Knowledge and Attitudes of Oral Health Students and Professionals Related to HPV-related Oropharyngeal Cancer and Selected Oral Mucosal Lesions

Marcella Renée Poelman

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1

Introduction

HPV-RELATED HEAD AND NECK CANCER

Head and neck cancers (HNC) are a broad spectrum of cancers that occur in the head and neck region and include the lip, oral cavity, nasopharynx, oropharynx, hypopharynx, larynx and salivary glands. More than 90% of HNCs arise from the mucosal lining and are squamous cell carcinoma (SCC). The overall incidence of HNC is increasing globally with a wide geographical variation [1-4]. In Europe, the annual incidence was 139,500 cases for the year 2012 and increased to 161,200 new cases in 2018 [1,5]. In the Netherlands, the annual incidence of new diagnosed HNC was 1,934 patients in 1989 and had increased to 3,159 patients in 2022. In 1989, 388 (20,1%) of these cancers were localized in the oral cavity and in 2022 this number was 1,039 (32,9%) [6]. The annual number of new cases of oropharyngeal cancer rose from 214 cases in 1989 to 689 cases in 2022 (Fig. 1). Classical risk factors for HNC are tobacco use, both smoked and smokeless, and excessive alcohol consumption, which have a synergetic correlation, and are estimated to account for 70% of all HNC SCC [7].

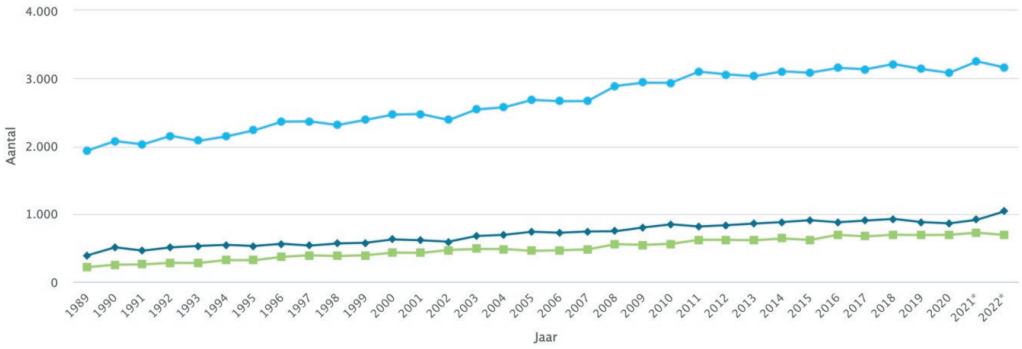

Figure 1. Number of patients diagnosed per year with head and neck cancer (light blue), oral cancer (dark blue) and oropharyngeal cancer (green), in The Netherlands [8].
*Provisional numbers.

In 2017, the International Agency for Research on Cancer (IACR) indicated infection with the human papillomavirus (HPV) as an independent risk factor for oropharyngeal cancer [9,10]. Oropharyngeal squamous cell carcinoma (OPSCC) are categorized into HPV-positive and HPV-negative OPSCCs. The anatomy of the pharynx is shown in figure 2.

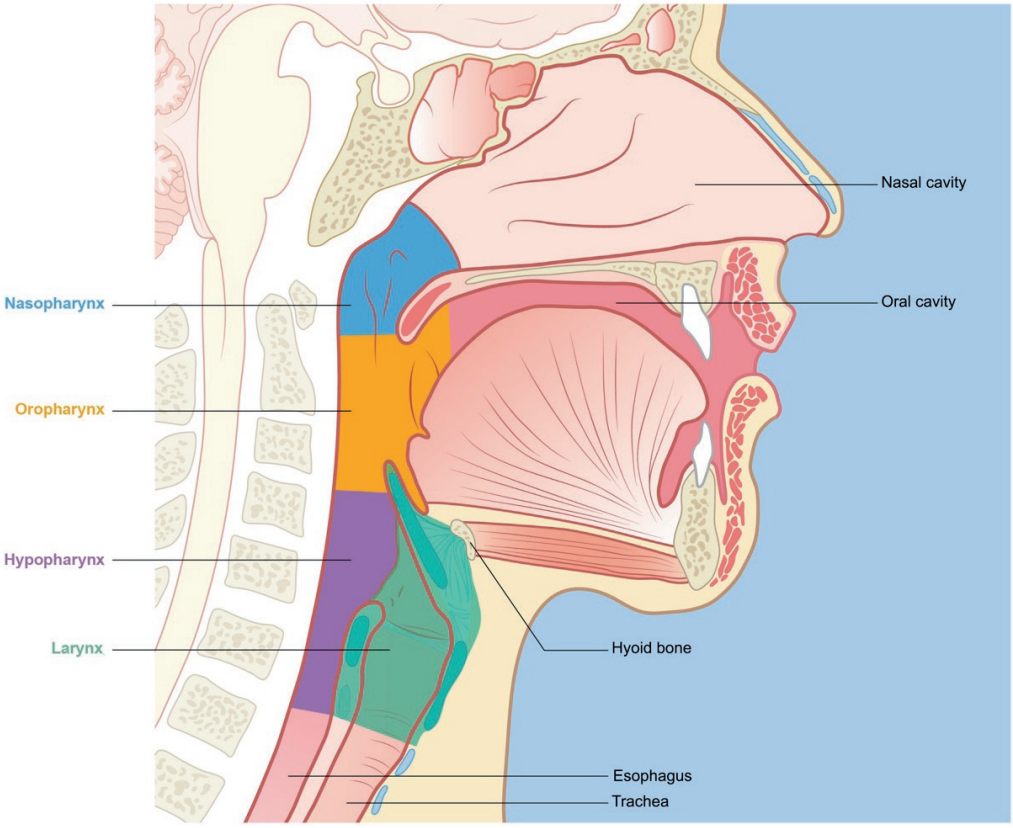

Figure 2. Anatomy of the pharynx. Illustrated by Maartje Kunen.

