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Age-group-specific trend analyses of oropharyngeal squamous cell carcinoma incidence from 1989 to 2018 and risk factors profile by age-group in 2015–2018: a population-based study in The Netherlands

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Incidence of oropharyngeal squamous cell carcinoma (OPSCC) is increasing globally and the human papillomavirus (HPV) has been linked to this increase. This study aimed to present a comprehensive overview of OPSCC trends in incidence rates by age group and investigate differences in risk factors profile. Netherlands Cancer Registry data from 1989–2018 were analyzed to calculate the annual percentage change (APC) over European standardized incidence rates by gender and age group using joinpoint regression software. Smoking, alcohol drinking and HPV-status were available for 2015–2018. During 1989–2018, 13 048 cases of OPSCC were reported with a male-to-female ratio of 2.1:1. The overall incidence rate increased by 5.4% (APC) annually from 1989 to 1996 but slowed thereafter by 1.2%. Significant declines were found in patients of 35–44 years (APCs −3.7%). Adults aged 45–59 years displayed significant increases from 1989 to 2001, followed by a significant decline. In patients ≥60 years, the incidence rates increased overall, with APC for women being consistently higher than men. The data on HPV status was available for 69% of the patients, of whom 47% were HPV+. Smoking and alcohol consumption were more prevalent, that is 75 and 76 % respectively. The declining trends of OPSCC for Dutch people aged 35–44 years from 1989 to 2018 and for those aged 45–59 years from 2002 onwards are inconsistent to trends reported elsewhere in the developed countries. The prevalence of smoking and drinking alcohol was quite high in all age groups, whereas the proportion of HPV-positivity was relatively low. *European Journal of Cancer Prevention* 31: 158–165

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Introduction

In 2018, the most recent year for which global data is available, the estimated number of oropharyngeal cancer cases was 92 887, and the number of deaths 51 005 (Bray *et al.*, 2018). Of note, a dramatic rise in oropharyngeal squamous cell carcinoma (OPSCC) in many developed countries, including the Netherlands has been observed in the last two decades (Chaturvedi et al., 2008, 2011, 2013; Braakhuis *et al.*, 2014). This shifted trend has mostly been attributed to an increasing number of human papillomavirus-positive (HPV+) OPSCC (Gillison *et al.*, 2015). HPV+ OPSCC is established as a unique disease with specific biological and epidemiological features distinct from HPV-negative (HPV–) OPSCC. First, HPV+ OPSCC commonly affects patients at a younger age with less tobacco exposure and has a high propensity to occur at the base of the tongue and tonsils (Chi *et al.*, 2015). Further, HPV+ tumors have a good response to chemoradiation therapy and a better survival rate (Chung and Gillison, 2009). However, OPSCC profiles in relation to HPV appear to be changing: a very recent study has shown a significant change in the demographics of HPV+ OPSCC patients and found that the incidence is not limited anymore to the younger population, but is expanding in the elderly groups as well (Rettig *et al.*, 2018).

The last report on the age-standardized incidence rate of OPSCC for the Dutch patients analyzed cancer registry data up to 2011 showed a significant increase in the incidence for those older than 45 years. In recent years,

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a steady increase in the prevalence of HPV+ OPSCC among Dutch patients was reported, ranging from 5.1% in 1990 to 29% in 2010 (Rietbergen *et al.*, 2013). The data were updated in 2015 and revealed an attributable fraction of about 50% in 2015 (Rietbergen *et al.*, 2018). However, these studies made estimates that were largely based on single-institution data, making it difficult to be considered as a national prevalence estimate. In the current study, we aimed to perform a population-based study to update and expand the epidemiological information on OPSCC and determine its burden on the Dutch society, based on data from the Netherlands cancer registry (NCR). First, we investigated time trends in OPSCC incidence by age group and gender between 1989 and 2018. Second, from 2015 to 2018, the NCR recorded information on HPV status, smoking and alcohol consumption, and the prevalence of these factors in patients with OPSCC was estimated.

