EPIDEMIOLOGICAL ANALYSIS OF LARYNGEAL CANCER HOSPITALIZATIONS IN THE BRAZILIAN PUBLIC HEALTH SYSTEM BETWEEN 2013 AND 2023

Análise epidemiológica dos pacientes internados por neoplasia maligna de laringe no Sistema Único de Saúde entre 2013 e 2023

Luís Otávio da Silva[1] | Jordana Rabelo Bergonso[2]

[1] Medical Student at Fundação Educacional do Município de Assis

[2] Professor of Medicine at Fundação Educacional do Município de Assis

Submission date: 01/21/2024 | Approval date: 04/24/2024

ABSTRACT

Objectives: Laryngeal cancer represents a significant public health problem, with more than 180,000 cases and 100,000 deaths per year worldwide. In Brazil, approximately 8,000 cases are diagnosed every year, causing 5,300 deaths. Considering this impact on public health, this study aims to analyze the number of hospitalizations of patients with this disease in the Brazilian Public Health System (SUS), providing data to support programs aimed at improving care for these patients. In addition, these data could also shed light on the strain laryngeal cancer places on the hospital network, which often falls short of meeting the demand for beds within the SUS. **Methods:** Using an ecological, cross-sectional, quantitative, and descriptive approach, data were gathered from the hospital information system (SIH/SUS) from 2013 to 2023. The TABNET tool, developed by the Department of Information Technology of SUS (DATASUS), was used for the analysis. The variables analyzed included the total number of hospitalizations, age group, region of the country, and sex. **Results:** From January 2013 to October 2023, a total of 131,021 hospitalizations for laryngeal cancer were recorded in Brazil. The Southeast region accounted for the highest proportion of hospitalizations (48.1%), followed by the Northeast (23.3%), South (19.1%), Central-West (6.2%), and North (2.9%). Of these hospitalizations, 85.4% involved male patients, with the most affected age group being 60 to 69 years, totaling 46,698 cases. There was no significant increase in hospitalizations during the COVID-19 pandemic. **Discussion:** The analysis identified a predominant profile among patients with laryngeal cancer admitted to the SUS, characterized by a higher proportion of male patients, primarily in the 60-69 age group and concentrated mainly in the Southeast region. The high number of hospitalizations relative to the disease's incidence in Brazil underscores the need for initiatives promoting early diagnosis, along with the development of effective prevention and treatment strategies to enhance patient care for this condition.

Keywords: laryngeal cancer, epidemiology, hospitalizations, SUS

DOI: 10.5935/2763-602X.20230001-en

INTRODUCTION

Globally, more than 180,000 cases of laryngeal cancer are reported each year, resulting in approximately 100,000 deaths annually. In Brazil, around 8,000 cases and 5,300 deaths from laryngeal cancer occur each year. The country has the highest mortality rate for laryngeal cancer in Latin America and ranks fourth in incidence worldwide, following the United States, China, and India[1].

Laryngeal cancer predominantly affects men, most of them in their seventh decade of life. Ranked as the third most common head and neck cancer, excluding non-melanoma skin cancer, its incidence is intrinsically associated with smoking and excessive alcohol consumption. Moreover, laryngeal cancer stands out as the ninth leading cause of death in men and the 20th in women[2].

Anatomically and clinically, the larynx is divided into three regions: glottic, supraglottic, and subglottic. Each region has distinct lymphatic drainage patterns, differing both in quantity and drainage pathways, which can affect the progression of laryngeal cancer based on the tumor's location[3]. Approximately two-thirds of laryngeal cancer cases involve the glottic region, about one-third affect the supraglottic region, and only a small fraction occur in the subglottic region. Squamous cell carcinoma is the most common histological type of laryngeal cancer, accounting for over 85% of cases. Symptoms vary based on tumor location, with dysphonia being the most frequent, though dysphagia and odynophagia are also significant.

Several risk factors are associated with laryngeal cancer, including smoking, alcohol consumption, HPV infection, gastroesophageal reflux disease (GERD) with laryngopharyngeal manifestations, and a nutrient-poor diet[3].

The tumor, node, and metastasis (TNM) staging system, established by the American Joint Committee on Cancer and the Union for International Cancer Control, is the gold standard for staging laryngeal tumors[4].

