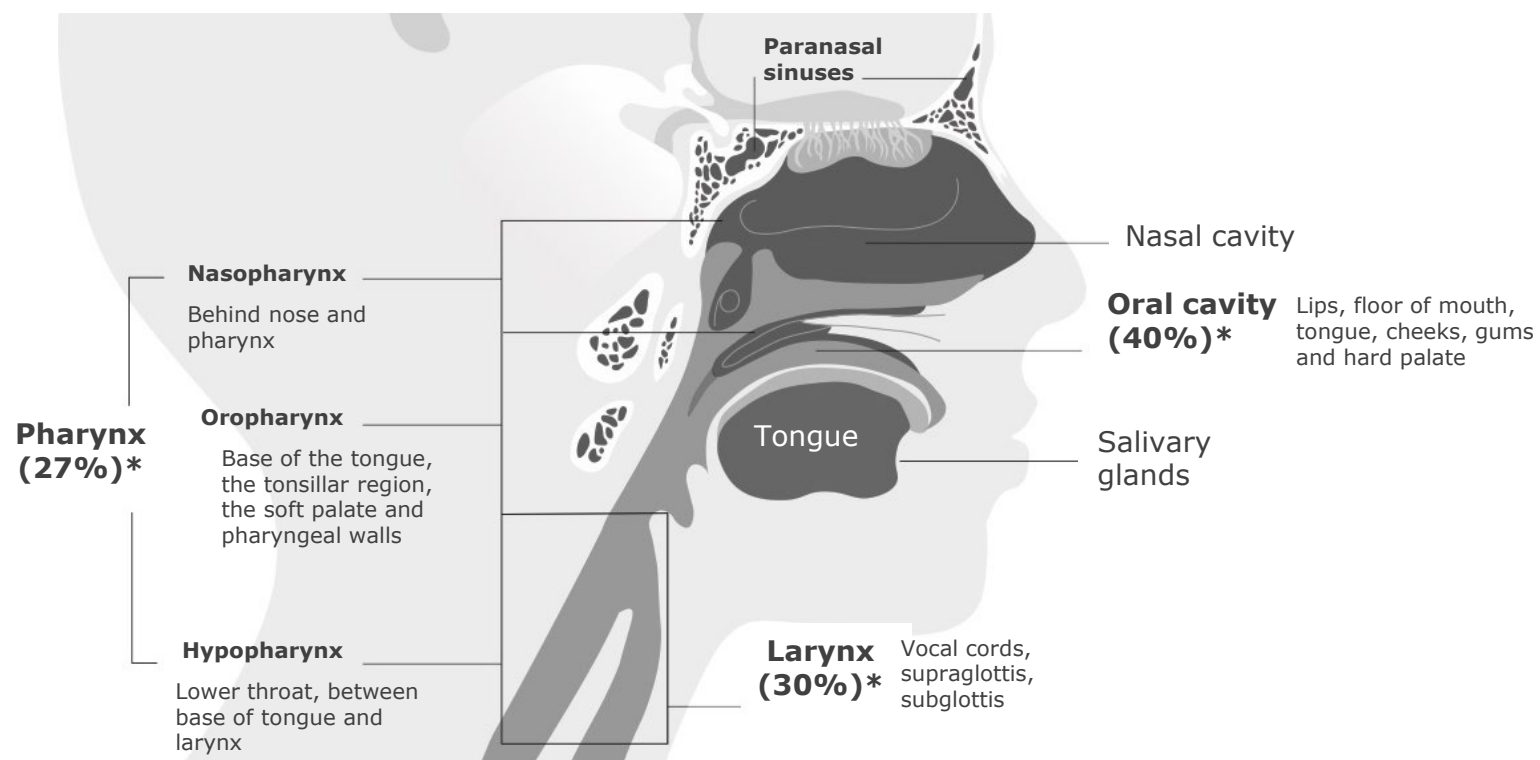
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Squamous Cell Carcinoma of the Head and Neck (SCCHN) Refers to a Group of Cancers Derived from Several Sites in the Head and Neck^{1,2}

- 90% of head and neck cancers are squamous cell carcinomas (SCCs)

Anatomical distribution of head and neck cancers^{1,2}



SCC: ~90%

- Oral cavity
- Larynx
- Pharynx
- Nasal cavity

Other types of head and neck cancer: ~10%

- Adenocarcinomas
- Lymphomas
- Sarcomas
- Melanomas

Typical localizations:

- Nasopharynx (NPC)[†]
- Salivary glands

There Are a Number of Environmental and Genetic Risk Factors for SCCHN

SCCHN develops in **the squamous cell epithelium** following exposure to **environmental factors** combined with **genetic changes**^{1,2}

- Patients with **high levels of EGFR** expression have a **worse prognosis** than those with low levels of expression³