Methods

Data source and population

Using the NCR, all newly diagnosed patients aged 20 years and older with OPSCC from 1989 to 2018 were included. A comprehensive evaluation of the data of NCR has shown that the registry database is complete and has recorded approximately 95.2% of all pathology-confirmed cancers, including OPSCC (van der Willik *et al*, 2020). We limited our analysis to cases diagnosed with squamous cell carcinoma (SCC) based on the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) and histology codes (M8050–M8084), localized at the following subsites: base of the tongue (C01.9, C024), soft palate (C05.1), uvula (C05.2), tonsil (C09) and other or unspecified parts of the oropharynx (C10). The collected data included all variables needed in the current analyses (histopathology, primary site, age at diagnosis and gender). Incidence rates for gender by age group were expressed as the European age-standardized rate (ESR) per 100 000 person-years and the data were classified into five age groups: young adult (20–34) years, adult (35–44) years, middle-age adult (45–59) years, early elderly (60–74) years and late elderly (+75) years.

The NCR began collecting data on risk factors in 2015. Thus, information about HPV-status, smoking and drinking habits was available only for the last 4 years of the study period (2015–2018). In the Netherlands, the national guideline for the detection of high-risk HPV in OPSCC tumors is performing P16 immunostaining, as a screening step followed by PCR for HPV type-specific DNA; both tests should be positive. P16-immunopositive is defined as strong and diffuse nuclear and cytoplasmic staining in 70% or more of the tumor cells. In the registry, patients were considered as positive if P16-immunostaining was positive and not followed by a negative HPV PCR test. Patients with a negative P16-immunostaining or negative HPV PCR were recorded as negative. Records without any information about HPV-testing were considered as unknown. With regard to smoking tobacco, it was defined in terms of cigarettes and cigars and was reported as smoking status (current/past smoker and never). Quantification of tobacco smoking was calculated in pack-year and 20 pack-year was chosen as a cutoff point for grouping the patients. Similarly, data on alcohol consumption were obtained and classified as follows: 'current drinker/past drinker' and 'never'. Regarding alcohol amount, because risky alcohol use was defined as >14 drinks/week among women and >21 drinks/week among men (Veerbeek *et al.*, 2019), and a new guideline has been adapted in the UK, in which 14 units/week is identified as a hazardous dose for both genders (Department of health, 2016),14 beverages per week was used as a cutoff point to dichotomize the patients into two groups. To facilitate understanding characteristics and risk factors for this disease, we analyzed differences between younger and older patients with regard to gender, subsites, clinical-stage, smoking, drinking and HPV status for that period.

Statistical analysis

Trends in the incidence rates for the five age-groups were assessed by the annual percent change (APC), average