Treatment choice is determined by factors such as the tumor's size, extent, location, and patient-specific characteristics like age, overall health, comorbidities, and psychosocial support. Additional considerations include laryngeal, pulmonary, and swallowing functions, the clinical expertise of the medical team, and access to rehabilitation services. Treatment-related toxicity and morbidity from chemoradiation or surgery must also be taken into account[5].

Given the public health challenges posed by the significant annual incidence of laryngeal cancer in Brazil, it is essential to monitor its epidemiological trends nationwide. The number of hospitalizations for laryngeal cancer within the Brazilian Public Health System (SUS) serves as a key indicator, potentially offering insights to inform targeted programs aimed at improving patient care. These hospitalization figures also shed light on the strain laryngeal cancer places on the hospital network, which often falls short of meeting the demand for beds within the SUS. Therefore, this study aims to conduct an epidemiological analysis of laryngeal cancer hospitalizations within the SUS over the past decade (2013-2023).

METHODS

This study is an ecological, cross-sectional, quantitative, and descriptive analysis. Data were obtained from the Hospital Information System (SIH/SUS) via the Department of Information Technology of SUS (DATASUS), utilizing the TABNET tool, covering the period from 2013 to 2023. The inclusion criteria consisted of patients hospitalized with malignant laryngeal neoplasms, classified under the code "C32" of the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). Variables analyzed included the number of hospitalizations, age group, country region, and sex. Ethical approval was not required for this research, as it relied solely on publicly available data.

RESULTS

Between January 2013 and October 2023, a total of 131,021 hospitalizations for laryngeal cancer were recorded in Brazil. The Southeast region had the highest number, with 63,129 hospitalizations (48.1%), followed by the Northeast with 30,589 (23.3%), the South with 25,139 (19.1%), the Central-West with 8,225 (6.2%), and the North with 3,889 (2.9%).

Men accounted for most cases, with 111,988 hospitalizations (85.4%), while women accounted for 19,033 (14.6%). In the Southeast, 54,886 (86.9%) of hospitalizations involved male patients, compared to 8,525 (13.1%) female patients.

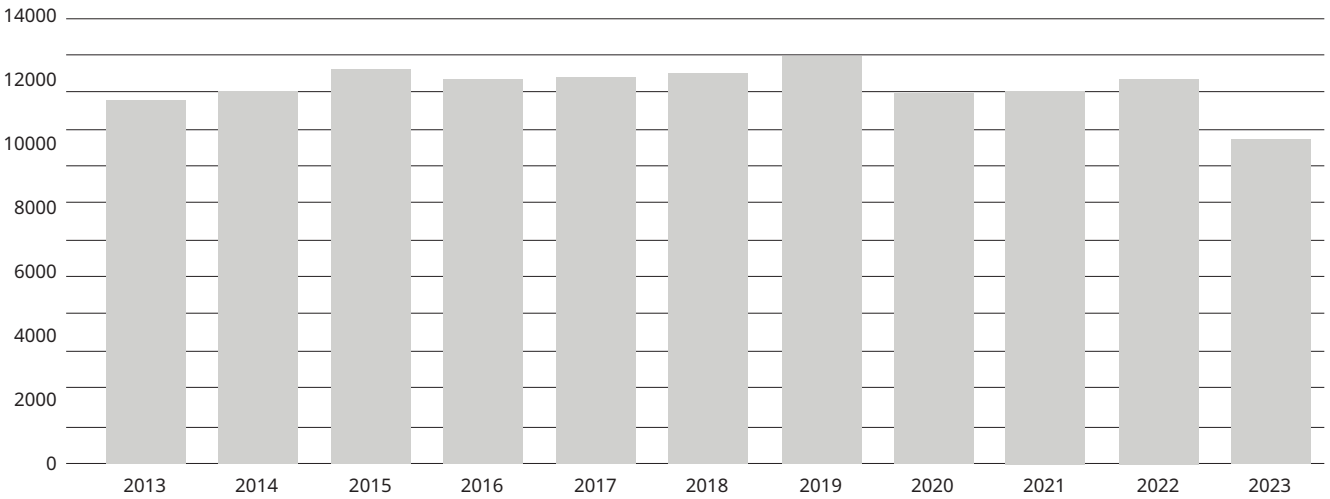
Hospitalizations spanned all age groups but were most prevalent among

TABLE 1 - Hospitalizations due to laryngeal cancer in Brazil between 2013 and 2023

