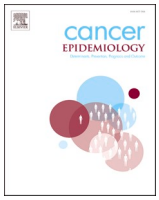
Cancer Epidemiology 93 (2024) 102686

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep



Trends in head and neck cancer incidence in Ho Chi Minh City, Vietnam between 1996 and 2015

Fiona Deutsch [a,*], Ngoc Ha Tran [a], Dung X. Pham [b], Nguyen Dinh Hien [b], V. Nguyen Tuan [a,b,c], Dayna Sais [a], Nham Tran [a,d,**]

[a] School of Biomedical Engineering, Faculty of Engineering and IT, University of Technology Sydney, Australia
[b] Bone and Muscle Research Group, Ton Duc Thang University, Ho Chi Minh City, Vietnam
[c] St Vincent's Clinical School, UNSW Medicine, UNSW Sydney, Sydney, Australia
[d] Sydney Head and Neck Cancer Institute, Sydney, Australia

ARTICLE INFO

Keywords:
Head and neck cancer
Incidence
Gender gap
Age gap
20 year study

ABSTRACT

Introduction: This study provides an analysis of head and neck cancer (HNC) cases over a 20-year period in Ho Chi Minh City, Vietnam. It aims to shed light on HNC's characteristics and trends in this highly populated urban region.

Methods: The analysis encompasses 8974 HNC cases, emphasising incidence rates, gender distribution, and the prevalence of different subtypes, including oral cavity, nasopharyngeal, oropharyngeal, and laryngeal/pharyngeal cancers. Ho Chi Minh City was chosen due to its extensive cancer reporting systems and its role as a major urban healthcare centre attracting a wide range of patients.

Results: The study reveals an increasing incidence of HNC in Ho Chi Minh City, with a notable predominance of male patients (73 %). The breakdown of HNC cases shows oral cavity cancer at 34 %, nasopharyngeal at 33 %, oropharyngeal at 12 %, and laryngeal/pharyngeal at 21 %. Compared to global averages, Vietnamese patients are diagnosed at an earlier age, with a noticeable trend of decreasing mean age of diagnosis over the study period.

Conclusion: This comprehensive study provides valuable insights into the HNC landscape in Ho Chi Minh City, revealing a slightly lower overall incidence but an earlier age of diagnosis compared to global trends. These findings suggest the need for region-specific public health initiatives and further research to clarify the epidemiological features of HNC in Vietnam.

1. Introduction

Head and neck cancers (HNC) represent more than 550,000 cases per year and are the sixth most common cancer type globally [1]. Head and neck cancers is a group of malignancies affecting the upper part of the respiratory and digestive tracts, which includes the lips, oral cavity, pharynx (oro-, naso-, and hypo- pharynx), nasal cavity, larynx, upper trachea, salivary glands, and associated lymph nodes [2]. The most common type is head and neck squamous cell carcinoma (HNSCC) [3]. There are 4 main subtypes of HNC: oral cancer, oropharyngeal cancer, nasopharyngeal cancer, and hypopharyngeal or laryngo-pharyngeal cancer [4].

The complex aetiology of HNC comprises both intrinsic and extrinsic factors. In addition to the two major risk factors associated with the development of HNC [5] particularly tobacco usage and alcohol consumption, it is now broadly accepted that viral infections (e.g., Human Papillomavirus, HPV) are also critical in this cancer's pathogenesis [6]. In Western populations, the decrease in combustible tobacco use and increased HPV prevalence have allowed an epidemiologic shift that has heightened the role of high-risk HPV strains in HNC pathology [7,8]. This subset of the disease is seen more often in younger patients and most commonly presents in the oral cavity, tongue, and oropharynx [9].

In developed countries, the lifetime risk of developing HNC is approximately 1 in 100 although these statistics are skewed towards men and people aged over 60 [10]. The cost of HNC, including diagnosis, treatment, and ongoing care, is significant. In the United States,

* Corresponding author.
** Corresponding author at: School of Biomedical Engineering, Faculty of Engineering and IT, University of Technology Sydney, Australia
E-mail addresses: Fiona.Deutsch@student.uts.edu.au (F. Deutsch), nham.tran@uts.edu.au (N. Tran).

https://doi.org/10.1016/j.canep.2024.102686
Received 8 May 2024; Received in revised form 1 August 2024; Accepted 6 October 2024
Available online 18 October 2024

the annual economic burden is estimated to exceed $3.2 billion [11]. Southeast Asia, this region has a higher prevalence of HNC due to risk factors like high tobacco and alcohol consumption. Many of these occurrences are attributed to the use of betel quid [4]. The lifetime risk of developing HNC in this region is higher than the global average, although precise data is lacking [12,13]. The economic burden is also substantial.

There is a geographic disparity in the distribution of HNC while it is noticeable that HNC is the most common cancer in economically disadvantaged countries, particularly observed in South and Southeast Asia. In Vietnam, the specific statistics for HNC are not clearly defined due to data availability. However, considering the prevalent risk factors similar to those in other Southeast Asian countries, it is likely that the incidence, lifetime risk, and economic burden of HNC are high.

Vietnam has very high smoking rates among its population; in 2015, the daily smoking rate among men was 38.7 % (estimated from the 2015 Global Adult Tobacco Survey) [14]. Furthermore, there is a large proportion of people exposed to second-hand smoke. In 2016, 63 % of the population reported living in households where tobacco is consumed [15]. Alcohol consumption for adults almost doubled from 2003–2005–2008–2010, increasing from 3.8 to 6.6 litres of pure alcohol. This rate is slightly above the global rate of per capita alcohol consumption per annum, which is estimated at 6.2 litres [16]. Understanding the impact of HPV16 on HNC in Vietnam presents a challenge due to limited specific data on HPV prevalence and its direct correlation with cancer rates, making it difficult to distinctly evaluate its role amidst high levels of tobacco and alcohol consumption. Additionally, the intertwining risk factors and developing health infrastructure further obscure the specific contributions of HPV16 to disease burden. Despite this, one notable study by the International Agency for Cancer Research (IACR) has provided some insight, suggesting a seropositivity rate of 21 % for HPV16 in Ho Chi Minh City [17].

Given the rapid economic and social changes in Vietnam and the observed increases in risk factors for HNC, it would be timely to report on the incidence of this disease. In our study, we sought to estimate the incidence of HNC in Ho Chi Minh City, the largest city in Vietnam with a population of 9 million inhabitants. Firstly, we looked to quantify the incidence of HNC and its four main subtypes in Ho Chi Minh City between 1996 and 2015. Secondly, we predicted age-standardised rates of HNC; and third, we examined defining points of incidence through joinpoint regression analysis.