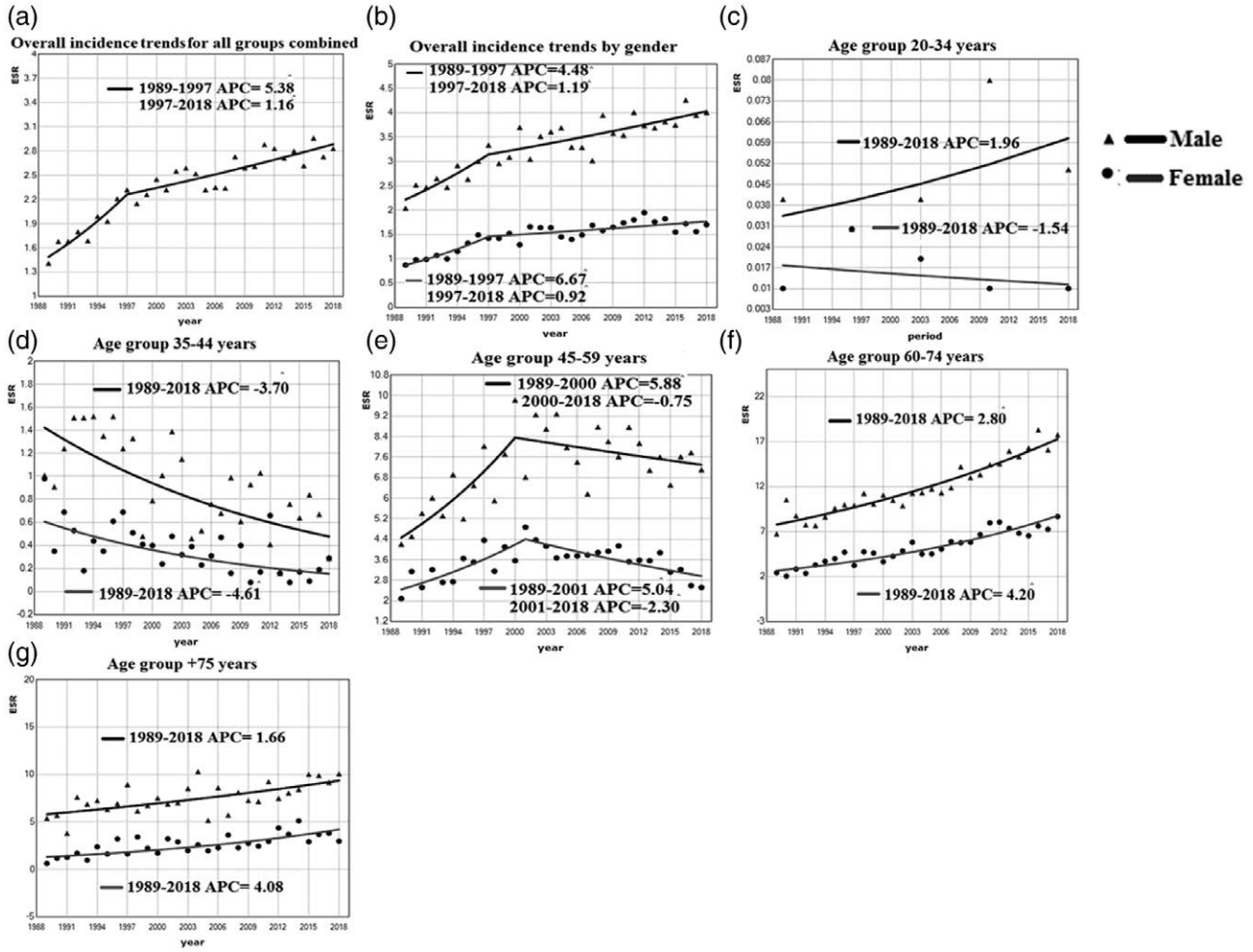
Table 1 General characteristics of 13 048 patients with oropharyngeal SCC diagnosed in 1989–2018 by age groups

	Age groups				
Variables All age	20–34 years	35–44 years	45–59 years	60–74 years	75+ years
Total *N* (row %) 13 048 (100)	32 (0.3)	470 (4)	5287 (41)	5845 (45)	1414 (11)
Gender *N* (column %)					
Male 8863(68)	24 (75)	339 (72)	3,591(68)	4,000 (68)	909 (64)
Female 4185 (32)	8 (25)	131 (28)	1,696 (32)	1,845 (32)	505 (36)
Anatomical sites *N* (column %)					
Tonsil 5074 (39)	8 (25)	202 (43)	2157 (41)	2154 (37)	553 (39)
Base of the tongue 3392 (26)	14 (44)	137 (29)	1357 (26)	1499 (26)	385 (27)
Soft palate and Uvula 1593 (12)	3 (9)	34 (7)	634 (12)	772 (13)	150 (11)
Other oropharynx/NOS 2989 (23)	7 (22)	97 (21)	1139 (21)	1420 (24)	326 (23)
Clinical stages[a] *N* (column %)					
local disease (stage I and II) 2893 (22)	8 (25)	91 (19)	1125 (21)	1346 (23)	323 (23)
advanced disease (stage III and IV) 9880 (76)	22 (69)	366 (78)	4056 (77)	4385 (75)	1051 (74)
Unknown 275 (2)	2 (6)	13(3)	106 (2)	114 (2)	40 (3)

NOS, not otherwise specified.

[a]During the study period of time, several editions of the International Union against Cancer (UICC) TNM classification were used to record tumor stages: 4th edition (1989–1998) 5th edition (1999–2002), 6th edition (2003–2009), 7th edition (2010–2017) and 8th edition (2018).