There is increasing evidence that the pathogenesis of HPV-positive carcinomas is different from HPV-negative, which is confirmed by molecular and clinical differences between these two categories [11]. HPV-positive OPSCCs appear to have a better response to chemo- and radiotherapy than HPV-negative OPSCCs, and patients with HPV-positive OPSCCs have better survival rates [12,13]. Therefore, HPV-testing has recently been proposed to be included in the standard procedure for diagnosis of OPSCC.

In 2012, approximately 40% of OPSCC in Europe was HPV-positive and in the United States 71%. This proportion of HPV-positive OPSCC in the overall incidence of OPSCC increases globally almost every year [2,14,15]. In The Netherlands, the incidence of OPSCC rises slightly over time (Fig. 2) with an increase in the portion of HPV-positive OPSCC; this amounted 5% in 1990, 29% in 2010 and 46% on average between 2015-2018 [16,17]. So, nowadays, in The Netherlands, half of the patients that are diagnosed with an OPSCC and tested for HPV, have an HPV-positive carcinoma [17].

More than 200 types of HPV have been recognized, based on DNA sequence data, showing genomic differences. Before infection with HPV was recognized as a risk factor

for OPSCC, it was known that HPV infection was related to anogenital diseases including cancer, precancerous lesions and genital warts. The virus is usually transmitted sexually and the infection is asymptomatic in most cases and usually cleared by the immune system within 2 years. Based on their association with cervical cancer and precursor lesions, HPVs can be grouped into high-risk and low-risk HPV types. Low-risk HPV types include types 6, 11, 42, 43, and 44. High-risk HPV types include types 16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, and 70. HPV 16 and 18 were the first types to be classified as having a carcinogenic potential for cervical cancer and a persistent infection with one of these types is responsible for almost all cases of cervical SCC, more than 90% of anal cancers and a smaller portion of vulvar, vaginal and penile cancer [9].

A persistent infection of the epithelium with a high-risk type of HPV can progress into a precancerous lesion and, in the long turn, to development of cancer [18]. This process starts with the infection of the basal epithelial cells of mucosal tissues, which get exposed through micro-wounds. After infection with HPV, these basal cells proliferate to HPV-positive differentiated cells in the epithelium. In cells that are infected with high-risk HPV types, the presence of oncoproteins E6 and E7 allows DNA damage. Both proteins function by targeting critical pathways that are essential for maintaining cellular homeostasis of the epithelial host cell and create an environment that is favourable for reproduction of the virus and DNA damage. Cells that are persistently infected with HPV, and undergo repeated rounds of DNA synthesis with presence of DNA damage, have a high risk for mutation. This mutation can be mild to moderate and cause lesions that regress spontaneously within 1 to 2 years. Failure of the immune system to clear this infection can result in development of cancer after 15 to 20 years [19,20].

HPV-positive OPSCCs preferentially arise in the tonsils and base of the tongue. This is assumed to be related to biological interactions between HPV and the lymph epithelium lining of the tonsillar crypts and in the base of the tongue. This tissue may provide an immune-privileged site that favours persistent HPV-infection [21]. Primary tumours are relatively small and asymptomatic and the first symptom observed by the patient is often a swelling in the neck, due to regional lymph node metastasis.

Patients diagnosed with HPV-positive OPSCCs have different characteristics compared to patients with HPV-negative OPSCCs; they are more often middle-aged white men, who use less tobacco and alcohol, have a good socioeconomic status and have more lifelong sexual partners. In contrast with the oropharyngeal site, only a small percentage of oral SCC is caused by HPV infection, just about 4% [22]. In the Netherlands, the HPV-prevalence is very low whereby 2.2% of oral SCC were HPV DNA-positive [23].

HPV-VACCINATION

HPV-related cancer is preventable through HPV vaccination. More than 100 countries have included HPV-vaccination in their national immunization programmes for girls with the aim of protecting against cervical cancer [24]. In The Netherlands, thirteen-year-old girls receive an invitation for this vaccination since 2010 and vaccination uptake rose from 52% in 2011 to 63% in 2020 [25]. Recent research shows that HPV-vaccination is also effective in preventing oropharyngeal and anogenital HPV infection and that introduction of pan-gender vaccination most likely will result in a significant decrease in HPV-related cancer at these specific anatomical locations [24,26]. Therefore, the United States, Australia and some European countries introduced the HPV-vaccination for boys; England introduced it in 2018 and in The Netherlands it is available since 2022 [25-27]. Some countries even lowered the age for routine vaccination from 11 or 12 years to 9 years of age [25].

There are currently three types of HPV-vaccinations available in many countries throughout the world, including the Netherlands. These are a bivalent (Cervarix®), a quadrivalent (Gardasyl®), and a nonvalent vaccination (Gardasil 9®). They are all highly effective in preventing infection with high-risk types HPV 16 and 18. The quadrivalent vaccination additionally provides protection against HPV 6 and 11, which cause oral and anogenital warts. The nonvalent vaccination provides protection against infection with high-risk types HPV 31, 33, 45, 52 and 58 [28].