2. Methods

2.1. Ho Chi Minh City cancer registry

The anonymised data for this study was extracted from the Ho Chi Minh City Cancer Registry [18–21] The Registry was established in 1990 to document all diagnosed cancer cases in the City. Cancer patients admitted to any hospital in the city were ascertained and checked for possible duplication. The coverage period was from January 1, 1996, to December 31, 2015. We focused on Ho Chi Minh City, as (i) it is the largest centre of commerce in the country, but more importantly patients often choose Ho Chi Minh city's hospitals for their treatment; (ii) the ascertainment and documentation of cancers in the city is more complete than any other provinces in the country. The study was approved by the Ethics Committee of the Oncology Hospital of Ho Chi Minh City (Ethic Number: X12–0346). The Ho Chi Minh City Cancer Registry adopted the International Classification of Diseases for Oncology, 3rd Edition (ICD0–3) for the classification of primary sites of morphology and guidelines from the International Agency for Research on Cancer and the International Association of Cancer Registries. Based on the ICDP-3, we identified head and neck cancer cases (including its four subtypes) from 1 January 1996–31 December 2015 inclusive. The identification was further ascertained by tumour site code, morphology code, and behaviour type.

2.2. Calculating ASR

Age and gender population statistics were obtained from census data managed by the General Statistics Office (GSO) of Ho Chi Minh City. Population statistics were available for 1999, 2004, 2009 and 2014. Age and gender population statistics in 1999 for Vietnam were obtained from the Bureau of Statistics of Vietnam. Using the population statistics of Ho Chi Minh City, we computed the point incidence rate of Head and Neck cancer (per 100,000 population) for each 5-year interval: 1996–2000, 2001–2005, 2006–2010, and 2011–2015. The reason for aggregating 5-year data was to improve the stability of statistical estimates. We used the direct method of standardisation to calculate the age-standardised rate (ASR), by applying the age-specific rates observed in a period to the national population in 1999. In this approach, the ASR can be thought of as a weighted average rate, with the weights being the proportion of the national population in each age group.

2.3. Logistic joinpoint regression model

Using the United States National Cancer Institute SEER*Stat software (https://seer.cancer.gov/seerstat/), we employed a logistic joinpoint regression model to identify temporal changes in the incidence of head and neck cancer incidence in the Vietnamese population between 1996 and 2015. Data was first formatted in SEER*Prep using the Global Incidence File Format. Age-and-gender population statistics were obtained from census data managed by the General Statistics Office (GSO) of Ho Chi Minh City. Population statistics were available for 1999, 2004, 2009, and 2014. Age-and-gender population statistics in 1999 for Vietnam were obtained from the Bureau of Statistics of Vietnam. Cases were restricted to the head and neck cancer site codes according to the International Classification of Diseases for Oncology, Third Edition (ICD-O-3).

Using the Joinpoint Regression Programme within SEER*Stat, we conducted a time-trend analysis to identify the years when significant changes occurred in the incidence rates. We used the Bayesian Information Criterion (BIC) to select the best-fitting joinpoint model, which detects the number and location of joinpoints (i.e., years where the rate of incidence changes) over the study period. We allowed for a maximum of 2 points in the model. We also calculated the annual percentage change (APC) and the average annual percentage change (AAPC) with 95 % confidence intervals (CIs) to quantify the magnitude and direction of trends. All statistical analyses were performed using SEER*Stat version 8.3.8 and R version 4.0.2. A p-value less than 0.05 was considered statistically significant.

3. Results

3.1. Recorded HNC cases in Ho Chi Minh City 1996–2015

Between January 1, 1996, and December 31, 2015, 8974 new cases of head and neck cancers with 6523 males and 2451 females had been registered in the Registry (Fig. 1 and Table 1). Based on the clinical grade, most cases were at Grade II for males and Grade I for females. Overall, 29 % of HNC cases were classified as Grade II. Most cases were diagnosed through histology of primary cancer (88.66 %), with 64.5 % and 24.16 % of cases for males and females, respectively.

By subtype, nasopharyngeal cancer was the most common cancer in males (23.08 %), whereas in females, cancer of the oral cavity was the prevalent cancer at 12.31 % (Table 1). Among all diagnosed cases of head and neck cancer, 14.53 % of Grade IV cases were found specifically in nasopharyngeal cancer, highlighting its severity at diagnosis compared to other subtypes where majority of cases were diagnosed as Grade I particularly in the larynx, pharynx, and oral cavity. For oropharyngeal cases, the majority were Grade II. For all cancer subtypes, the basis of diagnosis was performed by histology of the primary cancer: 18.56 %, 28.83 %, 30.63 % and 10.63 % for cancers in the larynx/