Environmental factors^{1,4}



Tobacco

Correlated with the duration and intensity of smoking¹



Alcohol

Synergizes with the effect of tobacco¹



HPV infection

Particularly associated with OPC⁴

Genetic changes^{2,4,5}



EGFR overexpression
(80–90% of patients)⁵



STAT activation⁵



Cyclin D1 overexpression⁵

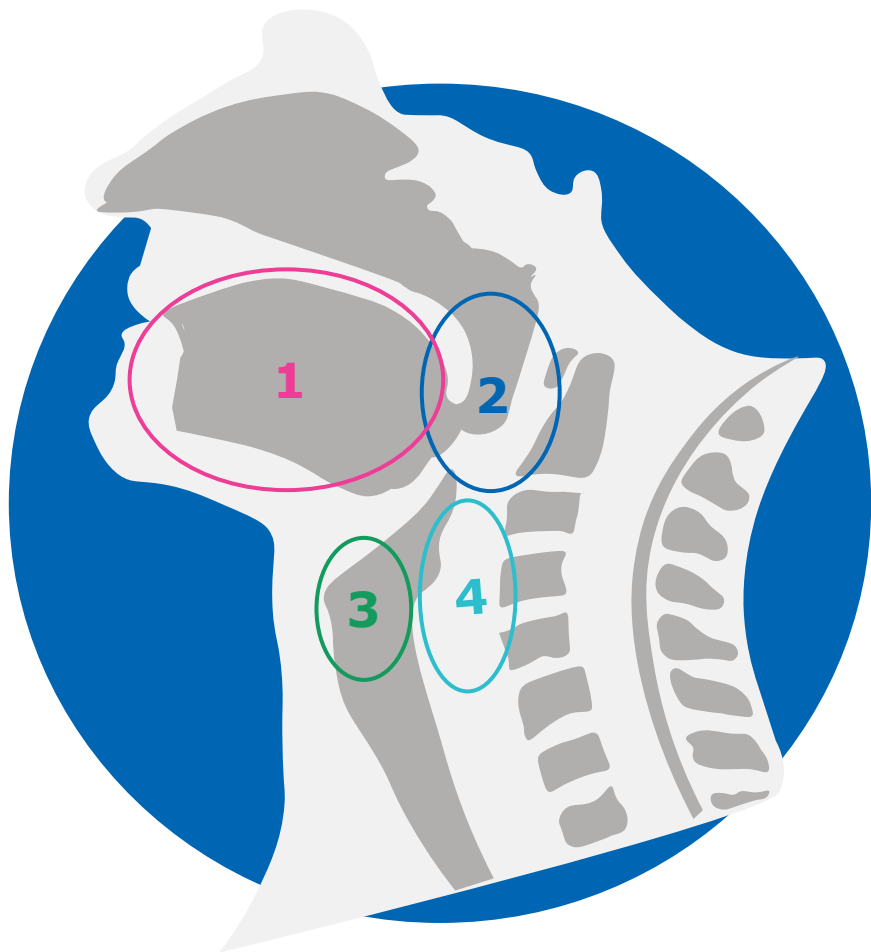


p16 expression alteration²



p53 mutation⁴

Typical Signs and Symptoms Differ Depending on the SCCHN Site¹



1 Oral cavity¹

- Patches on gums, tongue and lining of the mouth
- Bleeding
- Pain
- Ulcers

2 Oropharynx²

- Sore throat
- Chronic dysphagia
- Pain on swallowing
- Earache

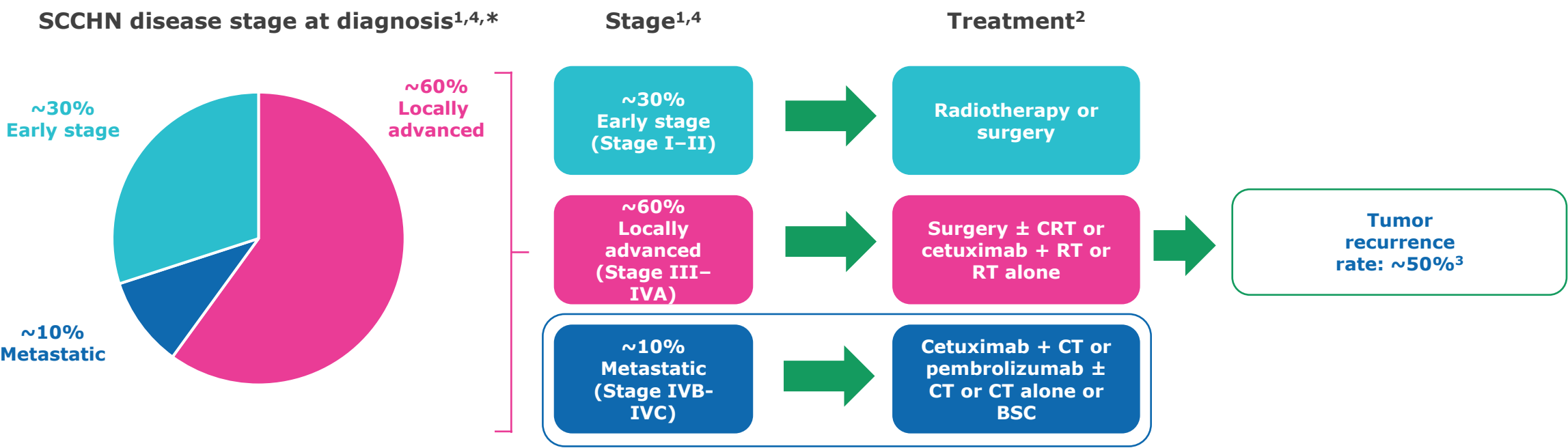
3 Larynx³

- Persistent hoarseness
- Neck mass (supraglottis)
- Earache

4 Hypopharynx⁴