Fig. 1



Joinpoint regression analysis shows trend of incidence of oropharyngeal squamous cell carcinoma (1989–2018), ESR: European age-standardized rate per 100 000 person-years. ^ indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha=0.05 level. The APC of age group of 20–34 years was calculated in period of five equally spaced calendar (1989–1994, 1995–2000, 2001–2006, 2007–2012 and 2013–2018). Note: Data on the confidence interval (CI) are presented in the supplementary table S1.

annual percentage change (AAPC) and the corresponding 95% CIs, with the Joinpoint Regression Analysis program (version 4.6.0.0), obtained from the National Cancer Institute *(http://surveillance.cancer.gov/joinpoint)* (Kim *et al.*, 2000; Joinpoint regression Program, 2018). This analysis program selected the best-fitting log-linear regression model to identify calendar years (i.e. the join points) when APC changed significantly, allowing for the minimum number of join points necessary to fit the data. However, because these tumors are rare, splitting up according to gender led to ESR-values of 0, specifically in the youngest population aged 20–34 years; therefore, the year of diagnosis in this group was clustered in five equally spaced calendar periods (1989–1994, 1995–2000, 2001–2006, 2007–2012 and 2013–2018)

To investigate differences in patient and tumor characteristics by age group for data of the years 2015–2018, Kruskal–Wallis was used for continuous variables (Kolmogorov–Smirnov test, $P<0.05$) and Pearson (χ^2) or Fisher's exact tests with the Monte Carlo simulation for categorical variables. Measured data of continuous variables were presented as a median and P25 and P75 (allows for interquartile range calculation), and count data as *N* (%). All statistical analysis was performed using SPSS version 24 (IBM Corp. New York, USA, 2016).

Results

A total of 13 048 OPSCC cases were registered in the Netherlands during the period 1989–2018: 8863 males (68%) and 4185 females (32%) with a male-to-female

Table 2 Prevalence of individual risk factors for different age groups for years 2015–2018

	Age groups						
Variables	All age	20–34 years	35–44 years	45–59 years	60–74 years	75+ years	*P* value
Total *N* (row %)	2539 (100)	3 (0.1)	34 (1.5)	773 (30)	1417 (56)	312 (12)	
HPV status *N* (column %)							**<0.001**[a]
Positive	820 (32)	1 (33)	19(56)	323 (42)	396 (28)	81 (26)	
Negative	938 (37)	2 (67)	7 (20)	254 (33)	565 (40)	110 (35)	
Unknown	781 (31)	0 (0.0)	8 (24)	196 (25)	456 (32)	121 (39)	
Smoking status *N* (column %)							**<0.001**[a]
Current or past	1899 (75)	0 (0.0)	22 (65)	577(75)	1083 (76)	217 (70)	
Never	236 (90029	3 (100)	7(20)	84(11)	105(7)	37 (12)	
Unknown	404 (16)	0 (0.0)	5 (15)	112 (14)	229 (16)	58 (18)	
Pack-years *N* (column %)							**<0.001**[a]
≤20 pack-year	241 (13)		9 (41)	69 (17)	114 (11)	22 (10)	
≥21 pack-year	931 (49)		5 (23)	276 (48)	557 (51)	93 (43)	
Unknown	727 (38)		8 (36)	232 (40)	412 (38)	102 (47)	
Median (P25, P75)[b]	40 (25,50)		18 (10, 25)	34 (20,40)	40 (25,50)	40 (23,52)	**<0.001**[c]
Alcohol status *N* (column %)							**<0.001**[a]
Current or past	1927 (76)	1 (33)	25 (73)	607(79)	1094 (77)	200 (64)	
Never	68 (3)	2 (67)	2 (6)	18 (2)	31 (2)	15 (5)	
Unknown	544 (21)	0 (0)	7 (21)	148 (19)	292 (21)	97 (31)	
Number of alcoholic beverages per week *N* (column%)		0.003[d]					**0.003**[d]
≤14	796 (41)	1 (100)	13 (52)	249 (41)	443 (40)	90 (45)	
≥15	753 (39)	0 (0)	5 (20)	231 (38)	448 (41)	69 (34)	
Unknown	378 (20)	0 (0)	7 (28)	127 (21)	203 (19)	41 (21)	
Median (P25,P75)[b]	14 (7,28)	1(1,1)	9.5 (2, 18)	14 (5, 35)	15 (7,28)	14 (7, 28)	**<0.001**[a]

Statistically significant *P* values are shown in Bold.
HPV, human papilloma virus.
[a]Fisher exact.
[b]Median calculated by Interquartile range (Percentile 25th, Percentile 75th).
[c]Kruskal wallis test.
[d]chi-square.