ORAL HEALTHCARE PROVIDERS AND HPV

Prevention of HPV-related cancer requires efforts of multiple kinds of healthcare providers. In addition to national health programmes, among others including HPV vaccination and screening for cervical cancer, oral healthcare providers could play a role in possible prevention and early detection of OPSCC. However, it is debatable to what extent oral healthcare providers in The Netherlands should engage in these prevention practices. The American Dental Association encourages oral health professionals to educate patients about the relation between HPV and oropharyngeal cancer and counsel patients about HPV-vaccination [29]. Dutch oral health professional organizations currently do not encourage oral healthcare professionals to engage in various aspects of HPV-related prevention. Providing patients with information about HPV and vaccination is covered by the government as part of the National Immunization Programme (Rijksvaccinatieprogramma), as well as by general practitioners. Recently, the government launched campaigns about HPV vaccination not only protecting against cervical cancer, but also protecting against a broader range of cancers, including OPSCC [25]. Research has shown that the introduction of HPV vaccination results in an increase of public HPV-related awareness and knowledge [30-32]. However, data of a recent study in The Netherlands

showed that public knowledge regarding the association of HPV with OPSCC is limited whereby only 27% of the interviewed reported to be aware of this relation [33]. This gap in public knowledge indicates a need to increase public education on HPV and OPSCC. Furthermore, campaigns of national immunization programmes may result in patients approaching their oral healthcare professional with questions about HPV-related OPSCC [25]. To provide patients with HPV-related information, knowledge of this topic among oral healthcare professionals needs to be sufficient and up to date. International research identified knowledge deficits among these professionals and observed that their HPV-related knowledge was insufficient [34-36]. In The Netherlands, research on HPV-related knowledge levels among oral healthcare professionals has not been conducted yet.

Answering patients' HPV-related questions is different from actively engaging in prevention. Besides sufficient HPV-knowledge, factors that influence whether professionals will engage in prevention practices are attitudes, subjective norms and perceived control [37]. Active involvement in preventive measurements on various aspects of HPV-related cancer requires positive attitudes towards HPV vaccination and the positive effect of prevention practices. Additionally, positive subjective norms are required, which include positive believes about what healthcare professionals would like their patients to do and patients' willingness to comply with this behaviour such as getting HPV vaccination or changing high-risk sexual behaviour. Patients' trust and beliefs about the professional knowledge, experience, involvement and dedication of oral healthcare professionals' carrying out this kind of prevention is of decisive importance. Perceived control is the amount of control that professionals experience when performing prevention, such as confidence in counselling skills about HPV or confidence in performing an examination for OPSCC.

Primary prevention includes reducing high risk behaviour in patients such as tobacco and alcohol use and is effective in reducing the incidence of oral cancer [38]. To reduce the risk for HPV-related OPSCC, providing patients with information about transmission of HPV, including high risk sexual behaviour and the added value of timely HPV-vaccination is necessary. Research in the United States has shown that oral healthcare professionals were willing to play a role in primary prevention [34,39]. However, they do not feel comfortable about discussing HPV and OPSCC with their patients and experienced barriers that were related to the practice environment and the sensitive topic of sexual transmission of HPV. They preferred using passive materials such as pamphlets, videos or posters to inform their patients about HPV, that would stimulate patients to initiate a conversation about HPV [40].

Secondary prevention involves clinical examination for the early detection of oral cancer. The potential effect of clinical examination by oral healthcare professionals on early detection of OPSCC is limited since primary tumours are relatively small and

complete visual inspection of the preferred locations, e.g. tonsils and base of the tongue, during normal dental examination is not very likely. A first symptom of OPSCC may be an enlarged lymph node in the neck, which could be detected during palpation of the neck region [12,41]. Regional lymph node metastasis often occurs in advanced stages of HPV negative OPSCC but is not uncommon to be the first manifestation in an early HPV positive OPSCC. Other more or less common clinical symptoms of OPSCC include a persistent sore throat, pain when swallowing, one-sided ear pain, hoarseness of a persistent lump in the throat [12]. Oral healthcare professionals should be aware of these symptoms when performing a dental check-up.

ORAL CANCER EXAMINATION

Clinical oral cancer examination consists of a white-light visual inspection and palpation of the oral cavity mucosa and the external face and neck. This examination does not intend to be diagnostic but aims to identify patients with abnormal findings, and accelerate referral and application of more specific diagnostic procedures by a specialist [42]. Evidence is lacking for the added value of screening methods for early detection of a tumour such as vital rinsing, light-based detection, mouth self-examination, remote screening and biomarkers [42]. Although strong evidence for an organized oral cancer screening programme for an asymptomatic population is lacking, oral healthcare professionals should perform an opportunistic examination for oral cancer at every regular check-up appointment [42,43].

Early stage OSCC and oral potentially malignant disorders (OPMD) are often asymptomatic and may mimic benign lesions, so patients often do not seek care [42]. Tumour size at diagnosis and especially the absence or presence of regional metastasis are the most important prognostic factors for survival [44]. The reported 5-year survival of patients with localised disease is 82% and with local and regional disease 51% [45]. When distant metastasis are present, survival rates are poor: the 2-year survival rate is reported to be only 26% [46]. Early detection and treatment of oral cancer results in high survival rates and limited health related quality of life and sequelae due to treatment [47,48]. The oral cavity is an anatomical region easy to be examined by oral healthcare professionals and therefore their knowledge needs to be sufficient to detect abnormalities of the oral mucosa and subsequently provide correct management or referral of patients [49]. Lack of knowledge among healthcare professionals is one of the factors that is associated with a delayed diagnosis [50].