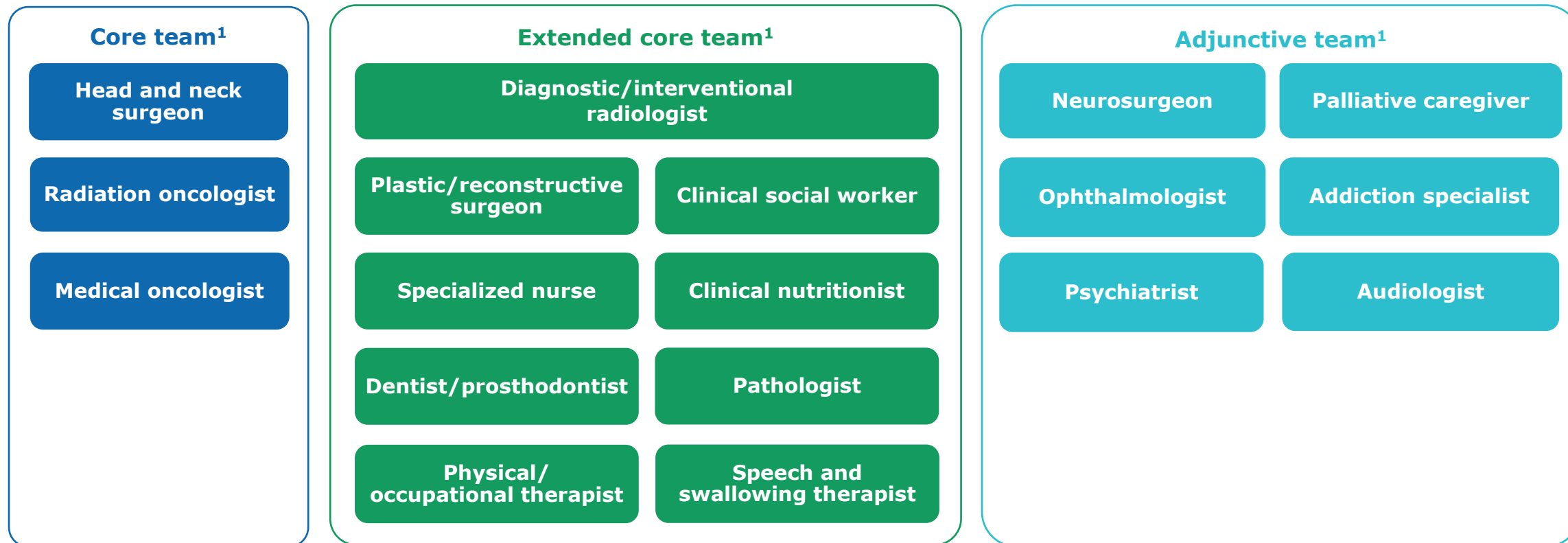
- Soreness
- Earache
- Dysphagia
- Change in voice

Most Patients Are Diagnosed With Locally Advanced SCCHN, but Nearly Half Will Experience Recurrence



*These data do not include the approximately 19% of patients with an unknown stage at diagnosis.
BSC, best supportive care; CRT, chemoradiotherapy; CT, chemotherapy; NCCN, National Comprehensive Cancer Network® (NCCN®); RT, radiotherapy; SCCHN, squamous cell carcinoma of the head and neck.
1. Corvò R. Radiother Oncol. 2007;85(1):156–170; 2. Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Head and Neck Cancers V.2.2022. © 2022 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way; 3. Machiels JP, et al. Ann Oncol. 2020;31:1462–1475; 4. Bean MB, et al. Oncologist 2019;24(12):1562–1569.