AGE RANGE	MALE	FEMALE	TOTAL
TOTAL	**112,029**	**19,036**	**131,065**
Less than one year	46	20	66
1 - 4 years	75	61	136
5 - 9 years	56	77	133
10 - 14 years	28	52	80
15 - 19 years	92	75	167
20 - 29 years	309	195	504
30 - 39 years	1,507	569	2,076
40 - 49 years	10,684	1,930	12,614
50 - 59 years	34,224	5,303	39,527
60 - 69 years	40,418	6,299	46,717
70 - 79 years	19,558	3,356	22,914
80 years and more	5,032	1,099	6,131

Source: Brazilian Health Ministry - Public Health System Hospital Information System (SIH/SUS)

CHART 1 - Hospitalizations due to laryngeal cancer in Brazil between 2013 and 2023



Source: Brazilian Health Ministry - Public Health System Hospital Information System (SIH/SUS)

those aged 60 to 69, with 46,698 cases. A notable increase in cases was observed across all regions of the country from this age onward.

During the COVID-19 pandemic, hospitalizations due to laryngeal cancer declined, with the lowest numbers recorded in 2020 (11,693) and 2021 (11,737). However, in the last five years (2019-2023), there were 59,603 hospitalizations (53.22%), with the highest annual figures in 2019 (12,852) and 2022 (12,139).

DISCUSSION

The larynx, positioned anteriorly in the median plane, at the level of the third to sixth cervical vertebrae and situated between the carotid sheaths[6], serves as the continuation of the airway that links the pharynx to the trachea. Besides facilitating airflow during breathing, its several functions include preventing food and liquids from entering the trachea and lungs during swallowing and producing vocal sounds.

Approximately two-thirds of laryngeal cancers originate in the true vocal folds, with some arising in the anterior commissure of the glottis. These tumors are typically associated with persistent dysphonia, which often emerges early in the disease course. Advanced tumors may present with symptoms such as dyspnea, dysphagia, referred otalgia, odynophagia, chronic cough, hemoptysis, and stridor[7]. In contrast, one-third of laryngeal tumors affect the supraglottic region. These are generally more aggressive and often diagnosed at later stages, as dysphonia is not an early symptom, making early detection more difficult. Furthermore, the supraglottic region, as opposed to the glottis, is rich in lymphatic vessels, which facilitates lymphatic spread of the cancer. In these cases, patients may present with signs of airway obstruction, such as stridor or dyspnea on exertion, along with dysphagia, pain, and metastatic lymphadenopathy[9]. Finally, subglottic tumors are rare, often asymptomatic initially, and usually detected only when locally advanced, frequently necessitating laryngectomy as a first-line treatment[10].

Squamous cell carcinoma is the predominant histological type in laryngeal tumors across all anatomic regions[11]. However, the larynx can also be affected by various other benign and malignant tumors, with truly benign tumors representing 5% or fewer of all cases. Indirect laryngoscopy is essential to evaluate suspected laryngeal cancer, followed by biopsy under direct laryngoscopy if a suspicious lesion is identified. Squamous cell carcinomas typically manifest as mucosal lesions, easily visualized during laryngoscopy, while non-squamous tumors are often submucosal, requiring further evaluation with imaging techniques such as computed tomography or magnetic resonance imaging[12].

Smoking is a major risk factor for head and neck cancer, increasing the risk by 5- to 25-fold compared to non-smokers[13]. A dose-response relationship has been observed, as demonstrated by a study that included 605 head and neck cancer cases and 756 controls, both drawn from the same population-based cohort. Among smokers, the relative risk for laryngeal cancer was 7.5, with risk increasing alongside greater smoking exposure. However, the risk decreased following smoking cessation and returned to baseline levels after 20 years of abstinence[14]. Similar studies also found that individuals who started smoking before age 18 and those with heavier smoking histories have a higher risk[15].

According to the 2013 Brazilian National Health Survey in Households, the Southern Region of Brazil had the highest smoking rate, with 16% of adults (over 18 years) smoking, while the Southeast, the most populous region of the country, had a rate of 15%. In the last survey, in 2019, the South continued to have the highest percentage, with 14.7%, compared to 13.5% in the Southeast[16]. This pattern may partly explain why the South Region recorded the highest number of hospitalizations, adjusted by population according to the 2022 census[17], with 0.84 hospitalizations per 1,000 inhabitants. In comparison, the Southeast recorded 0.74 hospitalizations per 1,000 inhabitants; the Northeast, 0.56; the Central-West, 0.5; and the North, 0.22.