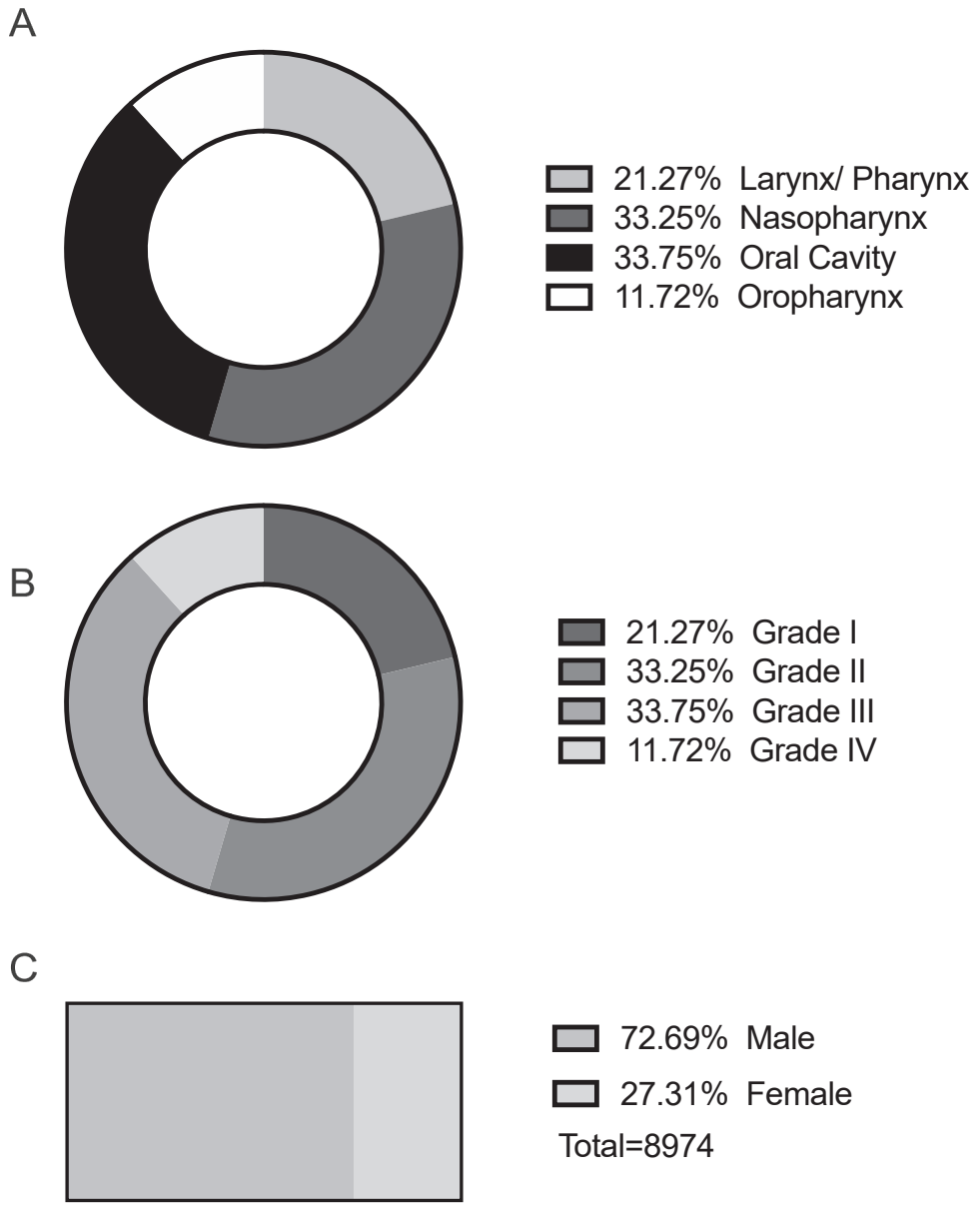


Fig. 1. Head and Neck Cancer (HNC) Cohort from 1995 to 2015 in Ho Chi Minh City. A) Distrurtion of HNC cases over 20 years B) HNC grading and diagnosis C) Male and Female HNC distribution.

pharynx, nasopharynx, oral cavity, and oropharynx, respectively.

3.2. Incidence rates of HNC in Ho Chi Minh City 1996–2015

From the data, it was clear that all four subtypes of HNC exhibited an increase in incidence over the 20-year period under investigation (Fig. 2). Notably, oropharyngeal cancer consistently demonstrated the lowest incidence. While there were minor fluctuations between 1998 and 2000, and again between 2008 and 2010, the incidence of oropharyngeal cancer exhibited a significant rise from 35 to 80. Nasopharyngeal cancer and oral cavity cancer accounted for the highest number of patients, with both types showing identical incidences in 1996 and 2015 (100 and 180, respectively), despite fluctuations in nasopharyngeal cancer cases, reaching a peak of 200 in 2010 and decreasing to 100 in 2006.

The median age of diagnosis for all HNC was similar between males and females, 56 and 57, respectively (Table 1). Males were diagnosed at a median age lower than that of females for laryngeal/pharyngeal cancers (61 years of age) and oral cavity cancers (56 years of age), presenting a difference of 6 and 11 years earlier for males compared to females, respectively (67 years of age for both cancer types in females). In contrast, women were diagnosed slightly younger than males for nasopharyngeal and oropharyngeal cancers, with respective median ages of 55 years and 47 years for females, compared to 56 years and 50 years for males. This difference was more pronounced for nasopharyngeal cancers, with females being diagnosed 3 years earlier and 1 year earlier for oropharyngeal cancers.

HNC showed an overall increase between 1996 and 2015 for both males and females. A detailed examination over a five-year span, categorised by age groups, revealed a rise in incidence for individuals between 40 and 69 years old, with the 50–59 age group being notably prevalent in both genders (Fig. 3, A and B). There was a notable shift in the distribution of incidence for both males and females between the periods of 1996–2000 and 2011–2015. In 1996, a quarter of HNC cases in males were reported in the age group of 60–69. Over the subsequent five-year period until 2015, this percentage increased to 35.39 %, with males aged 50–59 comprising a substantial portion. Similarly, among females with HNC, a quarter of cases diagnosed between 1996 and 2000

Table 1
Demographic and clinical characteristics by subtype and sex in Ho Chi Minh City, Vietnam. This table provides a detailed overview of median age of diagnosis, number of cases, cancer grade, and base of diagnosis for head and neck cancer subtypes in Ho Chi Minh City, Vietnam. It includes separate data for males and females to highlight gender-specific differences in clinical characteristics and diagnosis ages across subtypes.

Subtype	Sex	Median Age of Diagnosis	Number of Cases	Grade I (%)	Grade II (%)	Grade III (%)	Grade IV (%)	Unknown Grade (%)	Base of Diagnosis (%)
Laryngeal/ Pharyngeal	Male	61	1756 (19.57 %)	195 (2.17 %)	722 (8.05 %)	912 (10.16 %)	3 (0.03 %)	404 (4.50 %)	Histology of primary (18.56 %)
	Female	67	153 (1.70 %)	21 (0.23 %)	64 (0.71 %)	99 (1.10 %)	21 (0.23 %)	2 (0.02 %)	Clinical tests (1.56 %)
Oral Cavity	Male	56	1924 (21.44 %)	1288 (14.35 %)	960 (10.70 %)	200 (2.23 %)	7 (0.08 %)	574 (6.40 %)	Histology of primary (30.63 %)
	Female	67	1105 (12.31 %)	7 (0.08 %)	31 (0.35 %)	34 (0.38 %)	4 (0.04 %)	10 (0.11 %)	Clinical tests (2.16 %)
Oropharyngeal	Male	56	772 (8.60 %)	183 (2.04 %)	421 (4.69 %)	190 (2.12 %)	16 (0.18 %)	242 (2.70 %)	Clinical tests (0.78 %)
	Female	55	280 (3.12 %)	1 (0.01 %)	9 (0.10 %)	16 (0.18 %)	1 (0.01 %)	1 (0.01 %)	Histology of metastases (0.79 %)
Nasopharyngeal	Male	50	2071 (23.08 %)	49 (0.55 %)	504 (5.62 %)	661 (7.37 %)	1304 (14.53 %)	466 (5.19 %)	Histology of primary (28.83 %)
	Female	47	913 (10.17 %)	7 (0.08 %)	28 (0.31 %)	71 (0.79 %)	7 (0.08 %)	10 (0.11 %)	Clinical tests (2.86 %)
Head and Neck (all)	Male	56	6523 (72.69 %)	1469 (16.37 %)	2088 (23.27 %)	912 (10.16 %)	903 (10.06 %)	1151 (12.83 %)	Histology of primary (64.50 %)
	Female	57	2451 (27.31 %)	636 (7.09 %)	519 (5.78 %)	334 (3.72 %)	427 (4.76 %)	532 (5.93 %)	Clinical tests (2.11 %)