A Multidisciplinary Team Is Required for Optimal Care of Patients With Locally Advanced SCCHN¹



A significant increase in survival has been observed in patients seen by a multidisciplinary team vs patients who are not seen by one^{2,*}:

- **Stages 0–IV, HR=0.79, p=0.024**
- **Stage IV, HR=0.69, p=0.004**

*After controlling for stage, age at diagnosis and year of diagnosis. HR reported are from data collected over the 12-year study duration.

NCCN, National Comprehensive Cancer Network® (NCCN®).

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Incidence of SCCHN Globally

- Head and neck cancers are the **8th most common cancer** globally, and their incidence is predicted to rise^{1,2,*}



878,348

Estimated new cases
in 2020¹



444,347

Estimated deaths in
2020¹

Incidence and Risk Factors for SCCHN Vary by Geographical Region

Estimated no. new cases in the US (2022):

- 54,000 oral cavity and pharyngeal cancer¹
- 12,470 laryngeal cancer²

Stage at diagnosis in the US (2012–2018):

- 28% oral cavity and pharyngeal cancer at locally advanced stage¹
- 52% laryngeal cancer at locally advanced stage²



SCCHN is 2–5 times more common in men than in women^{1,2}



The risk of developing SCCHN increases with age; the majority of SCCHN cases occur in patients aged ≥50 years^{1,2,4}

Asia-Pacific: The risk of developing SCCHN is associated with **tobacco, alcohol and areca nut use**⁴

Western countries: Increasing rates of **SCCHN** in Canada, the US, the UK and parts of Europe, **despite a decline in smoking, likely due to increased HPV infection rates**³

Europe: Highest incidence of oral SCC in **France** (high rates also in Hungary, Slovakia and Slovenia)⁴