ORAL POTENTIALLY MALIGNANT DISORDERS

Oral squamous cell carcinoma (OSCC) is the most common form of oral cavity cancer and a proportion is preceded by oral potentially malignant disorders (OPMDs). This is a group of mucosal disorders that are diagnosed based on clinical alterations of the oral mucosa such as changes of colour, swelling or ulceration [51]. Not all OPMDs eventually develop into OSCC; they may remain stable and sometimes, however in a limited number of cases, the lesion disappears. OSCC may develop from clinical apparently normal mucosa or elsewhere in the oral cavity, outside the area of a precursor lesion. The World Health Organisation (WHO) presented a classification of OPMDs and recommended a nomenclature and definition for each [51]. The clinical manifestations of the most common and relevant OPMDs are presented in Table 1. The most common OPMD is oral leukoplakia (OL), which is defined as a predominantly white plaque of questionable risk, having excluded (other) known diseases or disorders that carry no increased risk for cancer. Recently, a Working Group of the WHO found no reason to change this definition since it is being used widely in the global literature [51]. When a white lesion of the oral mucosa is present and cannot be diagnosed based on the clinical presentation, a biopsy is indicated for histopathological diagnosis. This diagnosis can be hyperkeratosis, epithelial dysplasia or SCC, which determines further policy. Most patients with OL should be followed-up on a regular base because of the increased risk of developing oral cancer. In a recent study in the Netherlands, the annual malignant transformation rate of OL was 4.9% and remained stable during long follow-up [52].

Clinical manifestations of OL may vary over time and several factors may be predictive for an increased risk of malignant transformation. These factors include non-homogeneous leukoplakia, size and location of the lesion, habits such as smoking and histopathological features; especially the presence and degree of epithelial dysplasia. Predominantly red lesions, defined as erythroplakia, are much rarer, but have a higher overall malignant transformation rate of 33% [53]. Other, less common OPMDs are proliferative verrucous leukoplakia, lichen planus, lichenoid lesions, and submucous fibrosis [53].

Table 1. Definition of oral potentially malignant disorders and the 95% confidence intervals (CI) for malignant transformation.

Disorder	Definition	95% CI for malignant transformation
Leukoplakia	A predominantly white plaque of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer	7.9-11.7%
Proliferative Verrucous Leukoplakia	Progressive, persistent, and irreversible disorder characterized by the presence of multiple leukoplakia that frequently become warty	31.9-56.1%
Erythroplakia	A predominantly fiery red patch that cannot be characterized clinically or pathologically as any other definable disease	13.6-56.1%
Oral Submucous Fibrosis	A chronic, insidious disease that affects the oral mucosa, initially resulting in loss of fibroelasticity of the lamina propria and as the disease advances, results in fibrosis of the lamina propria and the submucosa of the oral cavity along with epithelial atrophy	2.7-5.6%
Oral Lichen Planus	A chronic inflammatory mucocutaneous disorder of unknown etiology, presumably immune-mediated, with characteristic relapses and remissions, displaying white reticular lesions, accompanied or not by atrophic, erosive and ulcerative and/or plaque type areas. Lesions are frequently bilaterally symmetrical. Desquamative gingivitis may be a feature	1.5-3.2%
Oral Lichenoid Lesion	Oral lesions with lichenoid features but lacking the typical clinical or histopathological appearances of OLP, that is, may show asymmetry or are reactions to dental restorations or are drug-induced	0.01-6.3%

Source: data are from Gonzales-Moles et al. [49], Warnakulasuriya et al. [51] and Iocca et al. [53].

The presence of OL increases the risk for cancer development anywhere in a patients' mouth during their lifetime; cancer does not necessarily develop at the site of the clinically altered mucosa. Especially in individual cases, there are no reliable risk factors or strategies predicting malignant transformation of an OL [53]. Most leukoplakias are asymptomatic. Unfortunately, it turns out that any kind of treatment for oral leukoplakia does not reduce the risk of malignant transformation, has a high recurrence rate and potentially serious adverse effects [52,55]. So, management often focusses on monitoring patients on regular basis with the aim of early detection of an OSCC, when prognosis of treatment is best [55].

AIM AND OBJECTIVES OF THIS THESIS

The incidence of HPV-related oropharyngeal cancer is rising thus the understanding of HPV-related infections and vaccination among oral healthcare professionals is of importance. It is debatable to what extent oral professionals should be engaged in prevention practices for HPV-infection of the oropharynx and OPSCC.

We aimed to explore HPV-related knowledge and attitudes towards engaging in HPV-related prevention practices among Dutch oral health professionals, and those studying for these professions, in **chapters 2, 3** and **4.** Subsequently, we explored various aspects such as perceived barriers and requirements for engaging in HPV-related prevention practices.

Additionally, we aimed to contribute to the prevention and early detection of head and neck cancer by oral health professionals. Therefore, we evaluated the content of the education on head and neck cancer at various dental schools in Europe in **chapter 5.** In **chapter 6**, the knowledge of diagnosis and management of selected oral mucosal lesions among dentists in The Netherlands was explored.

Chapter 7 discusses the topics and findings presented in this thesis and describes future perspectives. **Chapter 8** provides a summary.

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Prevention of HPV-related oral cancer by dentists: assessing the opinion of Dutch dental students

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ABSTRACT

Objective: To assess dental students' opinions of the dentists' role in primary prevention of human papillomavirus (HPV)-related oral cancer using a cross-sectional web-based survey.