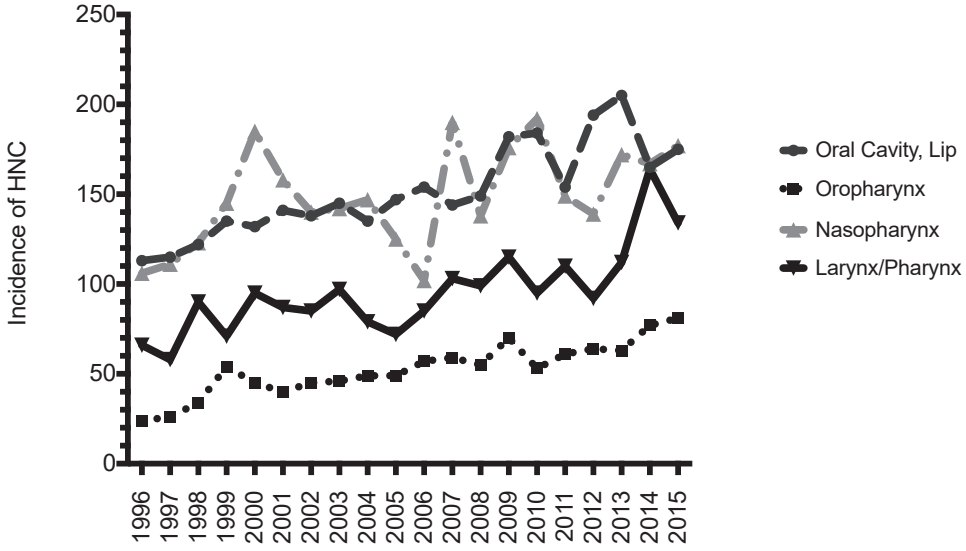


Fig. 2. Point incidence of four head and neck cancer subtypes in Ho Chi Minh City between 1996 and 2015. Oral cavity cancers and nasopharyngeal cancers were the most prominent cancer type, followed by laryngeal/ pharyngeal cancers and oropharyngeal cancers.

were in the age group of 70–79. From 2011–2015, there was a shift, with 25.53 % of cases observed in females aged 50–59 (Supplementary Table 1 A).

Nasopharyngeal cancer cases remained consistently prevalent in males and females aged between 40 and 59 (Supplementary Figure 1, A and B). Nasopharyngeal cancers peaked in the 5-year period between 2006 and 2010 in both males and females in the 40–49 age group, representing nearly one-third of nasopharyngeal cases in both males and females for that period (Supplementary Table 1B).

Oropharyngeal cancers affected males more than females (n = 2071 for males; n=913 for females), with males in the 50–59 age group affected substantially more than other age groups (Supplementary Figure 1, C and D). In the period between 1996 and 2000, 27.2 % of males with oropharyngeal cancers were diagnosed between 60 and 69 years old (Supplementary Table 1 C). From 2011–2015, 41 % were diagnosed in the 50–59 age range. In contrast, for females diagnosed with oropharyngeal cancers from 1996 to 2000, 18.97 % of cases were diagnosed in the 40–49 age range. From 2011–2015, 29.41 % of cases were diagnosed in the 60–69 age range.

Pharyngeal and laryngeal cancers incidence increased considerably in males and decreased in females between 1996 and 2015 (Supplementary Figure 1, E and F). In 2001–2015, a steep increase was observed for males aged between 50 and 59. In the 2001 period, this age group represented one fifth of pharyngeal/ laryngeal cases. By the 2011–2015 period, this age group represented 38 % of these cases. In contrast, there were only 153 cases of laryngeal/pharyngeal cancers in females over the 20-year period examined (n = 1756 in males), which saw a slight decrease in cases between 1996 and 2015 (Supplementary Table 1D).

Similar to pharyngeal/ laryngeal cancers, the incidence of cancers of the oral cavity increased considerably in males and decreased in females between 1996 and 2015 (Supplementary Figure 1 G and H). Between 1996 and 2000, 23.9 % of cases for males were diagnosed in the 70–79 age range (Supplementary Table 1E). This age range lowered between