Disparities in Cancer Care



Lack of transportation¹



Hesitation to enroll in clinical trials¹



Financial burden of cancer care^{1,2}



Lack of access to coverage and quality care^{1,2}



Need for housing near cancer center¹



Gaps in health and digital literacy¹



Unconscious biases in health care system¹

Disparities in SCCHN Outcomes



HPV infections¹



Radiotherapy interruptions⁴



Insurance²



Geographical location²



Race^{2,3}



Patient and hospital characteristics⁵

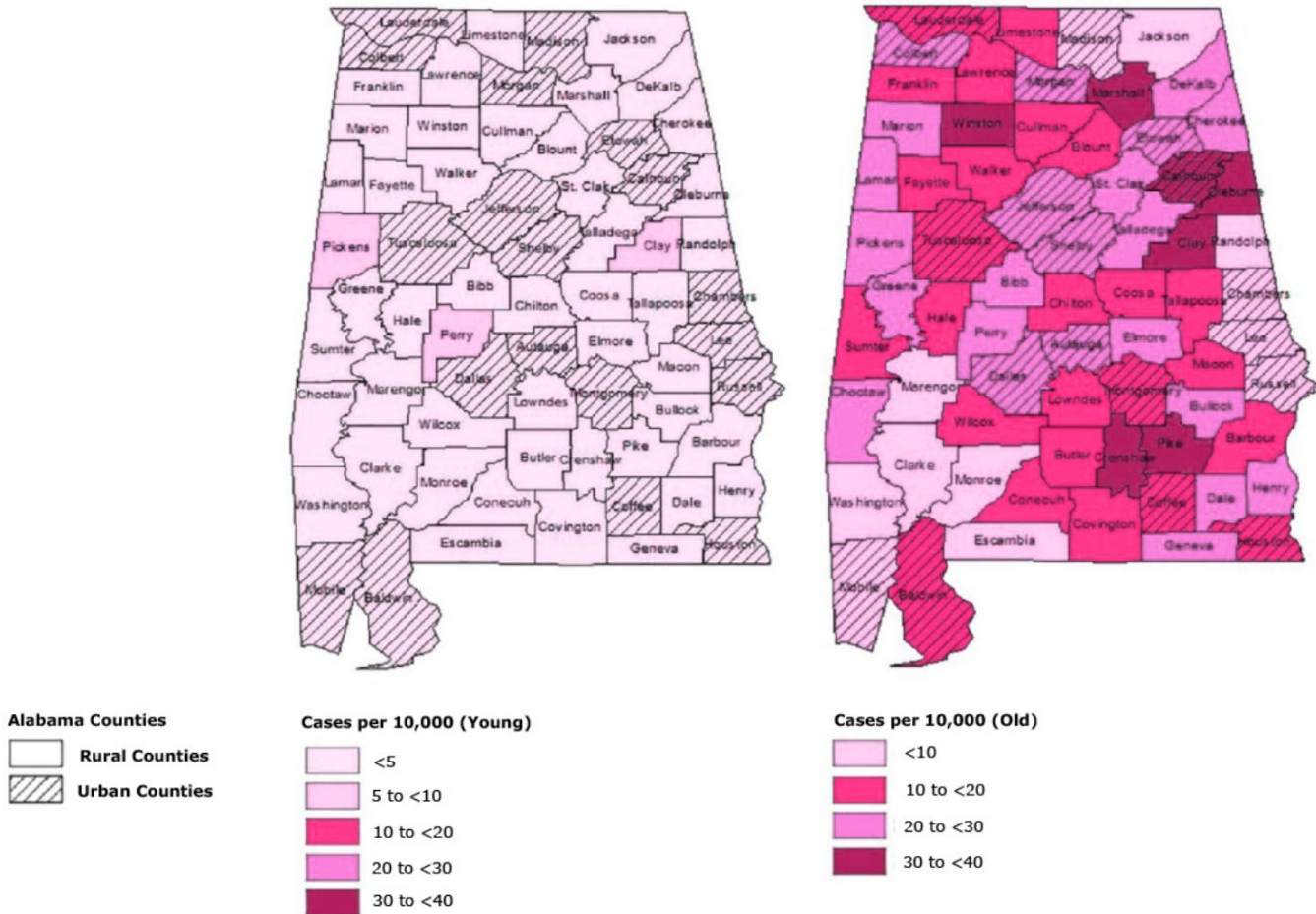


Ethnicity³



Marital status^{2,3}

Geographical and Racial Disparities in SCCHN^{1,2,*}



Race, smoking, alcohol consumption and insurance status were determinants of rural-urban differences observed in head and neck cancer cases¹



Patients from **rural counties** had **31% reduced odds** of getting diagnosed at a **young age**, compared with patients from urban counties¹



Most patients were diagnosed at **stage III/IV** (64.9% in rural and 60.2% in urban)¹



Black patients and **females** were more likely to get diagnosed at a **young age** compared with **White patients**¹

Hematologists and medical oncologists per 10,000 residents **aged 55 and older are limited** in certain states despite **higher** cancer incidence²

*Per a retrospective study using electronic medical records (Cerner) data of 4258 head and neck cancer patients from an NCI-designated cancer center in Alabama between January 2013 and March 2018. NCI, National Cancer Institute; SCCHN, squamous cell carcinoma of the head and neck.
1. Mukherjee A, et al. Health Equity. 2020;4(1):43–51; 2. ASCO interactive map. <https://asco-interactive-map-of-oncology-covid-19-asco1.hub.arcgis.com/> (accessed November 2022).



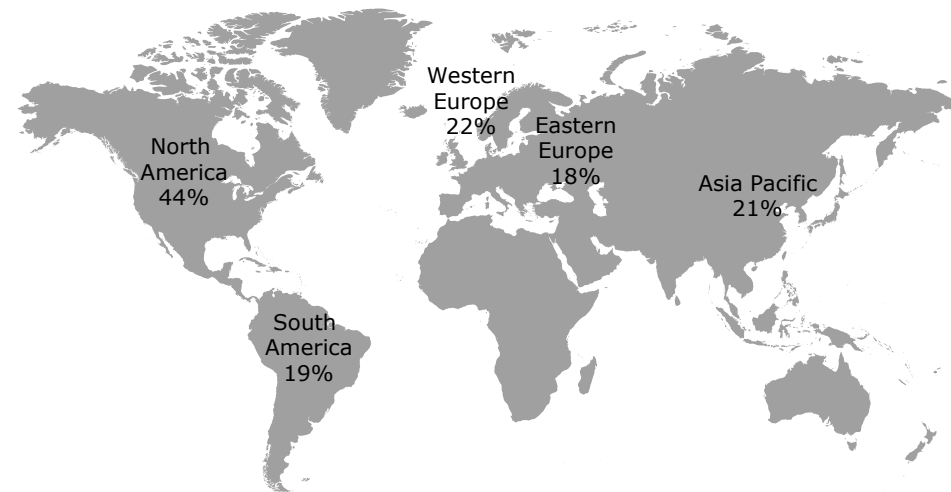
Disparities in HPV-positive SCCHN Rates Based on Geographical Region

- HPV-positive OPC incidence is increasing¹



Age-standardized incidence rates for HPV-positive cases is higher than that for HPV-negative cases^{1,†}

Rates of HPV-positive OPC by geographical region²

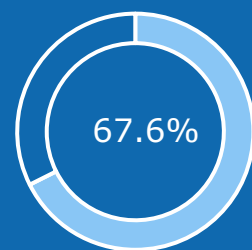


Prevalence of HPV-positive SCCHN



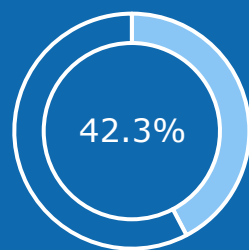
In a retrospective study, **34% of White** SCCHN patients tested positive for HPV vs **4% of Black** patients^{1,*}

