INTRODUCTION

Head and neck cancer (HNC) encompasses a heterogenous group of malignancies involving multiple sites including the oral cavity, pharynx, larynx, paranasal sinuses, and neck. The relative frequency of HNC is very low compared to other sites such as the lung and colon [1,2], however, HNC draws enormous attention because of potentially devastating consequences on quality of life [3,4]. Tobacco use remains the most important risk factor for HNC, followed by alcohol consumption [4]. In general, long-term use of both tobacco and alcohol account for the most cases of HNC. Recently, human papilloma virus has been found to play an important role in carcinogenesis, especially in HNC involving the tonsil, base of the tongue, and other parts of the pharynx [4-6].

Prior studies have reported on the worldwide incidence of HNC [1,2,7-16]. The type and frequency of HNC often varies considerably by region and country [1,2], likely due to ethnic and genetic differences, smoking and alcohol consumption habits, and occupational and environmental exposures [1,2,4]. In 1999, the Korean government launched The Korea National Cancer Incidence Database, recognizing the importance of systematic and comprehensive management of patients with cancer. By law, all hospitals in South Korea must report each new
cancer diagnosis to Korea Central Cancer Registry Center, which manages and analyzes the data. This registry provides a powerful tool to better understand the incidence and trends of HNC in Korea, much like the Surveillance, Epidemiology, and End Results tumor registry in the United States.

The objective of this study was to provide detailed estimates of population-based incidences of HNC between 1999 and 2012 in Korea and to evaluate cancer trends.

**MATERIALS AND METHODS**

**Cancer registration and population data**
A retrospective study was performed using The Korean National Cancer Incidence Database. Institutional review board approval was not required for this deidentified registry. The Korean National Cancer Incidence database codes information regarding the primary site and extent of disease. All patients diagnosed with HNCs from 1999 to 2012 were identified using site-specific codes defined below.

**Definition of HNCs**
Sites of HNC (identified by International Classification of Diseases code, 10th version) were reviewed from the database and included in this study included: lip (C00), oral tongue (C01, 02), oral cavity (C03–06), major salivary gland (C07, 08), nasopharynx (C11), nasal cavity and paranasal sinus (C30, 31), tonsil (C09), hypopharynx (C12, 13), oropharynx (C10), and larynx (C32). Oral tongue was defined separately from oral cavity, and tonsil from oropharynx. Thyroid cancer was not included in this study as it had been recently evaluated elsewhere. Cancer type and association with human papilloma virus (HPV) were not considered for this study.

**Statistical analysis**
Average of age-standardized incidence rates during 1999 to 2012 were calculated and provided with 95% confidence intervals for each tumor site. The increase ratio of HNCs for were calculated. We defined it as ratio of average incidence number during 2009–2011 to 1999–2001. Because the value of age-standardized incidence rate of HNCs was too small for the calculation, we used the incidence number instead. Total population of Korea was 46,136,000 at 2000 and increased to 48,580,000 at 2010, which means the population grew roughly 5.3% during 2000–2010. Therefore, we included this population increase in our calculations when comparing the incidence number in 2000 and 2010.

Population-adjusted ratio = average cancer incidence number from 2009–2011/average incidence number from 1999–2001 × 1.053

Male-to-female incidence ratios were also calculated by using the average incidence number during 1999–2001 and 2009–2011, respectively. We divided the average incidence number of male population by those of female population at same period and compared the ratios between 1999–2001 and 2009–2011 to investigate any potential trends in male-to-female ratio.

**RESULTS**

**Average age-standardized incidence rate per 100,000 during 1999 to 2012**
Table 1 shows the average age-standardized incidence rate per 100,000 of Korea during 1999 to 2012. Incidence rates of lip (0.07–0.10/100,000 people) and oropharyngeal cancer (0.09–0.12/100,000 people) remained low in the lip and oropharynx but high in the larynx.