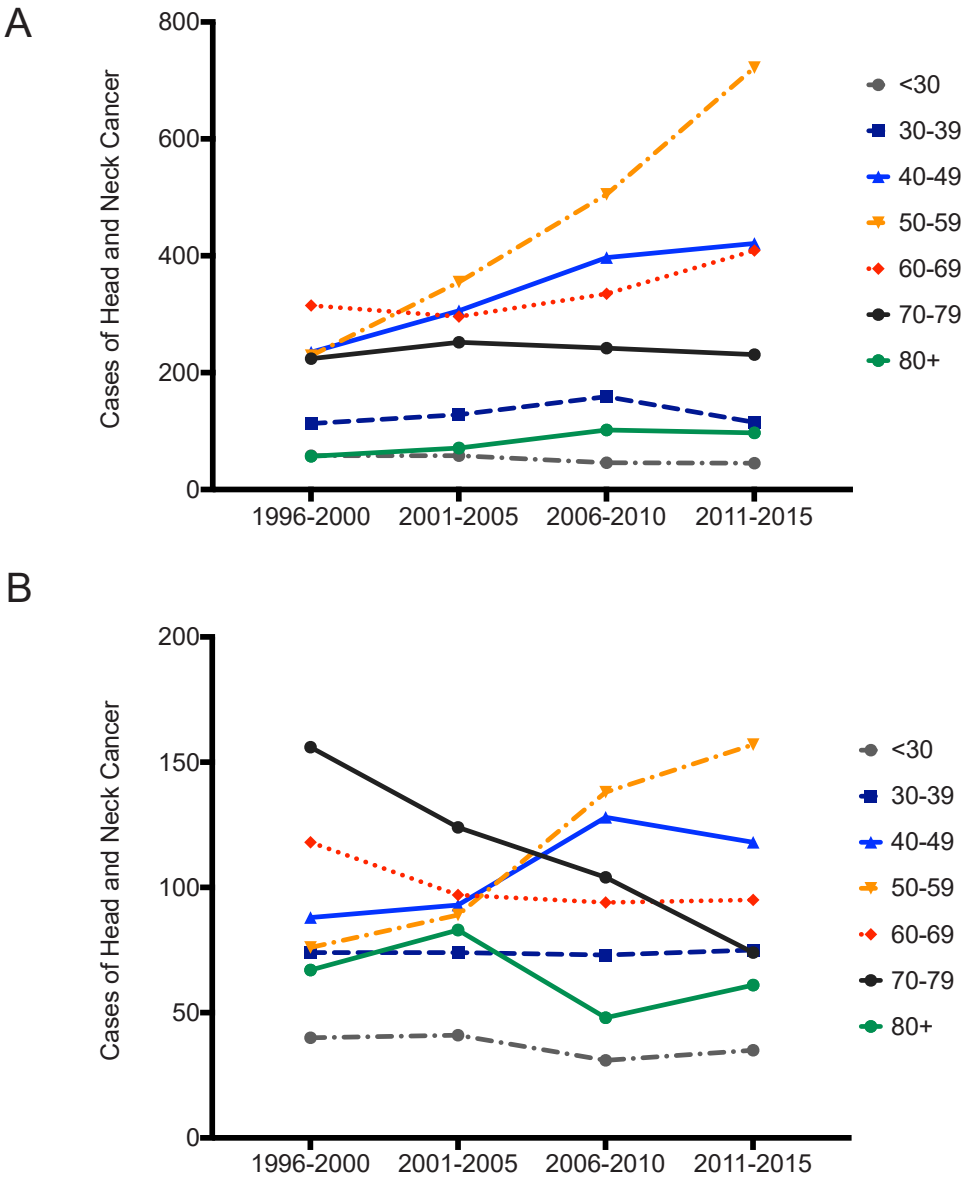


Fig. 3. Five-year incidence of Head and Neck cancers by age group. A) Head and neck cancer incidence in males by age group. 50–59 age group increases substantially over the 20 years examined; B) Head and neck cancer incidence in females by age group. 50–59 age group increases substantially over the 20 years examined. The 70–79 age group steadily decreased during the same period.

2011 and 2015, with the majority cases (34.08 %) cases seen in the 50–59 age range. Similarly, in females, 37.12 % of cases were diagnosed for patients between 70 and 79 in 1996–2000, however by 2011–2015, 27.61 % of cases were seen in the 50–59 age.

3.3. The 5-year age-standardised incidence rate (ASR) for HNC

Overall, the age standardised rates for the head and neck subtypes remained somewhat consistent over the 20 years examined, except for nasopharynx, which decreased from 3.2 per 100,000 population to 2.7 per 100,000 (see Supplementary Tables 2). When comparing our findings on ASR and crude rates for head and neck cancers patients in Ho Chi Minh City to GLOBOCAN statistics, HNC rates remain consistent for all subtypes, except again for nasopharyngeal cancer, where the overall crude rate and ASR between 1996 and 2015 was 2.3 and 2.7, respectively. The crude rate and ASR for the world in 2020 was 1.7 and 1.5 respectively (per 100,000 population). This correlates with nasopharyngeal cancers cases accounting for one third of overall HNC cases between 1996 and 2015.

The 5-year ASR for oral cancer was 3.5 cases per 100,000 population during the 1996–2000 period. This rate decreased slightly to 3.2 cases in 2011–2015. In males over the same time, ASR increased from 4.3 to 5.5 cases (per 100,000 population), while in females the ASR progressively decreased nearly a haft, from 2.9 to 1.6 (Supplementary Table 3, A). For cancers of the oropharynx, overall, the ASR increased between the period 1996–2000 and 2011–2015 from 1 case to 1.3 cases (per 100,000 population) (Supplementary Table 3, B). In males, this increased over the same period from 1.7 cases per 100,000 population to 2.2 cases per 100,000 population. In females, a smaller increase was seen of 0.5 cases to 0.6 (per 100,000 population) over the same time.

In nasopharyngeal cancer cases, the ASR decreased slightly per 100,000 population, from 3.2 cases to 2.6 cases over the 20-year period (Supplementary Table 3, C). Males were overrepresented between 1996 and 2000, with an ASR of 5.1 cases per 100,000 population. Incidentally, the ASR decreased in the period 2011–2015 with an ASR of 4.2. This rate was still more frequent than in females, which saw a slight

decrease in ASR from 1.8 to 1.3 in the same period. Lastly, laryngeal, and pharyngeal cancer cases slightly increased from 1996 to 2015, from 2.3 to 2.4 cases per 100,000 population (Supplementary Table 3, D). In males, the ASR increased from 5.0 cases in 1996 – 2000–5.5 in 2011–2015. For females, ASR decreased by half, from 0.4 cases to 0.2.

3.4. Joinpoint regression analysis

Joinpoint regression analysis did not identify breakpoints in any of the head and neck cancer subtypes from 1996 to 2015 (Supplementary Figure 2, A-D). Age-adjusted rates in males increased, whereas females decreased at the same time and were the least in overall. Male and female rates slightly declined from 3.4 to 2.9 (Supplementary Figure 2, A). Oropharyngeal age-adjusted rates have similar increasing trends, whereas males have the highest rates overall and females have the lowest (Supplementary Figure 2, B). Oropharyngeal and pharyngeal/laryngeal age-adjusted rates increased in both males and females (Supplementary Figure 2, B; Supplementary Figure 2, D), whereas nasopharyngeal age-adjusted rates decreased slightly for both genders (Supplementary Figure 2, C). In contrast with oropharyngeal cancer, for 20 years, the nasopharyngeal age-adjusted rates decreased steadily in both males and females but the rate in males is still the highest (Supplementary Figure 2, C). Laryngopharyngeal cancer rates in both males and females were quite stable, while the rates increased only 0.2, from 2.1 to 2.3 during the period. A decrease rates were seen in females from 0.5 to 0.2 (Supplementary Figure 2, D)

4. Discussion

This study represents a comprehensive 20-year analysis of head and neck cancer cases in Ho Chi Minh City, Vietnam. We focused on Ho Chi Minh City for the following reasons: (i) as the country's largest commercial centre, it draws many patients, many of whom opt for treatment in the city's hospitals. This concentration of patients offers a diverse sample for study. (ii) The city's cancer registration and reporting systems ensure more accurate and complete data collection compared to other rural provinces or regions, making it an ideal choice for an epidemiological analysis. Over this period, 8974 Vietnamese individuals were diagnosed with HNC.