HPV-positive OPC patients in the US^{2,†}



White patients

$p < 0.001$



Black patients

- HPV-related and HPV-unrelated SCCHN are **biologically different diseases**, with differing risk factors, tumor sites and prognosis³
- **HPV-positive SCCHN** patients have **better outcomes** than **HPV-negative patients**³
- **Prevalence of somatic mutations** including *EGFR*, *KRAS*, *HRAS* and *TP53* mutations were **higher in African Americans and Hispanic Whites** than in **non-Hispanic Whites**³
- One of the primary reasons for **high mortality and low response to chemoradiation therapy** in African American patients is due to **low HPV infection rates** compared with Whites³
- African American patients are also **less susceptible to oral, pharynx, nasal, or larynx squamous cell carcinoma**, the primary areas of HPV infection³

*Retrospective study conducted in roughly 2,000 patients with SCCHN treated at University of Maryland Marlene and Stewart Greenebaum Cancer Center between November 1995 and July 2006.

†Per a retrospective study in 22,693 patients with HPV-OPC and known HPV-status using the National Cancer Database and diagnosed between 2010 and 2013.

EGFR, epidermal growth factor receptor; HPV, human papillomavirus; *HRAS*, Harvey Rat sarcoma virus; *KRAS*, Kirsten rat sarcoma virus; OPC, oropharyngeal cancer; SCCHN, squamous cell carcinoma of the head and neck.

1. Settle K, et al. Cancer Prev Res (Phila). 2009;2(9):776–781; 2. Liederbach E, et al. Int. J. Cancer. 2017;140:504–512; 3. Chaudhary S, et al. JNCI J Natl Cancer Inst. 2019;111(3):djj207.

Survival in Black Patients With HPV-associated OPSCC*

- Black HPV-positive OPSCC patients had **worse OS** compared to White patients (HR 4.9, 95% CI 2.2–11.1, $p < 0.0001$) in the unadjusted survival analysis
- Racial disparity in 5-year OS remained **statistically significant** (HR 4.6, 95% CI 1.8–12.0, $p = 0.002$) even when adjusted for age, sex, T stage, N disease and distant metastases

5-year OS in HPV-associated OPSCC adjusted for demographics and stage

	Adjustment with demographics and stage [†]		
	HR	95% CI	P-value
Black (vs White)	4.6	1.8–12.0	0.002
Age (relative to <50)			
50–65	0.8	0.4–1.7	0.607
≥65	1.3	0.5–3.5	0.577
Female (relative to male)	0.8	0.3–2.0	0.653
T stage (relative to T1)			
T2	0.7	0.3–1.8	0.464
T3	1.6	0.6–4.2	0.321
T4	2.5	1.0–6.3	0.047
Nodal disease (relative to N0)	1.7	0.7–4.2	0.253
Distant metastases (relative to M0)	5.2	0.7–41.7	0.117

Factors Contributing to Radiotherapy Interruptions

- Early radiotherapy discontinuation increases the risk of **disease relapse** and **adversely influences survival** in SCCHN patients¹
- Black patients were **1.82 times more likely** than White patients (12.0% vs 6.6%; $p < 0.0001$) to face radiotherapy interruptions^{2,*}

Radiotherapy interruption was significantly higher in the following patients^{2,*}:

- | | | | |
|---|---------------------------------------|---|---|
| 1 | Uninsured patients (18.6%) | 4 | Patients with >25 prescribed radiotherapy fractions (14.3%) |
| 2 | Head and neck cancer patients (20.7%) | 5 | Patients treated in winter months (11.9%) |
| 3 | Gynecologic cancer patients (18.1%) | 6 | Aged >65 years (10.8%) |

Factors Contributing to Radiotherapy Interruptions* (continued)

Radiotherapy interruption was closely associated with:

- Patient insurance status: 3 times more likely in Medicaid patients relative to commercially insured patients
- Income: >2 times higher for patients with low predicted income
- Location of practice:
2 times higher at inner-urban facility than at suburban facility (12.0% vs 6.3%, respectively)

Vulnerable regions with >15% increased chances of radiotherapy interruptions were localized to:

- Inner-urban, majority Black, low-income regions
- Outer-rural, majority White, low-income regions

Contribution of the COVID-19 Pandemic to Disparities in SCCHN Outcomes

Potential drivers of disparate HNC survival resulting from the pandemic include:

- **Differential access to telemedicine, timely diagnosis, and treatment:** low uptake in African American and Hispanic Latino communities, hospitals of choice have less resources and capacity for a comprehensive telehealth program, limited access to software programs, inadequate English literacy
- **Implicit bias in initiatives to triage, prioritize, and schedule HNC-directed therapy:** latent threat to minorities in crisis standards of care (CSC) is that when comorbidities are used in prioritization schemes a proxy for health, minority patients who, in general, have higher base rates of comorbidities (and increased risk of mortality), may be deprioritized for access
- **The marked changes in employment, health insurance, and dependent care:** loss of employment, abrupt loss of insurance compounded by the financial need to absorb out-of-pocket costs, increased need for childcare due to school closings

