

Head and neck cancers: Evolving epidemiology, multidisciplinary care, and the road toward precision and prevention

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Head and neck cancers (HNCs) are undergoing a major transition, driven by the changing epidemiology and advances in multidisciplinary, precision-based care aimed at improving survival, function and prevention.

Head and neck cancers (HNCs), predominantly head and neck squamous cell carcinoma (HNSCC), remain a major global health challenge, accounting for nearly 890,000 new cases and more than 450,000 deaths annually worldwide.¹ In recent decades, cancer has emerged as one of the foremost public health challenges worldwide, imposing an escalating clinical, societal and economic burden. Despite advances in diagnosis and therapy, cancer mortality continues to rise, accounting for millions of deaths annually, with only modest gains achieved in overall survival. This limited progress reflects the complex, multifactorial nature of carcinogenesis, driven by interactions between genetic susceptibility, environmental exposures, lifestyle factors, infectious agents, and social determinants of health. A comprehensive understanding of modifiable risk factors, biological mechanisms and population-level determinants is therefore essential to inform effective prevention strategies, promote early detection, and guide the equitable implementation of the emerging therapeutic innovations.²

Despite advances in therapy, survival gains remain modest, reflecting late-stage presentation, biological heterogeneity and persistent exposure to modifiable risk factors. The contemporary landscape of HNC is defined by shifting epidemiology, evolving etiological profiles, expanding multidisciplinary care, and the promise and limitations of precision oncology and prevention.

Epidemiological shifts in a global context

The Global Burden of Disease (GBD) framework has become the principal reference for comparative cancer epidemiology, providing standardized estimates across 204 countries. Recent GBD 2023–2025 analyses confirm a sustained global transition toward non-communicable diseases, with the cancer burden rising in absolute terms due to population growth and aging.^{3,4} Although age-standardized mortality rates for many conditions have declined, disparities

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persist between high-income countries (HICs) and low- and middle-income countries (LMICs), where cancer mortality remains disproportionately high.⁵

Disability-adjusted life years (DALYs) estimates demonstrate a sustained shift from communicable to non-communicable diseases, with declining burdens from maternal, neonatal and infectious conditions, and a growing contribution from modifiable risk factors, such as hypertension, obesity, hyperglycemia, and pollution. Although total DALYs continue to rise globally due to population growth and aging, age-standardized rates have declined in high-socio-demographic index (SDI) regions while plateauing or increasing in low- and middle-SDI settings, reflecting persistent and widening health disparities.^{4,5}

Within HNC, contrasting trends are evident. In HICs, the incidence of human papillomavirus (HPV)-associated oropharyngeal cancer continues to rise, particularly among younger men, while tobacco-related tumors decline.⁶ Conversely, in LMICs, traditional exposures, such as tobacco, smokeless tobacco, betel quid, and alcohol, together remain as dominant drivers, sustaining high incidence and mortality.³ These regional contrasts underscore the dual burden of infection-related and lifestyle-related carcinogenesis, and highlight the central role of socioeconomic determinants in shaping outcomes.⁵

Etiology: From classical exposures to multifactorial risk

Tobacco and alcohol remain the most powerful and preventable risk factors for HNC, acting synergistically to amplify the carcinogenic risk by up to 30-fold.⁷ Human papillomavirus, associated with oropharyngeal cancer, represents one of the most significant paradigm shifts in head and neck oncology in recent history. Particularly, HPV-16 now accounts for approx. 60–70% of oropharyngeal squamous cell carcinomas (OPSCCs) globally, with HPV-positive tumors exhibiting distinct molecular profiles and superior treatment responsiveness.^{6,8} Importantly, HPV-attributable disease is no longer confined to the oropharynx, with the emerging evidence implicating subsets of oral cavity and laryngeal cancers.⁹ A systematic review and meta-analysis by Ndiaye et al. analyzed 148 studies involving 12,163 patients from 44 countries and found that HPV prevalence was the highest in OPSCC (45.8%), followed by oral cavity (24.2%) and laryngeal cancers (22.1%).¹⁰ HPV-16 accounted for 82.2% of all HPV-positive head and neck cancers, with approx. 40% of oropharyngeal cancers attributable to HPV when viral oncogenic biomarkers were considered, underscoring the central role of HPV-16 in oropharyngeal carcinogenesis.¹⁰