Materials and Methods: A questionnaire, containing questions about knowledge of HPV and oral cancer, confidence in head and neck examination and role of the dentist in preventing HPV-related oral cancer, was sent to all students of the Academic Centre of Dentistry Amsterdam (n=912).

Results: One hundred and twenty-six (n=126) students completed the questionnaire. Significantly more master students (75%) than bachelor students (54.3%) were aware that HPV is a causative factor for oral cancer. Master students had more knowledge of HPV than bachelor students, but knowledge about HPV vaccination was irrespective of the study phase. The majority of dental students agreed that it is important to discuss HPV vaccination with patients. 89% of the students think that more education about symptoms of oral cancer will increase screening for oral cancer. Development of a protocol for screening in dental practices was considered even more important.

Conclusion: According to dental students, dentists should discuss HPV as a risk factor for oral cancer with patients. Future dentists are willing to be involved in both primary and secondary prevention of HPV-related oral cancer. Therefore, screening for oral cancer and education about HPV vaccination should be integral elements of the dental curriculum.

INTRODUCTION

Head and neck cancer is the sixth most common cancer worldwide, with an annual incidence of approximately 600.000 cases [1,2]. The most common cancer in the head and neck area is the squamous cell carcinoma. In the past, head and neck cancer was most commonly seen in older adults with a history of tobacco and alcohol use. Due to a decrease in tobacco use, the number of newly diagnosed tobacco-related head and neck cancers is declining. However, the overall number of patients with head and neck cancer is still increasing, especially of patients with squamous cell carcinomas of the oropharynx[3]. Nowadays, patients diagnosed with head and neck cancer are more likely to be younger middle-aged men who may lack the previously significant risk factors as tobacco and alcohol use. These changes are relate to the human papillomavirus (HPV) [4]. The prevalence rates of HPV-positive oropharyngeal cancers has increased significantly over the last decades. HPV is the most common sexually transmitted virus, so one of the explanations of the increased prevalence rates, may be a change in sexual behaviour [5]. Engaging in orogenital sex with multiple sex partners is associated with HPV-related oral cancer [6].

The prevalence of HPV-related oropharyngeal cancer varies from 20 to 90%. The highest rates are reported in North America and Asia; the reported prevalence in Europe is usually lower [7,8,9]. This variation may be related to lack of a standardized HPV detection method, varying exposures to HPV in different geographical regions and referral bias in the populations tested [5,10].

There are many different sub-types of the HPV virus. The majority of HPV infections are asymptomatic and resolve spontaneously within two years. Persistent infection with a 'high-risk' sub-type is a risk factor for the development of cancer in various regions such as the oropharynx, cervix, anus, and penis. Regardless of anatomic site, most of these cancers are associated with HPV types 16 and 18 [11].

HPV-positive carcinomas are considered to be a different tumour entity, based on prominent biological and etiological differences, when compared with HPV-negative carcinomas [12]. In addition, HPV-positive carcinomas have a better response to therapy, lower rates of adverse events and better overall survival [13].

The World Health Organization (WHO) recommends HPV vaccination to be included in national immunization programmes with the specific aim of protecting women against cervical cancer [14]. The use of HPV vaccines is not recommended yet to prevent HPV-positive head and neck carcinomas. The two currently available HPV-vaccines prevent transmission of HPV type 16 and 18, the two strains attributable to 90-95% of HPV-positive oropharyngeal carcinomas. So hypothetically, the use of these HPV vaccines may cause a reduction in the increasing incidence of oropharyngeal cancer [15,16].

In the Netherlands, the HPV vaccine Cervarix is offered free of charge to preadolescent girls and uptake has been fairly consistent between 50% and 60% over the past five years.

When girls are vaccinated, heterosexual men could benefit indirectly from a reduced transmission of vaccine type HPV [17]. However, including boys in the HPV-vaccination program might be a more cost-effective strategy for the prevention of HPV-related cancer (oropharyngeal and anal) in the general population [17,18].

A systematic review of girls' and parents' information needs and views has shown that knowledge about the vaccination is poor and there are many misconceptions [19]. The association between individual knowledge and HPV vaccination makes providing information essential to increase uptake [20]. Therefore, health care providers must be prepared to provide patients with information on HPV vaccination, and discuss the sexual transmission of HPV [21,22]. In Florida, dentists are willing to play a role in primary prevention of HPV-related oral cancer, despite lack of high levels of knowledge [23.24].

Dentists are among the most visited health care providers. In the Netherlands almost 80% of the population visits the dentist annually. Clinical screening for oral cancer is a form of secondary prevention and is an important part of dental examination, because early diagnosis of (pre)malignant lesions increases the probability of cure [25]. Screening has been shown to be an effective and cost-effective way of improving early detection [26]. However, over 60% of oral cancers are diagnosed late, and many medical students report a lack of confidence in screening head and neck for cancer [27].

As the number of patients treated for HPV-related oral cancer increases, it is likely that dentists will be asked questions that were previously considered taboo and potentially cause embarrassment. The possible psychosocial impact of diagnosis of HPV-related oral cancer should not be overlooked either. So, dentists need to develop advanced communication skills to address these topics [28].

It could be difficult to achieve a preventative role in HPV infection for dentists, because it requires public recognition and professional acceptance. Professional organisations can enable advancement by providing the profession with information and tools. Strengthening content on this topic in the dental curriculum may also be beneficial [23,29,30].