Males accounted for 73 % of these cases, indicating a gender gap of 3:1 (males to females), mirroring global trends. The study investigated four subtypes of HNC: oral cavity cancer (34 % of cases), nasopharyngeal cancers (33 %), oropharyngeal cancer (12 %), and laryngeal/pharyngeal cancers (21 %), demonstrating that HNC subtype prevalence in Vietnam is not dissimilar to that observed globally [22]. There was a significant age gap, with diagnosis typically occurring around 10 years earlier than global averages. There was also a decrease in the mean age of diagnosis over the 20-year period investigated, a contrast to increasing diagnosis age trends observed in Western countries [23].

Similarly, our analysis revealed a notable trend where HNC is diagnosed at a younger age in Vietnam compared to the global average. This finding aligns with studies conducted in other regions, such as a study in the USA which reported that Asian diasporas were diagnosed at younger ages, with a 3–5 times higher likelihood of being diagnosed by age 40 compared to white patients [24].

Our findings are also consistent with observations in other Asian countries. Similar to Taiwan and the Philippines, oral cancer is a significant health burden, with more than 5000 new cases every year in Taiwan [25] and a crude rate of 2 per 100,000 in the Philippines [26]. Nasopharyngeal cancer, the leading HNC subtype in China and Hong Kong, also accounted for a considerable proportion of Vietnamese cases [27,28]. However, unlike Western countries, where oropharyngeal cases have sharply risen due to increasing HPV infections [7], this subtype only accounted for a smaller fraction of HNC cases in Vietnam.

Our analysis showed a consistent rise in the incidence of oropharyngeal cancers in Vietnam over the 20-year period. This trend might be attributed to prevalent habits in Asian countries, such as tobacco use and alcohol consumption.[8,29]. Consumption of foods high in nitrites is another distinct risk factor, commonly observed among the economically disadvantaged. In Vietnam, there is a widespread custom of buying homemade alcohol with high concentration at low costs, rendering it readily available to the general populace. Moreover, domestically produced tobacco, known for its affordability, is increasingly becoming prevalent in communities, affecting not just men but also women. This trend is partly due to the government's regulations, which are not stringent enough to effectively curb this issue. Additionally, betel quid and areca nuts are culturally utilised by older individuals in rural areas of Vietnam.

Furthermore, the distribution of HNC subtypes in our study, where oropharyngeal cancer was found to be the least common, mirrors findings from Khosla et al., which observed a similar distribution pattern among Asian diasporas in the USA [24]. This consistency across studies suggest that certain biological or environmental factors associated with Asian populations may influence the prevalence of specific HNC subtypes [24].

There has been a lack of information regarding accurate rates for HPV16 infections in Vietnam, particularly for males, with previous studies looking at HPV infection rates among Vietnamese women [30,31]. It was recently reported that HPV in Vietnamese males was common with high-risk HPV genotypes, although this study looked at penile cell samples [32]. As such, we cannot eliminate that HPV may play a role in specific HNC cases.

Our study revealed differences in the median age of diagnosis. For laryngeal and oral cancers, the median age of diagnosis was higher in females (67 years for both subtypes) than in males (61 and 56 years, respectively. Conversely, for oropharyngeal and nasopharyngeal cancers, males presented at a median age of 56 and 50 years, respectively, which was slightly older than their female counterparts diagnosed at 55 and 47 years. The median age of diagnosis for males and females was similar (56 and 57).

In a global context, the median age of diagnosis for non-virally associated HNC is typically 66 years [33]. Viral-associated HNCs, such as HPV-associated oropharyngeal cancer and Epstein-Barr virus-associated nasopharyngeal cancer, exhibit a lower median age of diagnosis, around 53 and 50 years, respectively [3]. Data specific to median age of diagnosis in Asia remains limited, but there exists a 10-year disparity between the global median age of diagnosis and that observed for both sexes in Ho Chi Minh City. This does not imply that Vietnamese people develop HNC earlier than the global average. While many Western countries have advanced healthcare infrastructure facilitating early detection, the observed trend in Vietnam may also be influenced by differing healthcare access and lifestyle factors. Notably, smoking remains prevalent in many Asian countries, including Vietnam, contrary to declining trends in the West, which have influenced disease patterns. Therefore, our observations may reflect both enhanced access to diagnostic services in urban areas like Ho Chi Minh City, and persistent high-risk behaviours, rather than an inherent predisposition to earlier onset disease.

In contrast, Western countries have seen an upward trend in the mean age of HNC diagnosis over the past several decades [34]. The U.S. has seen an increase in mean age at diagnosis for all HNC subtypes from 1975 to 2016, with the sole exception of oropharyngeal cancer [35]. This subtype saw a decrease in the mean age of diagnosis, paralleled by a surge in proportional prevalence, potentially attributable to a rise in HPV-related oropharyngeal cancers.

Vietnam has experienced an upward trend in both smoking and alcohol consumption, particularly among men [15]. These lifestyle factors could contribute to the observed higher ASR of HNC in men. Efforts to reduce the prevalence of these risk factors could potentially lead to a decrease in the incidence of HNC [36]. Furthermore, given that Vietnam is a developing country and Ho Chi Minh City encompasses individuals from all social strata, oral hygiene tends to be lower among

those in impoverished conditions. This highlights the urgency for public health measures in this region to mitigate these risk factors, and, thus, potentially reduce the incidence of HNC among men.

While this study covers a 20-year period, there are several limitations that must be considered. One primary constraint is its focus solely on Ho Chi Minh City. This potentially limits the generalisability of the findings to other areas of Vietnam, particularly rural or less urbanised regions where lifestyle, environmental factors, and healthcare access may differ significantly. Another aspect pertains to data collection. If the study relies heavily on existing medical records or cancer registries, it may face challenges related to the completeness and accuracy of these records.

An important factor to consider in the observed rise in HNC cases in Ho Chi Minh City is the potential influence of improved transportation infrastructure over the past two decades. As Vietnam's largest commercial centre, the city not only attracts a large resident population but also draws patients from across the country seeking higher-quality medical care. Since 1996, significant improvements in transportation facilities and the increasing accessibility of the city may have contributed to a rise in the number of patients having to travel to the city for diagnosis or treatment. This factor could partly explain the observed increase in HNC incidence; however, the available data does not allow us to directly quantify the proportion of cases attributable to non-residents.

Over the span of 20 years, inconsistencies or gaps in data collection methods could have implications for the reliability of the trend analysis presented. Any limitations in this regard could also affect the accuracy of HNC incidence. Patient selection biases represent another potential limitation. The study might inadvertently focus on patients with access to healthcare facilities in Ho Chi Minh City, potentially skewing data towards certain demographics or disease severity. This aspect may impact the study's findings. Additionally, without longitudinal follow-up, individual outcomes could not be analysed.