Additional risk factors, including betel quid and areca nut chewing, poor oral hygiene, nutritional deficiencies, occupational exposures (like wood dust and certain chemicals), oral microbiome dysbiosis, chronic metabolic and

inflammatory states, and genetic and epigenetic susceptibility markers, increasingly appear to modify the risk, tumor behavior and treatment response.^{10,11} These insights expand the conceptual framework of HNC beyond environmental carcinogenesis toward a complex interplay of host, microbial and metabolic determinants.

Clinical presentation and diagnostic challenges

Head and neck cancers often present with non-specific symptoms like non-healing ulcers, dysphagia, hoarseness, or neck masses, leading to frequent diagnostic delays and advanced-stage disease at presentation.¹² While technological machine learning diagnostic models for thyroid cancer detection,¹³ the use of artificial intelligence (AI) in HNC diagnosis,¹⁴ advances in imaging, digital pathology, and liquid biopsies offer promise, their integration into routine practice remains uneven. Population-wide screening is not recommended; instead, contemporary consensus favors risk-based and opportunistic screening by dental and primary care professionals, particularly in high-risk populations. Volatile sulfur compounds (VSCs),¹⁵ as well as 5 key interactome hub genes (*RSPO4*, *CDHR2*, *DDAH2*, *HLA-J*, and *IRF3*)¹⁶ were identified as molecular links between chronic periodontitis and oral cancer. In a study by Banthia et al., a causal relationship could not be established due to the cross-sectional design employed; yet, the findings demonstrate a significant association between periodontal disease and the overall cancer risk, while no clear link with metastasis was observed.¹⁷

Treatment modalities and evolving therapeutic paradigms

Modern HNC management is inherently multidisciplinary, integrating surgery, radiotherapy, systemic therapy, and rehabilitation to optimize oncologic and functional outcomes. Transoral robotic surgery (TORS) has refined surgical precision and improved quality of life (QoL) in selected patients.¹⁴ Radiotherapy remains central for locally advanced disease, while immune checkpoint inhibitors (ICIs) targeting the PD-1/PD-L1 axis have transformed the management of recurrent and metastatic HNC.¹⁵

The expansion of immunotherapy into neoadjuvant and definitive settings marks a pivotal shift, yet outcomes remain heterogeneous, and access remains uneven across regions.^{15,16} A central controversy persists in treatment de-escalation for HPV-positive disease. While reduced-intensity strategies aim to limit long-term toxicity, recent trials caution against indiscriminate de-intensification without robust biomarker-based selection.¹⁷ This tension exemplifies the broader challenge of balancing therapeutic innovation with oncologic safety.

Head and neck squamous cell carcinoma requires multidisciplinary management, with surgery and radiotherapy as the mainstays of treatment for locally and regionally advanced disease and platinum-based chemotherapy serving as an important adjunct. Therapeutic options for relapsed or metastatic disease have expanded substantially with the introduction of biologics and ICIs, while ongoing trials are evaluating novel immunotherapies, targeted agents, vaccines, antibody–drug conjugates, and cellular therapies. Despite these advances, outcomes remain heterogeneous, underscoring persistent knowledge gaps and the need for continued innovation in systemic therapy for HNSCC.¹⁸

Current evidence for HPV treatment suggests limited benefit from chemotherapy reduction, uncertain toxicity and outcomes with TORS as compared to radiation, and the greatest promise in carefully selected adjuvant and radiation de-escalation strategies, although definitive level I evidence is still lacking. Data supports the de-escalated adjuvant therapy after TORS, but consensus on treatment indications is still needed.¹⁹