In contrast to other European countries and the United States, dental professional organisations in the Netherlands do not yet support the dentists' role in prevention of HPV-related oral cancer [31]. Furthermore, it is not yet known what role dentists in the Netherlands see for themselves. Therefore, the aims of this study among dental students were: (1) to assess awareness of the association between HPV and oral cancer; (2) to explore their readiness for playing a role in primary prevention of human papillomavirus (HPV)-related oral cancer by discussing the HPV vaccine with patients; and (3) to assess their confidence in screening the oral cavity for (pre)malignant lesions.

METHODS

Study design

A cross-sectional web-based research was performed, using a 19-item questionnaire, based on a validated questionnaire from a previous study among dentists in the USA [23]. This questionnaire was translated, reformulated according to regulations for dentists in the Netherlands and adapted for dental students. Dental education, in the Netherlands, comprises a 3-year bachelor program and a subsequent 3-year master program. Both programs have to be completed before one can register as a dentist according to the Professionals in Individual Health Care Act of the Netherlands. Next to the master in dentistry degree (MSc) there are two dental-specialists recognized by the Ministry of Education, Culture and Science of the Netherlands: maxillofacial surgery and orthodontics. Furthermore, there are a number of board-certified postgraduate programs such as (maxillofacial)prosthodontics, periodontics, pedodontics, gnathology, endodontics and special care dentistry. The postgraduate programs are recognized by the related scientific associations but not recognized as dental specialists.

A preliminary version of the questionnaire was tested on two dental students. Their feedback led to some small adjustments of the questionnaire. The results of these two students were not included in the statistical analysis. The final version of the questionnaire took approximately 5-10 minutes to complete.

Instrument

To assess students' knowledge of HPV and the HPV vaccine, statements used required one of the following responses: 'correct', 'incorrect' or 'I do not know'. Items included were 1) awareness of relation between HPV and oral cancer; 2) risk factors for oral cancer; 3) transmission of HPV; 4) target group for vaccination; and 5) safety of the HPV vaccine.

Furthermore, four- and five-point Likert-scales were used to assess students' opinion about 1) their skills for screening for oral cancer; 2) need to development professional guidelines; 3) discomfort discussing sexual history topics with patients; and 4) the role for dentists regarding primary prevention of HPV-related oral cancer. All items translated from the previous questionnaire [22] were maintained on the original four-point Likert-scales to enable comparison. Items added to the original questionnaire were on five-point Likert-scales, as these have a higher reliability than the four-point version [32,33].

Multiple-choice questions, with the possibility of selecting multiple options, contained items about current education about HPV and factors motivating dentists to discuss HPV-vaccination with patients. Additionally, demographic variables (e.g., sex, ethnicity, age, year in dental school, received HPV-vaccine) were included.

Data collection and analyses

The questionnaire was administered via Cognitoforms (Cognito, Columbia, SC, USA), using a universally accessible web address, and an electronic invitation was emailed to all registered students of the Academic Centre of Dentistry Amsterdam (n = 912). Student participation was voluntary and responses were processed anonymously. After three and four weeks, students received an email with a reminder requesting participation in the survey.

Data were analyzed with SPSS, version 22.0 (IBM Corp, Armonk, NY, USA) using unpaired t-tests and Chi-square goodness of fit test to investigate the difference in responses between bachelor and master students. When the requirement of a minimum of 5 or more expected frequencies in each category was not met, a Fisher's exact test (FET) was used. A p-value of 0.05 or lower was considered statistically significant.

RESULTS

The total number of registered dental students at October 1st 2015 was 914. The survey was emailed to their student-email account and 2 emails were returned 'undeliverable'. A response of 126 surveys was obtained, resulting in a response rate of 14%. Respondents were primarily female (68.3%) and one third of the female students were vaccinated against HPV (31.7%). Approximately half of the respondent students were in the bachelor programme (first three years of a six-year curriculum) (55.6%).

Before participation in the present survey, 63.5% of the students were aware of the relation of HPV with oral cancer. Significantly more master students (75.0%) than bachelor students (54.3%) had this knowledge (χ^2 (2, N = 126) = 6.08, p = 0.048) (Fig 1). Knowledge about availability of HPV vaccination was reported by 46.3% of the students.

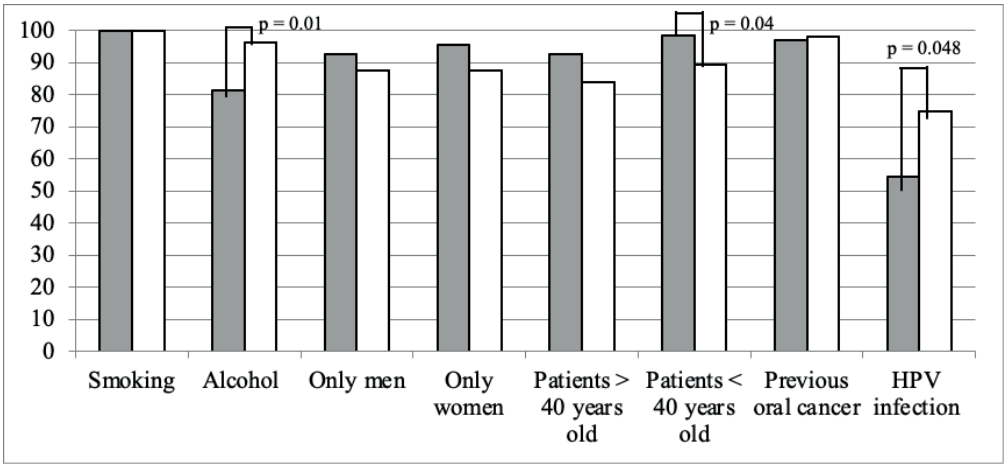

Figure 1. Percentages correct answers to questions on potential factors of oral cancer. Significant differences between Bachelor and Master students are indicated.