**Cancer trends from 1999–2012**
Fig. 1 illustrates trends in HNC from 1999–2012 in South Korea. The incidence of oral tongue, major salivary gland, tonsil, and hypopharynx increased steeply compared to other HNCs during this time period. Increase ratios of HNCs for 10 years ranged from 1.00 (for laryngeal cancer) to 2.34 (for tonsil cancer). The increase ratios for 10 years of all HNCs except laryngeal cancer (1.00) and lip cancer (1.02) were over 1.10. The difference of increase ratios between two genders were great (over 0.3) for tonsil, hypopharynx, and larynx cancer, which means that the male incidence of HNCs has been increased more steeply than female incidence for those HNCs. Especially for laryngeal cancer, the increase ratio was 1.04 for male, while only 0.64 for female. This data is summarized in Table 2.

**Male-to-female ratio**
Male-to-female ratio was over 1.0 for all HNCs. Tonsil, hypopharynx, oropharynx, and larynx cancers had a ratio of >5.0, signifying a heavy predominance of these cancers in Korean men. Comparing the ratios between 1999–2001 and 2009–2011, those of nasopharyngeal cancer (2.44 to 1.31) decreased.
Table 1. Average age-standardized incidence rate per 100,000 of head and neck cancer during 1999 to 2012 in Korea

| Primary site                  | ICD-10 code | Total   | Male   | Female  |
|-------------------------------|-------------|---------|--------|---------|
| Lip                           | C00         | 0.07–0.10 | 0.10–0.10 | 0.00–0.04 |
| Oral tongue                   | C01, 02     | 0.72–0.80 | 1.07–1.18 | 0.42–0.51 |
| Oral cavity<sup>a</sup>       | C03–06      | 0.71–0.92 | 1.09–1.40 | 0.41–0.58 |
| Major salivary gland          | C07, 08     | 0.54–0.64 | 0.66–0.76 | 0.45–0.56 |
| Nasopharynx                   | C11         | 0.62–0.68 | 0.96–1.03 | 0.31–0.36 |
| Nasal cavity and paranasal sinus | C30, 31    | 0.48–0.52 | 0.67–0.73 | 0.32–0.37 |
| Tonsil                        | C09         | 0.36–0.46 | 0.66–0.84 | 0.10–0.13 |
| Hypopharynx                   | C12, 13     | 0.54–0.59 | 1.17–1.26 | 0.07–0.10 |
| Oropharynx<sup>c</sup>        | C10         | 0.09–0.12 | 0.22–0.29 | 0.00–0.00 |
| Larynx                        | C32         | 1.75–2.08 | 3.71–4.38 | 0.21–0.29 |

Values are presented as 95% confidence interval.
<sup>a</sup>International Classification of Diseases, 10th version. <sup>b</sup>Oral cavity cancer site: gum, floor of mouth, palate, and other and unspecified parts of the mouth, except for oral tongue. <sup>c</sup>Oropharyngeal cancer sites: base of tongue, lingual tonsil, pharynx not otherwise specified, and Waldeyer ring, except for tonsil.

Fig. 1. Trend of incidence number of head and neck cancers in Korea from 1999 to 2012. (A) Lip, (B) oral tongue, (C) oral cavity, (D) major salivary gland.

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Fig. 1. Continued. (E) nasopharynx, (F) nasal cavity/paranasal sinus, (G) tonsil, (H) hypopharynx, (I) oropharynx, and (J) larynx.
The prevalence of smoking among Korean adults is very high, especially for men. According to the data of the Korea National Statistical Office, the prevalence of smoking was 66.3% for men and 6.5% for women in 1998, since then continuously decreased to 42.1% for men and 6.2% for women in 2013. Jee et al. [17] reported some data in which consumption amount of tobacco increased steeply from mid-1950’s to mid-1990’s in South Korea and lung cancer mortality started to increase with similar proportion from 1980. The authors argued that the effect of smoking on lung cancer statistics would appear decades later due to a lag period between the exposure and the onset of disease [17]. The effects of smoking would results in similar trends of HNCs in Korea. Saito el al. [18] found that smoking over 40 years is poor prognostic factor for oropharyngeal cancer. A study by International Agency for Research on Cancer also reported that the relative risk for laryngeal cancer was greater than 10 for subjects who had smoked for greater than 40 years [19]. Therefore we can assume that the lag period between smoking exposure and the incidence of some HNCs is approximately 40 years. Considering this data, we could infer that the incidence of some HNCs in Korea will continue to increase until the mid-2030’s when considering decreased rates of tobacco use in the county.