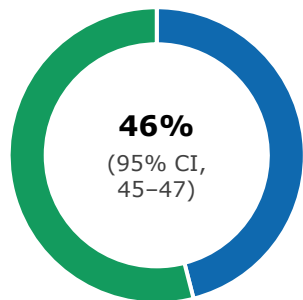
Patient and Hospital Characteristics Contributing to Disparities in SCCHN Outcomes*

Influence of patient and hospital characteristics on hazard of mortality excluding OPC cases

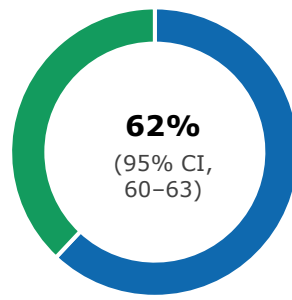
Factor	Overall survival (Black vs White)	
	HR	95% CI
Unadjusted	1.30	1.24–1.36
Adjusted individually for		
Nononcologic patient factors [†]	1.36	1.30–1.43
Oncologic factors [‡]	1.02	0.97–1.07
Hospital factors [§]	1.25	1.19–1.31
Adjusted sequentially for		
Unadjusted	1.30	1.41–1.54
Nononcologic patient factors	1.36	1.30–1.43
Oncologic factors	1.11	1.05–1.16
Hospital factors	1.09	1.04–1.14

- Black patients had a 48% **higher mortality** than White patients (HR 1.48; 95% CI, 1.41–1.54)

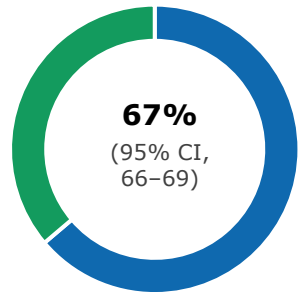
Racial and Ethnic Disparities in SCCHN Outcomes*



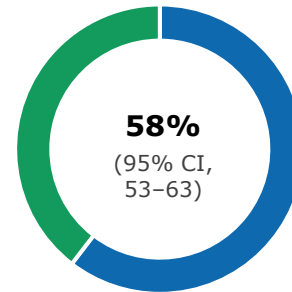
Non-Hispanic Black



Hispanic



Asian/Pacific Islander



American
Indian/Alaska Native
individual

- Five-year OS rate was **significantly lower** among non-Hispanic Black individuals with head and neck cancer as compared to Hispanic, Asian/Pacific Islander and American Indian

OPC Outcomes in Non-Hispanic Black and Hispanic Males

Mean survival of males with HPV-related OPC by race/ethnicity, US, 2005–2011 (N=60,886)*

Change to race/ethnicity	Mean (95% CI), months
Overall	96.58 (96.16–97.00)
Hispanic	91.89 (89.87–93.91)
Non-Hispanic White	99.63 (99.18–100.07)
Non-Hispanic Black	69.72 (68.14–71.31)
Non-Hispanic other [†]	96.55 (93.25–99.84)

Non-Hispanic Black males had the **lowest cumulative survival** relative to other racial/ethnic groups[‡]

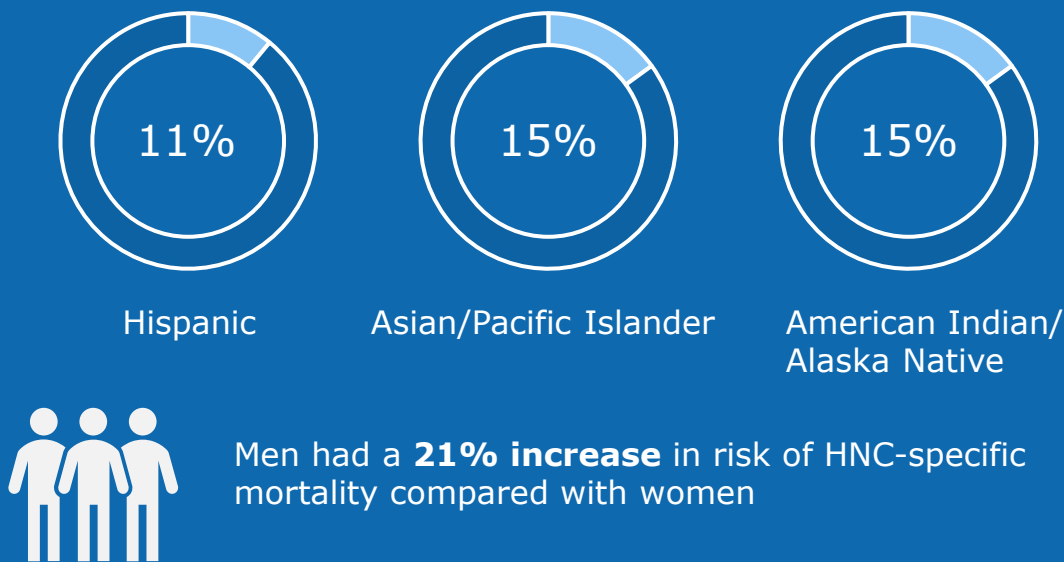
Non-Hispanic Black and Hispanic males had **lower unadjusted mean survival times** compared to non-Hispanic White males, with non-Hispanic Black males having **30 months shorter survival** (p<0.01)