It is also noteworthy that tobacco production is predominantly concentrated in Brazil's South Region, likely impacting the social, political, and economic landscape and contributing to greater acceptance and consumption of tobacco in this area. Additionally, the high presence of European immigrant descendants in southern Brazil and its sociocultural influences may be linked to smoking behaviors observed in this region[18]. Regarding gender distribution, smoking rates in 2013 were estimated at 18.9% for men and 11.0% for women[19], which may partly explain the higher rates of hospitalization among men in this study.

In terms of alcohol consumption, Brazil's annual per capita intake of pure alcohol among individuals over 15 years old surpasses the average observed in the Americas[20]. It is estimated that men consume two to ten times more alcohol than women[21]. Considering that alcohol consumption and smoking have an interactive and multiplicative effect on the risk of developing head and neck cancer, these figures may also account for the higher hospitalization rates for laryngeal cancer among men in this study.

Despite these conclusions, it is not possible to definitively establish an association between laryngeal cancer and smoking or alcoholism based solely on the data from this study, as it only accounts for hospitalizations related to the disease. Nevertheless, the findings align with existing literature, suggesting that men have higher exposure to these risk factors than women, as discussed earlier. Future research using longitudinal data and direct measures of exposure will be crucial to explore further the potential correlation between smoking, alcohol consumption, and the risk of hospitalization for laryngeal cancer.

Another important risk factor for laryngeal cancer is infection with human papillomavirus (HPV), a sexually transmitted disease that causes anogenital and oropharyngeal conditions in both men and women[22]. Epidemiological and molecular evidence has confirmed HPV's causal role, particularly type 16, in head and neck cancer. A comprehensive meta-analysis of 148 studies, covering 12,163 cases of head and neck squamous cell carcinoma, found HPV DNA in 22.1% of laryngeal tumors, compared to 45.8% in oropharyngeal cancers and 24.2% in oral cavity cancers[2]. An observational study using the National Cancer Database (NCDB), which included over 24,000 patients with head and neck squamous cell carcinoma, detected HPV DNA in 11% of laryngeal tumors[24]. In Brazil, the SUS offers the HPV vaccine to males and females aged 9 to 14 years, as well as to transplant recipients, patients undergoing chemotherapy or radiotherapy, people living with HIV/AIDS, and victims of sexual violence[25]. While HPV vaccination has been linked to a reduction in oral HPV infections, there is still no conclusive evidence of its impact on decreasing the risk of head and neck cancer. In this study, we observed a decline in hospitalizations among female patients with laryngeal cancer aged 10 to 30 years, with 47 cases in 2013 compared to ten in 2023. Despite the limitations mentioned earlier and the inability to make causal inferences, this trend could suggest a possible protective effect of vaccination in this subgroup, which was among the first to be vaccinated by the SUS. Additionally, the risk of HPV-related head and neck carcinoma outside the oropharynx, particularly laryngeal cancer, remains lower than that seen in oropharyngeal cancers[27].

GERD, a well-established risk factor for esophageal cancer, may also be linked to laryngopharyngeal tumors through laryngopharyngeal reflux, as indicated by studies using 24-hour pH monitoring[28]. GERD is one of the most common gastroenterological diagnoses, affecting around 12% of the Brazilian population, with similar prevalence in men and women[29]. Although findings in the literature are conflicting, the proposed pathophysiological mechanism suggests that gastric acid reaching the upper airways induces chronic inflammation by generating reactive oxygen and nitrogen species and intracellular acidification. This process may activate proliferative signaling pathways and cause cellular damage in the laryngeal epithelium, potentially leading to malignant transformation and the development of laryngopharyngeal squamous cell carcinoma[28]. Additionally, alcohol consumption can lower the tone of the lower esophageal sphincter, making it a dose-dependent risk factor for GERD30 and suggesting an interaction between risk factors for laryngeal cancer. Despite the potential role of GERD in the pathophysiology of laryngeal cancer, this study could not provide further conclusions on this association, given that the data were limited to hospitalizations and did not account for patients' comorbidities.

During the COVID-19 pandemic, delays in cancer screening and diagnosis became evident across several countries, leading to an increase in late-stage diagnoses, many of which were made in emergency settings. Additionally, significant delays were noted in initiating treatment for patients recently diagnosed with laryngeal cancer[31]. These trends align with the findings of this study, which showed a decline in hospital admissions for laryngeal cancer in 2020 and 2021.