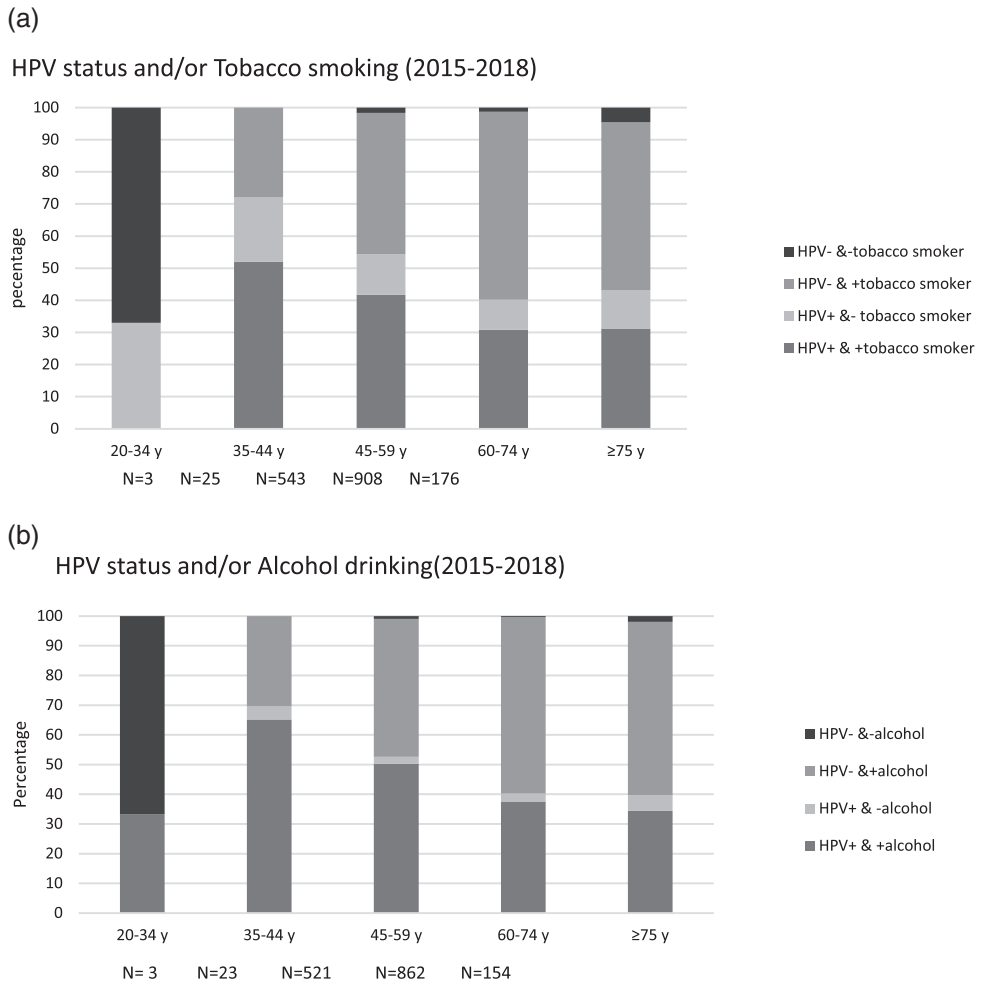
ratio of 2.1:1. Tonsil (39%) and base of the tongue (26%) accounted for two-thirds of all cases that occur in the Netherlands. The young adult groups aged 20–44 years accounted for 502 cases (4%). The results also showed that 76% of the OSCC patients presented with an advanced stage disease (Table 1).

The results of joinpoint analysis on the trend of OPSCC among the Dutch population between 1989 and 2018 are presented in Fig. 1 (and Supplementary Table S1, Supplemental digital content 1, *http://links.lww.com/EJCP/A321*). The analysis revealed a clear upward trend in the overall incidence with an AAPC of 2.3%. A significant cutoff point was noted in 1997; before which a steep APC increase of 5.4 % was observed (Fig. 1a). During the same period, the corresponding AAPC was 2.1% per year in males overall and 2.5% per year in females overall.