Even with these limitations, our study is one of the few to describe the incidence of HNC over an extended time. It revealed a significant gender disparity, with a higher incidence in males, mirroring global trends. Notably, the average age of HNC diagnosis in Vietnam is about 10 years earlier than in other parts of the world. This could be due to a combination of factors, including improvements in healthcare and increased awareness. These findings point to the need for public health initiatives, including cancer screening, tailored to Vietnam's specific health landscape. The study may provide important information that could inform future healthcare policies and cancer control strategies in Vietnam, considering the country's unique demographic and economic context.

5. Conclusion

The study conducted a thorough 20-year analysis of head and neck cancer cases in Ho Chi Minh City, Vietnam, highlighting several key findings. The city's role as a major commercial centre provided a diverse patient population. The incidence of head and neck cancer cases in the city was found to be lower than global rates but demonstrated a significant gender gap, with males accounting for 73 % of cases, consistent with global trends. The study identified four main subtypes of HNC, with oral cavity and nasopharyngeal cancers being the most prevalent, aligning with global patterns.

A notable finding was the age gap, with head and neck cancer diagnosis occurring 10 years earlier in Vietnam compared to global averages and decreasing mean age of diagnosis over the study period. This contrasts with Western countries, where diagnosis age trends are increasing, particularly for oropharyngeal cases due to rising HPV infections.

The study's limitations include its focus on Ho Chi Minh City, its limited generalisability to other regions of Vietnam, and potential biases in patient selection. Despite these limitations, the study provides valuable insights into head and neck incidence and demographics in Vietnam over an extended period of 20 years.

Ethical approval and consent to participate

The research was conducted in accordance with the Declaration of Helsinki. The study was approved by the Ethics Committee of the Oncology Hospital of Ho Chi Minh City.

Authors' contributions

FD and NT developed the original idea and drafted the initial manuscript. FD, NT, DP, NDH, TVN, DS, and NHT performed data analysis and provided input into the manuscript. All authors provided intellectual input and reviewed the final submission.

Funding

This project was funded by a Translational Cancer Research Network PhD Scholarship Top-Up Award, supported by the Cancer Institute NSW Australia.

CRediT authorship contribution statement

Nham Tran: Writing – review & editing, Writing – original draft, Supervision, Investigation, Conceptualization. **Fiona Deutsch:** Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation. **Ngoc Ha Tran:** Writing – review & editing, Validation. **Dung X Pham:** Data curation. **Nguyen Dinh Hien:** Writing – review & editing, Software, Formal analysis, Data curation. **Dayna Sais:** Writing – review & editing, Resources.

Declaration of Competing Interest

No interest to declare

Acknowledgements

N/A

Consent for publication

Not applicable.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.canep.2024.102686.

Data availability

All data generated or analysed during this study are included in this published article and its supplementary information files.

References

[1] Y. Sharma, G. Mishra, V. Parikh, Quality of life in head and neck cancer patients, Indian J. Otolaryngol. Head. Neck Surg. 71 (Suppl 1) (2019) 927–932.
[2] D. Owens, V. Paleri, A.V. Jones, Head and neck cancer explained: an overview of management pathways, Br. Dent. J. 233 (9) (2022) 721–725.
[3] D.E. Johnson, B. Burtness, C.R. Leemans, V.W.Y. Lui, J.E. Bauman, J.R. Grandis, Head and neck squamous cell carcinoma, Nat. Rev. Dis. Prim. 6 (1) (2020) 92.
[4] A. Barsouk, J.S. Aluru, P. Rawla, K. Saginala, A. Barsouk, Epidemiology, risk factors, and prevention of head and neck squamous cell carcinoma, Med Sci. 11 (2) (2023).
[5] A.R. Kreimer, A.K. Chaturvedi, L. Alemany, D. Anantharaman, F. Bray, M. Carrington, J. Doorbar, G. D'Souza, C. Fakhry, R.L. Ferris, et al., Summary from an international cancer seminar focused on human papillomavirus (HPV)-positive