Since Theodor Billroth's first total laryngectomy in 1879, treatment approaches have advanced considerably. Modern options include endoscopic laser laryngectomy for early-stage tumors and radiation therapy, which can be used alone in early cases or as adjuvant therapy in more advanced stages[3]. Currently, even for many patients with locally advanced laryngeal cancer (stages III or IV), organ-preserving strategies involving chemoradiotherapy are often preferred over total laryngectomy, as they offer better functional outcomes, although

they do not provide a survival advantage compared to total laryngectomy[32]. With proper treatment, five-year disease-specific survival rates are high, reaching 100% and 96% for stages I and II, respectively, in leading centers[33]. Furthermore, care by a multidisciplinary team specialized in head and neck cancer has been associated with better outcomes, especially concerning vocal and swallowing rehabilitation[34].

This study, however, did not include data on treatment modalities or their potential outcomes. Generally, non-surgical cancer treatments can be administered on an outpatient basis, which tends to result in lower hospitalization rates, except in cases of complications. Analyzing the therapeutic modalities used could help explain trends in hospitalization rates over time. Additionally, examining treatment-related complications, including the number of hospitalizations, could enable comparisons of the morbidity linked to each therapeutic strategy. Common complications include xerostomia, dental disease, hypothyroidism, and osteoradionecrosis. Other critical outcomes to monitor post-treatment are voice and swallowing rehabilitation, nutritional status, continued use of alcohol and tobacco, depression, and other comorbidities.

This study was also unable to obtain data on relapse and recurrence rates among hospitalized patients, which are key contributors to hospital admissions. Understanding these rates is essential for evaluating treatment effectiveness and informing clinical follow-up strategies. Most recurrences (around 90%) occur within the first three years after curative treatment, underscoring the need for more frequent follow-up during this period. However, maintaining long-term monitoring, even at reduced frequency, is beneficial due to the potential for late recurrence and the development of new primary head and neck cancers, which share common risk factors[35].

Despite the study's limitations, some preliminary conclusions can be drawn regarding the profile of laryngeal cancer patients hospitalized at the SUS over the past decade. The predominance of male patients (85.4%) and those aged 60-69 can be attributed to higher rates of tobacco use and alcohol consumption in this population. While the Southeast region recorded the highest absolute number of hospitalizations of patients with laryngeal cancer, the South had the highest rate of hospitalizations adjusted for population size.

This study was limited to data from public hospitals, a significant constraint since private hospitalizations were not accounted for. Additionally, the data do not allow for statistical correlations with risk factors, habits, or comorbidities. Nonetheless, the findings provide insights that can inform future research using other databases, such as those from the National Cancer Institute (INCA) and the Global Cancer Observatory (GCO), which offer more detailed information on risk factors.

Finally, it is also crucial to emphasize the importance of health promotion in preventing laryngeal cancer, particularly by reducing smoking and alcohol consumption. Educating the public about the symptoms of laryngeal cancer is equally important, as it encourages patients to seek medical care at early stages, which is critical for timely diagnosis and better treatment outcomes.

CONFLICT OF INTEREST

The authors attest they have no conflict of interest to declare.

FUNDING SOURCE

This research did not receive any type of funding.

INFORMATION ABOUT THE ARTICLE

Fundação Educacional do Município de Assis (FEMA)

Mailing address:
Rua Cardoso de Melo, 940, bloco 11, apto 23 – Assis, SP, CEP 19807-140

Corresponding author:
Luís Otávio da Silva
Otavio_uro@hotmail.com

REFERENCES

[1] International Agency for Research on Cancer. Global Cancer Observatory [Internet]. Geneve, Switzerland: World Health Organization; 2023. Available at: https://gco.iarc.fr/ (accessed on 12/18/2023).

[2] Instituto Nacional de Câncer. Tipos de câncer - Laringe [Internet]. Rio de Janeiro: Instituto Nacional de Câncer; 2022. Available at: https://www.gov.br/inca/pt-br/assuntos/cancer/tipos/laringe (accessed on 12/18/2023).

[3] de Castro Jr FM. Cirurgia de Cabeça e Pescoço: Tópicos Essenciais [Internet - Ebook]. Rio de Janeiro: Thieme Revinter Brasil; 2019. Available at: https://www.thieme.com.br/produto/cirurgia-de-cabeca-e-pescoco-1045 (accessed on 04/23/2024).