Of the 16 questions assessing dental students' knowledge about HPV, five questions were answered incorrectly by more than 50% of the students (Table 1). Master students knew significantly more often the correct answer on five items than bachelor students ($p< 0.05$). Of the six questions testing the knowledge about the HPV vaccine (Table 2), two items were answered correctly by only one third of bachelor and master the students (38.6%, 30.4% and 30.4%, 30.4%).

Female students were more often aware of the fact that in the Netherlands HPV vaccine is only available for girls (χ^2 (2, N = 126) = 12.7, p = 0.002). More female students who had been vaccinated against HPV answered more knowledge questions correctly than unvaccinated female students, but this was not significant χ^2 (2, N = 126) = 0.40, p = 0.82).

A large majority of the students were aware of the risk factors for oral cancer; all students correctly identified tobacco, 81% of the bachelor and 96% of master students identified alcohol consumption and almost all students (bachelor students 97%, master students 98%) identified previous oral cancer as risk factors (Fig 1). Significantly more master students acquired their knowledge from theoretical education at the dental school (80.4%) compared to bachelor students (47.1%) (χ^2 (1, N = 126) = 14.6, $p < 0.001$). Internet and social media and professional literature are relatively important resources for acquiring information for dental students (33.3% and 34.1%, respectively). Clinical practice was hardly a source of information for students (4%).

Dental students reported a low level of confidence in performing a screening for oral cancer. On a 4-point Likert scale (1 = very confident, 4 = not confident) students rated their confidence in visual inspection on average at 3.2 (SD = 0.8) and manual palpation on average at 3.5 (SD = 0.6).

To stimulate students to perform a screening for oral cancer in all patients, a large proportion of the students would like to have additional training during their education (88.9%). Furthermore, availability of reliable screening devices was suggested (50.8%) as well as enhancement of knowledge about HPV and oral cancer in the general public (42.9%). According to students, the best way to inform patients about HPV was to present it as a risk factor for oral cancer (65.1%) followed by presenting HPV as an infectious disease (20.4%). Incorporation of a question into the written medical protocol about the sexual history of the patient was only recommended by 14.3% of the students. Discussing personal topics with the patient, such as lifestyle and substance abuse, were considered 'easy' (*mean* = 3.9, SD = 0.9) and *M*= 3.6 (SD 0= 0.9) respectively on a 5-point Likert-scale from 1 = not easy to 5 = very easy. Topics as domestic violence, sexually transmitted infections and eating disorders were considered 'less easy' to talk about (respectively *mean* = 2.2 (SD = 0.8); *mean* = 2.5 (SD = 0.9); *mean* = 2.6 (SD = 1.0). There was no significant difference in discomfort in discussing these topics with patients between male and female students, except for general health which male students found less comfortable to discuss than female students (χ^2 (4, N = 126) = 9.79, p = 0.04).

Table 1. Sixteen questions assessing dental students' knowledge about HPV, stratified for bachelor and master students. The correct answers for each item are indicated with an asterisk. Data are expressed as percentages.

N = 126	Bachelor n = 70 (%)			Master n = 56 (%)			χ^2 (1, N = 126)
	Correct	Incorrect	I don't know	Correct	Incorrect	I don't know	
1. Approximately 50% of patients who get oral cancer will die from this disease	22.9	41.4*	35.7	26.8	46.4*	26.8	1.16, p = 0.561
2. Some types of HPV cause oral cancer	84.3*	1.4	14.3	89.3*	1.8	8.9	0.87, p = 0.649
3. Oral cancer is often preceded by the presence of clinically identifiable premalignant changes	70*	5.7	24.3	94.6*	3.6	1.8	13.67, p = 0.01
4. An increasing number of patients diagnosed with oral cancer lack risk factors as tobacco and alcohol use	28.6*	18.6	52.9	41.1*	35.7	23.2	11.80, p = 0.03
5. The average age of patients diagnosed with oral cancer is declining	38.6*	10	51.4	46.4*	21.4	32.1	5.85, p = 0.054
6. The majority of malignant lesions in the oral cavity is diagnosed in an advanged stage of progression.	54.3*	7.1	38.6	83.9*	8.9	7.1	16.67, p < 0.001
7. There are more than 100 types of HPV	30*	12.9	57.1	35.7*	19.6	44.6	2.16, p = 0.34
8. A person can have HPV without knowing it	81.4*	0	18.6	96.4*	0	3.6	6.68, p = 0.012
9. Most HPV infections resolve within a short time	17.1*	37.1	45.7	16.1*	53.6	30.4	3.80, p = 0.15
10. Some types of HPV cause cervical cancer	74.3*	4.3	21.4	85.7*	3.6	10.7	2.70, p = 0.26
11. HPV causes herpes and cold sore	27.1	47.1*	25.7	32.1	60.7*	7.1	7.49, p = 0.024
12. HPV causes HIV/aids	2.9	75.7*	21.4	3.6	89.3*	7.1	4.96, p = 0.084
13. HPV is a sexually transmitted virus	67.1*	11.4	21.4	83.9*	10.7	5.4	6.18, p = 0.033
14. Antibiotics can cure a HPV infection	10	61.4*	28.6	8.9	73.2*	17.9	2.19, p = 0.34
15. There is a vaccine that prevents against certain types of HPV	65.7*	10	24.3	78.6*	12.5	8.9	5.10, p = 0.078
16. Using a condom decreases the chance of transmitting HPV	61.4*	10	28.6	76.8*	7.1	16.1	3.48, p = 0.176

Table 2. Six questions assessing dental students' knowledge about HPV vaccination, stratified for bachelor and master students. The correct answers for each item are indicated with an asterisk. Data are expressed as percentages.