oropharynx cancer, convened by scientists at IARC and NCI, Oral. Oncol. 108 (2020) 104736.
[6] N. Tran, B.R. Rose, C.J. O'Brien, Role of human papillomavirus in the etiology of head and neck cancer, Head. Neck 29 (1) (2007) 64–70.
[7] A.K. Chaturvedi, E.A. Engels, R.M. Pfeiffer, B.Y. Hernandez, W. Xiao, E. Kim, B. Jiang, M.T. Goodman, M. Sibug-Saber, W. Cozen, et al., Human papillomavirus and rising oropharyngeal cancer incidence in the United States, J. Clin. Oncol. 29 (32) (2011) 4294–4301.
[8] A.K. Chaturvedi, B.I. Graubard, T. Broutian, W. Xiao, R.K.L. Pickard, L. Kahle, M. L. Gillison, Prevalence of oral HPV infection in unvaccinated men and women in the United States, 2009-2016, JAMA 322 (10) (2019) 977–979.
[9] G.C. Blitzer, M.A. Smith, S.L. Harris, R.J. Kimple, Review of the clinical and biologic aspects of human papillomavirus-positive squamous cell carcinomas of the head and neck, Int. J. Radiat. Oncol. Biol. Phys. 88 (4) (2014) 761–770.
[10] S. Warnakulasuriya, Global epidemiology of oral and oropharyngeal cancer, Oral. Oncol. 45 (4-5) (2009) 309–316.
[11] M.S. Landwehr, S.E. Watson, C.F. Macpherson, K.A. Novak, R.H. Johnson, The cost of cancer: a retrospective analysis of the financial impact of cancer on young adults, Cancer Med. 5 (5) (2016) 863–870.
[12] R.H. Patterson, V.G. Fischman, I. Wasserman, J. Siu, M.G. Shrime, J.J. Fagan, W. Koch, B.C. Alkire, Global burden of head and neck cancer: economic consequences, health, and the role of surgery, Otolaryngol. Head. Neck Surg. 162 (3) (2020) 296–303.
[13] Q.B. Rahman, O. Iocca, K. Kufta, R.M. Shanti, Global burden of head and neck cancer, Oral. Maxillofac. Surg. Clin. North Am. 32 (3) (2020) 367–375.
[14] T.P.T. Tran, J. Park, T.N.P. Nguyen, V.M. Hoang, M.K. Lim, Association between perceived harm of tobacco and intention to quit: a cross-sectional analysis of the Vietnam Global Adult Tobacco Survey, BMC Public Health 22 (1) (2022) 909.
[15] P.T. Phan, G.V. Vu, C.Q. Ngo, Q.L.T. Pham, L.P.T. Doan, T.H.T. Nguyen, H.L. T. Nguyen, T.H. Nguyen, B.X. Tran, C.A. Latkin, et al., Tobacco smoking and nicotine dependence among patients with respiratory diseases in Vietnam: status and correlated factors, J. Subst. Abus. Treat. 135 (2022) 108562.
[16] L.M. Kaljee, B.L. Genberg, T.T. Minh, L.H. Tho, L.T. Thoa, B. Stanton, Alcohol use and HIV risk behaviors among rural adolescents in Khanh Hoa Province Viet Nam, Health Educ. Res. 20 (1) (2005) 71–80.
[17] S. Vaccarella, S. Franceschi, G.M. Clifford, A. Touze, C.C. Hsu, S. de Sanjose, T. H. Pham, T.H. Nguyen, E. Matos, H.R. Shin, et al., Seroprevalence of antibodies against human papillomavirus (HPV) types 16 and 18 in four continents: the international agency for research on cancer HPV prevalence surveys, Cancer Epidemiol. Biomark. Prev. 19 (9) (2010) 2379–2388.
[18] D.X. Pham, T.H. Ho, T.D. Bui, L.T. Ho-Pham, T.V. Nguyen, Trends in breast cancer incidence in Ho Chi Minh City 1996-2015: a registry-based study, PLOS One 16 (2) (2021) e0246800.
[19] D.X. Pham, H.D. Nguyen, A.H.T. Phung, T.D. Bui, T.S. Tran, B.N.H. Tran, L.T. Ho-Pham, T.V. Nguyen, Trends in incidence and histological pattern of thyroid cancer in Ho Chi Minh City, Vietnam (1996-2015): a population-based study, BMC Cancer 21 (1) (2021) 296.
[20] D.X. Pham, A.H.T. Phung, H.D. Nguyen, T.D. Bui, L.D. Mai, B.N.H. Tran, T.S. Tran, T.V. Nguyen, L.T. Ho-Pham, Trends in colorectal cancer incidence in Ho Chi Minh City, Vietnam (1996-2015): Joinpoint regression and age-period-cohort analyses, Cancer Epidemiol. 77 (2022) 102113.
[21] T.N. Truong, T.N.D. Pham, L.B. Hoang, V.T. Nguyen, H.V. Dao, D.V.B. Dao, S. Alessy, H.B. Pham, T.T.T. Pham, L.D.D. Nguyen, et al., Surveillance and treatment of primary hepatocellular carcinoma (aka. STOP HCC): protocol for a prospective cohort study of high-risk patients for HCC using GALAD-score, BMC Cancer 23 (1) (2023) 875.
[22] N. Cohen, S. Fedewa, A.Y. Chen, Epidemiology and demographics of the head and neck cancer population, Oral. Maxillofac. Surg. Clin. North Am. 30 (4) (2018) 381–395.
[23] E.P. Simard, L.A. Torre, A. Jemal, International trends in head and neck cancer incidence rates: differences by country, sex and anatomic site, Oral. Oncol. 50 (5) (2014) 387–403.
[24] S. Khosla, R.C. Hershow, S. Freels, G.D. Jefferson, F.G. Davis, C.E. Peterson, Head and neck squamous cell carcinomas among males of the three largest Asian diasporas in the US, 2004-2013, Cancer Epidemiol. 74 (2021) 102011.
[25] K.J.Y. Wan-Lun Hsu, Chun-Ju Chiang, Tseng-Cheng Chen, Cheng-Ping Wang, Head and neck cancer incidence trends in Taiwan, 1980 ~ 2014, Int. J. Head. Neck Sci. 1 (3) (2017) 180–189.
[26] P.M. Albano, D. Holzinger, C. Salvador, J. Orosa 3rd, S. Racelis, M. Leano, D. Sanchez Jr., L.M. Angeles, G. Halec, M. Schmitt, et al., Low prevalence of human papillomavirus in head and neck squamous cell carcinoma in the northwest region of the Philippines, PLOS One 12 (2) (2017) e0172240.
[27] Z. Anwei, S. Xin, T.Q. Fei, J. Ziyu, F.Y. Liu, Management practices of head and neck cancer in chinese tertiary care hospitals: a multicenter questionnaire-based survey among oncologists, Cancer Control 27 (1) (2020), 1073274820902264.
[28] P. Thomson, R. Su, S.-W. Choi, Oral cancer in Hong Kong: identifying and managing the 'high-risk' population, Fac. Dent. J. 9 (3) (2018) 116–121.
[29] M.L. Gillison, T. Broutian, R.K. Pickard, Z.Y. Tong, W. Xiao, L. Kahle, B.I. Graubard, A.K. Chaturvedi, Prevalence of oral HPV infection in the United States, 2009-2010, JAMA 307 (7) (2012) 693–703.
[30] T.C. Bui, L.T. Tran, C.M. Markham, T.T. Huynh, L.T. Tran, V.T. Pham, Q.M. Tran, N.H. Hoang, L.Y. Hwang, E.M. Sturgis, Self-reported oral health, oral hygiene, and oral HPV infection in at-risk women in Ho Chi Minh City, Vietnam, Oral. Surg. Oral. Med Oral. Pathol. Oral. Radio. 120 (1) (2015) 34–42.
[31] L. Vu, H. Le, O. Luong, H. Tran, N. Nguyen, H. Luu, Prevalence of cervical human papillomavirus infection among married women in Hanoi, Vietnam, 2010, Asia Pac. J. Public Health 24 (2) (2012) 385–390.
[32] B.N. Hoai, T.N. Cao, L.A. Luong Thi, M.N. Nguyen, H.Q. Duong, V.T. Than, Human papillomavirus prevalence and genotype distribution in Vietnamese male patients between 2016 and 2020, J. Med. Virol. 94 (6) (2022) 2892–2896.
[33] R.L. Siegel, K.D. Miller, H.E. Fuchs, A. Jemal, Cancer statistics, 2021, CA Cancer J. Clin. 71 (1) (2021) 7–33.
[34] J.M. Vahl, M.C. Wigand, M. Denkinger, D. Dallmeier, C. Steiger, C. Welke, P. Kuhn, C. Idel, J. Doescher, A. von Witzleben, et al., Increasing mean age of head and neck cancer patients at a German tertiary referral center, Cancers 13 (4) (2021).
[35] S. Bajpai, N. Zhang, D.G. Lott, Tracking changes in age distribution of head and neck cancer in the United States from 1975 to2016, Clin. Otolaryngol. 46 (6) (2021) 1205–1212.
[36] C. de Martel, D. Georges, F. Bray, J. Ferlay, G.M. Clifford, Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis, Lancet Glob. Health 8 (2) (2020) e180–e190.