When age-specific trends were analyzed, the incidence trend of OPSCC was stable in those 20–34 years of age (APC = 2.2; CI, −4.8 to 9.6) (Fig. 1c), whereas a significant decline in the group aged 35–44 years for both males and females with APC −3.7 and −4.6, respectively, was observed (Fig. 1d). Combining the two young adult groups (20–44 years), showed a significant annual decrease of −3.4 % (Supplementary Table S1, Supplemental digital content 1, *http://links.lww.com/EJCP/A321*). For the cohort 45–59 years, the incidence rate increased significantly from 1989 to 2001 (APC = 5.2), but showed a decline thereafter (2001–2018; APC of −1.4%), specifically among females. In the older age groups, the AAPC increased significantly in both genders, though the AAPC was consistently higher in females than in males. The largest positive AAPC was observed in females aged 60–74 years (APC = 4.2), followed by females aged 75 years and older (APC = 4.08) (Fig. 1g and f).

Table 2 presents data of the last 4 years of the study period (2015–2018) and shows the prevalence of classical risk factors at diagnosis in different age groups. The table shows that 75% of the patients were current or former smokers and 76% were alcohol consumers. It is also apparent from this table that the 60–74 years old patients had the highest level of alcohol consumption; 41% drank >15 beverages per week. The proportion of OPSCC that tested positive for HPV was 32% (76% were males; data not shown), 37% was negative and 31% was unknown. Considering variation among different age groups, noticeably, the young adult aged 35–44 years had nearly 3 times the rate of being positive than being negative (56 vs. 21%). Likewise, in adults aged 45–59 years old, we found 42% of the patients were positive vs. 33% who were negative. For the older groups, although a high percentage of the data was missing, the percentage of the patients with HPV-negative tumors was higher than that who had HPV+. The data also revealed that high proportions of the HPV+ patients were concomitantly smokers or drinkers (Fig. 2a and b).

Fig. 2



(a) Percentage of patients with different human papilloma virus (HPV) status and/or tobacco smoking across different age groups. Patients were not included if either HPV-status or tobacco smoker was unknown. (b) Percentage of patients with different HPV status and/or alcohol drinking across different age groups.Patients were not included if either HPV-status or alcohol drinking was unknown. +alcohol, ever drinker; —alcohol, never drinker; + tobacco smoker, ever smoker; —tobacco smoker, never smoker; HPV+, human papilloma virus positive; HPV—, human papilloma virus negative; N, absolute number of the patients.

Discussion

This study aimed to assess the national trends of OPSCC incidence over three decades, with emphasis on age-specific trends, and to report on risk factor proportions by age group. The data confirm that the overall incidence rate of OPSCC in the Dutch population increased significantly during the past 30 years (AAPC = 2.3%). This increasing incidence over the years was most pronounced in patients 60 years or older. Intriguingly, from 1997, the overall annual rate still showed an increase but at a very slow pace (AAPC = 1.2%). In the last 4 years of the studied period, HPV status data were available only for 69% of OPSCC Dutch patients, of whom 47% were HPV+.

The increasing trend of OPSCC for all cohorts combined in the current study is consistent with two previous reports from the Netherlands (Braakhuis *et al.*, 2014; van Monsjou *et al.*, 2015). This result is also similar to several figures reported in economically developed nations (Chaturvedi *et al.*, 2011; Ariyawardana & Johnson, 2013; Mork *et al.*, 2010; Denson *et al.*, 2016; Owosho *et al.*, 2019; Tota *et al.*, 2019), though the increase in the annual rate for Dutch patients (2.3%) was much lower than the average level reported in Taiwan (6.9%) (Hwang *et al.*, 2015), Denmark (5.3%) (Jensen *et al.*, 2018) and Canada (4.6%) (Mifsud *et al.*, 2017). A noteworthy finding of the current study was that from 1997 the AAPC still showed an increase, though at a much smaller rate than before.