Our data also illustrates that the incidence of all HNCs except laryngeal cancer increased from 1998 to 2012. The prevalence of smoking among Korean women did not vary much between 1998 and 2013, ranging from 5.2% to 7.4%. Our data found that the incidence of all HNCs for men outnumbered those for women significantly (male-to-female ratio, 1.23 to 18.35). However, the rates over 10 years did not show much change between men and women except in regards to laryngeal cancer (1.04 for men and 0.64 for women). For oral tongue, oral cavity, oral salivary gland, and oropharynx cancers, the rates of increase were greater among women than men. We have no specific explanation for this finding, except an increasing prevalence of women smoking during mid-1950’s to mid-1990’s.


disubstantially, while those of hypopharynx (13.70 to 18.35) and larynx cancers (9.54 to 15.53) became much greater. This data is summarized in Table 3.

**DISCUSSION**

The incidence of HNCs can vary considerably by country and gender [1,2,4]. According to an international comparison study by Simard et al. [1], the incidence of oral cavity cancer increased among both genders in some European countries, remained stable in a number of Asian countries, and decreased in Canada and the United States. In this study, the incidence of oropharyngeal cancer increased among both genders in eastern, some northern European nations, and some Asian countries, while declined in China and India [1]. For laryngeal cancers, incidence and trends varied by sex in other areas [1]. The exact reason for these differences are not fully understood, however differences in the level of consumption of tobacco and alcohol are believed to be the main reason [4].
Alcohol is also well-known risk factor for HNCs even though the effect is much smaller than tobacco [4]. Heavy drinking is not uncommon in Korea for both men and women. The prevalence of heavy alcohol use for men over the last 10 years is 24.9%, and 6.8% for women. According to World Health Organization [20], the annual amount of hard liquor consumption per person over 15 years is 9.57 liters in Korea, which is the highest of all surveyed countries. We did not have data about alcohol consumption in the Korean database, but we presume that alcohol use likely played an important role in the incidence of HNC in Korea, independently or synergistically with tobacco.

HPV also likely plays a role in the incidence of HNCs in Korea. The exact rate of oral infection with HPV is unknown, however, one study on Korean mothers and their neonates reported that HPV was detected in cervix of 72 among 469 pregnant women (15.4%) and in the mouth of 15 neonates (3.2%), with a rate of vertical transmission of 20.8% [21]. Another study based on Korean patients showed that the HPV was detected in 36% (13 of 36) of oral tongue cancer patients, compared with 4% (1 of 25) of normal controls [22]. Considering this data, we can infer that HPV likely contributes to the incidence of HNCs in Korea. Our study also showed that over the last 10 years the incidence for oral tongue (1.67 times) and tonsil cancers (2.46 times) increased rapidly compared to cancers of other HNCs. For laryngeal cancer, which is not known to be strongly associated with this virus, the incidence rate was stable for men (1.04 times) and even dropped steeply for women (0.64 times).

In conclusion, the incidence of all the HNCs except for laryngeal cancer has steadily increased for both men and women in Korea since 1998. Among the different types of HNC, oral tongue, major salivary gland, and tonsil cancer have seen the most rapid increase. Cancer in Korean males is higher than females for all types of HNCs, especially for cancer of the tonsil, hypopharynx, oropharynx, and larynx.

**CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

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