[4] Patel SG, Lydiatt WM, Glastonbury CM, Mukherji SK, Ghossein RA, Brandwein-Gensler M, *et al.* Larynx. In: Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, *et al.* (Eds). AJCC Cancer Staging Manual. 8th ed. New York: Springer. 2017; p. 149-161.

[5] Baird BJ, Sung CK, Beadle BM, Divi V. Treatment of early-stage laryngeal cancer: a comparison of treatment options. *Oral Oncol.* 2018; 87:8-16.

[6] Netter NN. Atlas de Anatomia da Cabeça e Pescoço [Internet - Ebook]. Rio de Janeiro: Guanabara Koogan/Grupo GEN; 2018. Available at: https://www.grupogen.com.br/netter-atlas-de-anatomia-da-cabeca-e-pescoco (accessed on 12/18/2023).

[7] Lahav Y, Burns JA, Feinberg S, Heaton JT, Zeitels SM. Initial anatomic geographic presentation of glottal dysplasia. *Ann Otol Rhinol Laryngol.* 2009; 118(5):321-325.

[8] Steuer CE, El-Deiry M, Parks JR, Higgins KA, Saba NF. An update on larynx cancer. *CA Cancer J Clin.* 2017; 67(1):31-50.

[9] Raitiola H, Pukander J, Laippala P. Glottic and supraglottic laryngeal carcinoma: differences in epidemiology, clinical characteristics and prognosis. *Acta Otolaryngol.* 1999; 119(7):847-851.

[10] Mann H, Seligman K, Colwell N, Burr A, Glazer TA. Management of Subglottic Cancer. *Otolaryngol Clin North Am.* 2023; 56(2):305-312.

[11] Coskun H, Mendenhall WM, Rinaldo A, Rodrigo JP, Suárez C, Strojan P, *et al.* Prognosis of subglottic carcinoma: Is it really worse? *Head Neck.* 2019; 41(2):511-521.

[12] Dogan S, Vural A, Kahriman G, Imamoglu H, Abdülrezzak Ü, Öztürk M. Non-squamous cell carcinoma diseases of the larynx: clinical and imaging findings. *Braz J Otorhinolaryngol.* 2020; 86(4):468-482.

[13] Wyss A, Hashibe M, Chuang SC, Lee YC, Zhang ZF, Yu GP, *et al.* Cigarette, cigar, and pipe smoking and the risk of head and neck cancers: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *Am J Epidemiol.* 2013; 178(5):679–690.

[14] Lewin F, Norell SE, Johansson H, Gustavsson P, Wennerberg J, Biörklund A, *et*

al. Smoking tobacco, oral snuff, and alcohol in the etiology of squamous cell carcinoma of the head and neck: a population-based case-referent study in Sweden. *Cancer*. 1998; 82(7):1367–1375.

[15] Andre K, Schraub S, Mercier M, Bontemps P. Role of alcohol and tobacco in the aetiology of head and neck cancer: a case-control study in the Doubs region of France. *Eur J Cancer B Oral Oncol.* 1995; 31B(5):301–309.

[16] Brazil. Health Ministry. National Health Survey. Panel of indicators. 2013-19 [Internet]. Brasilia: Brazilian Health Ministry; 2021. Available at: https://www.pns.icict.fiocruz.br/painel-de-indicadores-mobile-desktop/ (accessed on 01/03/2024).

[17] Brazilian Institute of Geography and Statistics. Brazilian Demographic Census [Internet]. Brasilia: Brazilian Institute of Geography and Statistics; 2023. Available at: https://www.ibge.gov.br/estatisticas/sociais/trabalho/22827-censo-demografico-2022.html (accessed on 04/22/2024).

[18] Brazil. Health Ministry. Special Survey on Smoking – PETab. Brazil Report. [Internet]. Brasilia: Brazilian Health Ministry; 2011. Available at: https://bvsms.saude.gov.br/bvs/publicacoes/pesquisa_especial_tabagismo_petab.pdf (accessed on 01/03/2024).

[19] National Cancer Insitute. Observatory of the National Policy for the Control of Smoking: data and figures of smoking prevalence [Internet]. Rio de Janeiro: INCA; 2019-2020. Available at: https://www.inca.gov.br/observatorio-da-politica-nacional-de-controle-do-tabaco/dados-e-numeros (accessed on 01/05/2024).