Even though we do not have a clear explanation on why the APC increased less steeply since 1997, this might be a reflection of the decline in the number of people that smoked in the Netherlands which started in the 1960s (Janssen and van Poppel, 2015). Because the impact of tobacco use on cancer incidence becomes manifest only after a latency period of approximately 25–30 years the effect of smoking cessation would therefore become visible in the late 90's indeed (Kleinsmith, 2005). It is also worth noting that the reported upsurge in the prevalence of HPV-infection globally (Chaturvedi *et al.*, 2011; Hong *et al.*, 2016; Carlander *et al.*, 2017) during the last two decades was not conspicuous in the Netherlands (Stein *et al.*, 2015), suggesting tobacco and alcohol use still being the leading risk factors related to Dutch incidence trends.

In contradiction with several reports from the USA that have shown a rise in the incidence of OPSCC for white patients younger than 45 years, our data revealed a significant decrease in the annual incidence rate for this age group, in particular within those aged 35–44 years (APC of –3.7%) (Shiboski., 2005; McGorray *et al.*, 2012; Gayar *et al.*, 2014). This result matches with a reported previous observation in the Netherlands (Braakhuis et al., 2006, 2014). A decline in OPSCC incidence rates in young adults was also reported in France (Ligier *et al.*, 2011). This regional discrepancy is most likely not related to smoking or drinking because smoking and drinking rates declined in these three countries (Janssen *et al.*, 2019; Stivoro, 2013; Wang *et al.*, 2019). Of interest, however, it was found that increasing trends in young patients were mainly observed in HPV-related sites (Chaturvedi *et al.*, 2008; Shiboski *et al.*, 2005). This is in accordance with other findings that the prevalence of HPV in biopsies of tonsil carcinoma in patients younger than 40 years was high (10/11 = 91%) (El-Mofty and Lu, 2003). Therefore, this progressive trend in this age group is believed to be linked to the presence of an oncogenic HPV infection. Although the prerequisite persistent infection period appears quite short in this young patient group, it has been assumed that either or all of virulence of HPV strains, site-specificity and methods of transmission have significant roles in the promotion of malignant clones (El-Mofty and Lu, 2003; Gayar *et al.*, 2014).

In 2010, a substantial increase in the proportion of OPSCC in the patients aged 40–59 years was found, that is from 35 to 45% of all oropharyngeal carcinoma patients based on SEER data (Mehta *et al.*, 2010). This is supported by several studies around the globe, which showed a faster pace increase for OPSCC incidence rate at the median age of 50 years, solely in HPV-related sites (Chaturvedi *et al.*, 2008; Forte *et al.*, 2012; Hwang *et al.*, 2015; Mifsud *et al.*, 2017). Therefore, a conventional belief of increasing the trend of HPV-driven OPSCC exclusively in the people aged 45–59 years emerged (Chaturvedi *et al.*, 2013). Surprisingly, for those aged 45–59 years, our findings closely mirrored those studies during the 1990s only. However, since the year 2000, there was a significant decline in the trends for this subpopulation of Dutch patients which was most prominent in women. It remains unclear to us what could be the reason behind this phenomenon, and we do not have an explanation other than the relation to cessation of smoking as argued above. However, the importance of this finding within this timeframe may lie in the fact that the casual role for HPV is minimal in the Netherlands, suggesting cultural diversity in regard to HPV-infection among western societies.

In the current article, we observed the highest increase in APC in those 60–74 years of age at diagnosis. This is consistent with what was reported for England by Owosho *et al.* 2019. The authors reported a significant increase in OPSCC annual rate for the patients in the 6th and 7th decade of life with APC of 3.06 and 4.98%, respectively (Owosho *et al.*, 2019). Also in England, a doubling in the incidence of OPSCC for the patients aged 60–69 years in the period of 2002–2011 was reported (McCarthy *et al.*, 2015). Of interest, in the US divergent results on the SEER database were reported and no significant increase in OPSCC incidence for the population ≥60 years between 1973 and 2004 was found (Chaturvedi *et al.*, 2008). However, in a recent publication based on SEER data from later years (2000–2012), there was a significant increase in the age-adjusted incidence of OPSCC in the patients aged 65 years and older (Zumsteg *et al.*, 2016). A shifted paradigm of the typical HPV-positive OPSCC patients and increasing prevalence of HPV-infection among elderly patients with oropharyngeal carcinoma has been reported in the last 10 years in the USA (Rettig *et al.*, 2018). It was reported that the proportion of HPV+OPSCC increased from 41% during 1995–2000 to 70% during 2007–2013 in those aged 65 years and above (Windon *et al.*, 2018). A similar pattern has also been observed for the period of 2010–2015, where the prevalence of HPV+ OPSCC increased among patients 70 years or older from 45.1 to 63.3% (Lu *et al.*, 2018). This evolving picture is unclear for the Dutch population, in which our data revealed that the lowest proportion of HPV-related OPSCC was found among patients aged 60 years and older.