*Unadjusted; all log rank Mantel-Cox tests were statistically significant at p<0.01. [†]Includes Asian, American Indian, Alaska Native and Pacific Islander. [‡]Adjusted for age, insurance, stage at diagnosis, country of residence, percent persons below poverty at country of residence, geographic region and treatment modality. CI, confidence interval; HPV, human papillomavirus; OPC, oropharyngeal cancer. Villalona S, et al. Ann Cancer Epidemiol 2022;6:4.

Factors Associated with Racial and Ethnic Disparities in SCCHN Outcomes*

Non-Hispanic Black patients have **poorer survival outcomes** than Asian/Pacific Islander, American Indian/Alaska Native and Hispanic patients

Lower sdHR of HNC-specific mortality



Factors associated with HNC-specific survival[†]

Factor	sdHR (95% CI)
Age, years	1.02 (1.01–1.02)
Race and ethnicity: vs non-Hispanic Black	
Hispanic	0.89 (0.83–0.95)
Asian/Pacific Islander	0.85 (0.78–0.93)
American Indian/Alaska Native	0.85 (0.71–1.01)
Sex: male vs female	1.23 (1.16–1.31)
Marital status: unmarried vs married	1.30 (1.23–1.37)
Insurance: vs private insurance	
Medicaid	1.43 (1.35–1.51)
Uninsured	1.41 (1.28–1.54)
Geographical region: vs South	
West	0.91 (0.84–0.98)
Northwest	0.97 (0.88–1.06)
Midwest	0.96 (0.86–1.06)
SES: vs high	
Medium	1.13 (1.05–1.23)
Low	1.22 (1.12–1.32)
Very low	1.22 (1.13–1.33)

*Per a population-based retrospective cohort study in 21,966 patients using SEER data from 2007 to 2016 that included non-Hispanic Black, Asian Pacific Islander, American Indian/Alaska Native and Hispanic patients with head and neck cancer. [†]Fine and Gray Cox regression model was adjusted for cancer site and treatment regimen, including chemotherapy, radiation and surgery (not shown). CI, confidence interval; HNC, head and neck cancer; SCCHN, squamous cell carcinoma of the head and neck; sdHR, subdistribution hazard ratio; SEER, Surveillance, Epidemiology, and End Results; SES, socioeconomic status
Taylor DB, et al. JAMA Otolaryngol Head Neck Surg. 2022;148(2):119–127.

Efforts to Address Disparities in Cancer Care



Address provider-level barriers¹



Access to tobacco cessation programs¹



Grow patient navigator program¹



Engage in advocacy groups¹



Reduce geographic barriers¹



Implementation of system changes that promote health equities²



Provide culturally and linguistically tailored programs focused on cancer awareness to address patient-level barriers^{1,2}

Addressing Disparities in Cancer Clinical Trials

Analyses of cancer therapeutic trials found that only 4–6% of trial participants are Black and 3–6% are Hispanic, despite representing 15% and 13% of people with cancer, respectively¹



- Efforts to address these disparities have come across various stakeholders

FDA^{2,3}

- Project Equity assures medicinal products work for **all demographics** by recruiting patients into trials for data and provide access to potentially promising drugs in clinical trials
- FDA Draft Guidance recommends that sponsors of medical products develop and submit a **Race and Ethnicity Diversity Plan** to the agency early in clinical development and support Clinical Trial Diversity
- Provide ongoing **public education and outreach campaign** to help address some of the barriers preventing diverse groups from participating in clinical trials

ASCO and ACCC jointly released resources⁴

- ASCO-ACCC Equity, Diversity and Inclusion Research Site Self-Assessment
- Just ASK™ Training Program

Diversity, Equity and Inclusion in Clinical Trials at EMD Serono

Our objective

To better reflect in our clinical trials and provide benefit to the diverse patient populations that are in need and would most likely use our drug(s) for treating their disease

An inclusive approach

Our focus includes, but is not limited to, age, sex, gender, gender identity, race, ethnicity, religion and their intersections

Our commitment

To address key barriers and limitations negatively impacting the diversity, equity and inclusion of minority populations in clinical trials with an end-to-end strategic mindset

Our 4 key pillars



Partner with health care providers who are diverse or provide care to diverse communities



Awareness and community outreach



Facilitate patient participation in clinical research



Protocol design and the use of real-world data