[20] Machado IE, Monteiro MG, Malta DC, Lana FCF. Brazilian Health Survey (2013): relation between alcohol use and sociodemographic characteristics by sex in Brazil. *Rev Brasil Epidemiol.* 2017; 20(3):408-422.

[21] Monteiro MG. Alcohol y Salud Pública en América Latina: ¿Cómo impedir un desastre sanitario? *Adicciones*. 2013; 25(2):99-105.

[22] Doorbar J, Egawa N, Griffin H, Kranjec C, Murakami I. Human papillomavirus molecular biology and disease association. *Rev Med Virol.* 2015; 25:2-23.

[23] Ndiaye C, Mena M, Alemany L, Arbyn M, Castellsagué X, Laporte L, *et al.* HPV DNA, E6/E7 mRNA, and p16INK4a detection in head and neck cancers: a systematic review and meta-analysis. *Lancet Oncol.* 2014; 15(12):1319–1331.

[24] Tian S, Switchenko JM, Jhaveri J, Cassidy RJ, Ferris MJ, Press RH, *et al.* Survival outcomes by high-risk human papillomavirus status in non oropharyngeal head and neck squamous cell carcinomas: a propensity-scored analysis of the National Cancer Data Base. *Cancer*. 2019; 125(16):2782–2793.

[25] Levi M. Atualizações das vacinas HPV em uso no Brasil: introdução da nonavalente (HPV9) [Internet]. São Paulo, Brazil: Sociedade Brasileira de Imunizações; 2023. Available at: https://sbim.org.br/images/files/notas-tecnicas/nt-sbim-vacina-hpv9-231103.pdf (accessed on 01/09/2024).

[26] Zhang Y, Fakhry C, D'Souza G. Projected Association of Human Papillomavirus Vaccination With Oropharynx Cancer Incidence in the US, 2020-2045. *JAMA Oncol.* 2021; 7(10): e212907.

[27] Petrelli F, Cin ED, Ghidini A, Carioli D, Falasca V, De Stefani A, *et al.* Human papillomavirus infection and non-oropharyngeal head and neck cancers: an umbrella review of meta-analysis. *Eur Arch Otorhinolaryngol.* 2023; 280(9):3921-3930.

[28] Langevin SM, Michaud DS, Marsit CJ, Nelson HH, Birnbaum AE, Eliot M, *et al.* Gastric reflux is an independent risk factor for laryngopharyngeal carcinoma. *Cancer Epidemiol Biomarkers Prev.* 2013; 22(6):1061–1068.

[29] Mehta RS, Song M, Staller, K Chan AT. Association Between Beverage Intake and Incidence of Gastroesophageal Reflux Symptoms. *Clin Gastroenterol Hepatology.* 2020; 18(10):2226–2233.

[30] Meireles LS, Holanda BLS, de Faria MA, Castro DL, Coutinho IHILS, Mucari TB. Prevalência e fatores agravantes do sintoma de refluxo gastroesofágico em estudantes de medicina da Universidade Federal do Tocantins. *Sci Med.* 2014; 24(3):274-277.

[31] Akbari M, Motiee-Langroudi M, Heidari F, Beheshti A, Karimi E. Impact of the COVID-19 pandemic on the stage and the type of surgical treatment of laryngeal cancer. *Am J Otolaryngol.* 2022; 43(2):103319.

[32] Gourin CG, Conger BT, Sheils WC, Bilodeau PA, Coleman TA, Porubsky ES. The effect of treatment on survival in patients with advanced laryngeal carcinoma. *Laryngoscope*. 2009; 119(7):1312-1317.

[33] Tamura Y, Tanaka S, Asato R, Hirano S, Yamashita M, Tamaki H, *et al.* Therapeutic outcomes of laryngeal cancer at Kyoto University Hospital for 10 years. *Acta Otolaryngol.* 2007; 127(supp557): 62–65.

[34] Kelly SL, Jackson JE, Hickey BE, Szallasi FG, Bond CA. Multidisciplinary clinic care improves adherence to best practice in head and neck cancer. *Am J Otolaryngol.* 2013; 34(1):57-60.

[35] Ritoe SC, de Vegt F, Scheike IM, Krabbe PF, Kaanders JH, van den Hoogen FJ, *et al.* Effect of routine follow-up after treatment for laryngeal cancer on life expectancy and mortality: results of a Markov model analysis. *Cancer*. 2007; 109(2):239-247.