Several publications have reported higher proportions of HPV+OPSCC among never tobacco/alcohol users than former or ever users, which has resulted in a common conception that HPV-driven OPSCC is a distinctive disease in nonsmokers/nondrinkers (Deschler *et al.*, 2014). By contrast, our results showed that HPV+ patients were frequent tobacco/alcohol users. This is consistent with a recent study in the USA that evaluated the burden of HPV+OPSCC among never and ever smokers at the population-level and found a significant increase in the

incidence of this type of tumor among ever smokers compared to never smokers for both genders (Chaturvedi *et al*., 2016). It was also found that the prevalence of high-risk oral HPV type 16 was higher in current smokers (2%) than in never smokers (0.6%) (Fakhry *et al*., 2014). Although the potential role of smoking in the development of HPV+ OPSCC has been a subject of debate, it has been suggested that HPV– infection alone is not a sufficient cause of the development of OPSCC, but that smoking substantiates the risk of malignancy in both HPV+ and HPV– individuals (Smith *et al*., 2010).

To our knowledge, we report the first population-based data on HPV-status among Dutch OPSCC patients. Despite the fact that the data was only available for the last 4 years, it provides critical information. Of note, we report a relatively large proportion of unknown cases. Whether patients are not tested or the results are not to be found in the patient file, we do not know, because we have to rely on reporting in the patient file. Nonetheless, the proportions of unknown cases decreased year after year (from 40% in 2015 to 23% in 2018) (Data not shown). Hopefully, with the introduction P16/HPV status in the TNM8-staging classification, completeness will become a problem of the past soon. The data on HPVstatus was available for 69% of the patients, of whom 47% were HPV+ (2015–2018). This result broadly supports earlier publications reporting that HPV positivity attributed to 48% of OPSCC among Dutch patients (Rietbergen *et al*., 2018). Nonetheless, the proportion observed in the current study is considerably lower than the proportions reported from the national datasets of New Zealand (77.9 %)(Lucas-Roxburgh *et al*., 2017) and Denmark (62%) (Carlander *et al*., 2017). Such disparity between different populations might be a reflection to various methods of viral detection, but geographical differences in cultural practices and sexual behavior may also be of influence.

A strength of this study is the presentation of a comprehensive image of age- and gender-specific incidence trends OPSCC, including Dutch patients for a long period (30 years). Unfortunately, splitting up national data by year, sex, and age group leads to small numbers, preventing additional analyses by subsite. Although our major focus was put to analyze changing incidence trends by calendar year of diagnosis, extending the model to consider birth cohort effect would be a useful direction for future work to help in understanding the contribution reasons beyond changes in trends. Our data on risk factors does not help to explain the observed trends and trends breaks, because these data were only available for the last 4 years. However, the information on HPV-status, smoking and alcohol consumption does give an insight into the difference between age groups. Finally, though we could illustrate the differences by age group, we cannot make definitive statements about cause-effect links. This is because patient and tumor characteristics, including lifestyle habits, were only available at the time of diagnosis of the tumor

In conclusion, the incidence patterns of OPSCC show significant decline for age groups of 35–44 years and 45–59 years, indicating OPSCC is predominantly a disease of the elderly in the Netherlands. The prevalence of smoking and drinking alcohol was quite high in all age groups, whereas the proportion of HPV-positivity was relatively low, showing that tobacco and alcohol use remain leading factors in OPSCC for Dutch patients.

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Conflicts of interest

There are no conflicts of interest.

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