Precision oncology: Promise constrained by reality

Molecular profiling has illuminated profound distinctions between HPV-positive and HPV-negative tumors, enabling biomarker-driven strategies and targeted therapeutics. Yet, despite scientific progress, precision oncology has achieved limited penetration into routine care. The reproducibility of biomarkers, uncertain cost-effectiveness and infrastructural inequities restrict implementation,

particularly in LMICs.¹⁸ The gap between molecular discovery and population-level impact remains substantial, reinforcing the need for translational frameworks that integrate precision with pragmatism. Table 1 depicts the key insights of the editorial. It summarizes the global burden, the evolving epidemiology, major etiological factors, clinical presentation, treatment paradigms, and prevention strategies in HNCs, highlighting the dual impact of lifestyle-related and HPV-associated disease, persistent global disparities, and the central role of multidisciplinary care and prevention in reducing future disease burden.

Future directions for prevention and public health

Prevention remains the most effective strategy to reduce the HNC burden. The HPV vaccination has demonstrated population-level reductions in oral HPV prevalence, with the greatest benefit anticipated from gender-neutral programs.⁶ Tobacco control, alcohol reduction and harm-reduction strategies continue to offer the greatest opportunities for cancer prevention.^{7,20} GBD modelling suggests that a substantial proportion of future HNC cases could be averted through combined vaccination and risk-factor modification.^{3,4}

Equally important are the social determinants of health. Socioeconomic disadvantage, limited access to care and educational inequities drive late presentation and poor outcomes.⁵ Addressing these structural determinants is essential to translating scientific advances into equitable survival gains.

Table 1. Key contemporary insights in head and neck cancers (HNCs)

No.	Domain	Key findings	Significance
1.	Global burden	~890,000 new cases and >450,000 deaths annually worldwide	confirms that HNC is a major and growing global health challenge
2.	Epidemiological transition	the absolute burden rising due to population growth and aging; persistent disparities between HICs and LMICs	highlights inequities and the need for region-specific strategies
3.	Etiological shift	declining tobacco-related cancers in HICs; rising HPV-associated oropharyngeal cancer	demonstrates the dual burden of lifestyle- and infection-driven disease
4.	HPV-associated disease	HPV-16 causes ~60–70% of OPSCC; HPV-positive tumors show better treatment response and survival	alters prognosis, staging and therapeutic strategies
5.	Traditional risk factors	tobacco and alcohol act synergistically, increasing risk up to ~30-fold; betel quid and smokeless tobacco prominent in LMICs	identifies major targets for prevention
6.	Emerging risk modifiers	oral microbiome dysbiosis, periodontal disease, metabolic and inflammatory states, genetic/epigenetic susceptibility	expands disease model beyond classical carcinogens
7.	Clinical presentation	frequently diagnosed at advanced stages due to non-specific symptoms	explains limited survival gains despite treatment advances
8.	Treatment paradigm	multidisciplinary care with surgery, radiotherapy and chemotherapy; immunotherapy for recurrent/metastatic disease	reflects the complexity of modern HNC management
9.	Precision oncology	molecular profiling reveals biological heterogeneity, yet routine clinical implementation is limited	shows a gap between molecular discovery and population-level benefit
10.	Prevention potential	HPV vaccination, tobacco and alcohol control could prevent a substantial proportion of future cases	positions prevention as the most effective long-term strategy

HICs – high-income countries; LMICs – low- and middle-income countries; HPV – human papillomavirus; OPSCC – oropharyngeal squamous cell carcinoma.

Conclusion

Head and neck cancers exemplify the intersection of shifting epidemiology, complex etiology and the evolving therapeutic paradigms. The contemporary trajectory of HNC care is defined by integrated multidisciplinary management, expanding immunotherapy, emerging precision strategies, and renewed emphasis on prevention and equity. Yet, the greatest opportunity lies not solely in molecular innovation, but in implementing the proven public health interventions, strengthening early detection and closing global disparities.

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