N = 126	Bachelor n = 70 (%)			Master n = 56 (%)			χ^2 (1, N = 126)
	Correct	Incorrect	I don't know	Correct	Incorrect	I don't know	
1 The vaccine prevents transmission of some types of HPV	**51.4***	24.3	24.3	**55.4***	25	19.6	0.40, p = 0.819
2. The HPV-vaccine protects women against cervical cancer	**71.4***	10	18.6	**67.9***	16.1	16.1	1.07, p = 0.585
3. Individuals vaccinated against HPV do not have to practice safe sex (e.g. using condoms)	0	**90***	10	0	**92.3***	7.1	0.32, p = 0.572
4. In the national immunization programme the HPV-vaccine is only available for females	**64.3***	10	25.7	**73.2***	8.9	17.9	1.27, p = 0.527
5. Men can request their general practitioner for HPV-vaccination, however this is not covered financially	**38.6***	1.4	60	**30.4***	10.7	58.9	5.44, p = 0.066
6. The HPV vaccine is only effective for individuals who have never had sex before	37.1	**31.4***	31.4	39.3	**30.4***	30.4	0.061, p = 0.970

According to dental students, it is important for dentists to discuss HPV as a risk factor for oral cancer on a 5-point Likert-scale of 1 = very important to 5 = not important (*mean* = 2.1, SD = 0.8). Dental students considered a protocol for oral cancer screening very important (*mean* = 1.02, SD = 0.2) on a 5-point Likert-scale of 1 = very important 5 = not important. Female students considered the development of a protocol significantly more important than male students (χ^2 (2, N = 126) = 11.7, p = 0.003).

DISCUSSION

The prevalence rates of HPV-positive oral cancers are increasing rapidly and the demographic profile of patients with oral cancer is changing [5]. The dentists may be a key healthcare provider for prevention of HPV-related oral cancer in patients. Discussing HPV as a risk factor, providing information about sexual behaviour to prevent infection and early detection of (pre) malignant lesions, might help to stop the increase in prevalence of HPV-positive oral cancers.

As dental students are future dentists, their opinion about the dentists' role in primary prevention of oral cancer is important. To fulfil this role in the future, adequate education of dental students is essential. Several studies have demonstrated that medical students have insufficient knowledge of oral cancer. Recent studies in America showed poor baseline knowledge among medical students, with only 18% to 59% and 44% to 67% correctly identifying alcohol consumption and tobacco as risk factors for oral cancer. Less than a quarter (24%) of the medical students correctly identified HPV as a potential risk factor [27,34]. The results from the Dutch dental students did not corroborate this knowledge deficit: 100%, 88% and 64% named tobacco, alcohol and HPV as risk factors for oral cancer. Although the dental students' knowledge about HPV as risk factor for oral cancer was reasonable, basic knowledge about HPV was considerably less. One third of the knowledge questions of HPV were answered correctly by less than 50% of the students (Table 1). They did not know that the average age of patients diagnosed with oral cancer is declining and patients are more likely to lack risk factors such as alcohol and tobacco use. This information is crucial in diagnosis of oral lesions. Master students answered significantly more items correctly than bachelor students. This may be related to the incorporation of theoretical education about HPV in the master curriculum. This suggestion is supported by the fact that 80% of the master students reported that the theoretical education of their dental school is their source of information about HPV. These findings suggest that theoretical knowledge about HPV of future dentists is reasonable.

Students who are vaccinated against HPV did not have more knowledge about HPV than non-vaccinated students. In the Netherlands, girls are invited for HPV-vaccination at an age of 13 years (www.rijksvaccinatieprogramma.nl) and therefore need approval of

their parents. Maybe the opinion and knowledge of their parents about vaccination plays a more important role in the decision to be vaccinated than their own opinion. It is also possible that both parents and girls have limited understanding about the HPV vaccine, when they decide whether or not to take the vaccination [19].

In America, 66% of medical schools do not include screening for head and neck cancer in their curricula. Even when students learn to perform this screening, the quality of this teaching is inconsistent [27]. It is likely that this contributes to the fact that 47% of medical students in America reported feeling 'not very confident' or less in examining the oral cavity for oral cancer [27]. The Dutch dental students reported the same lack of confidence. Insufficient education at dental schools may explain the reported lack of screening skills for oral cancer in dentists [29]. It also explains why a large majority of dental students (89%) suggested inclusion of more clinical training in screening for oral cancer in their curriculum. Education which contains discussions on HPV and clinical training by experienced dentists or oral surgeons has shown to be effective [27]. These educational methods have also been successful in educating dental students on the Human Immunodeficiency Virus (HIV) [35].

Dental students express a need for development of protocols for screening for oral cancer. This opinion is shared by dentists in Florida [23]. Dental professional organisations could help in the development and introduction of these protocols. Patient information leaflets relating to the topic may also be a tool for providing accurate information. Furthermore, investment in advanced communication skills courses for dentists will help the practitioner in addressing sexual related topics that were previously considered a taboo.

Although dentists in Florida stated that their profession had a clear role and responsibility in discussing the relation between oral cancer and HPV with patients, they were not 'ready' to discuss the HPV vaccine with their patients [23,29]. On the contrary, Dutch dental students thought dentists should discuss this subject with their patients, which suggests students are ready to discuss the HPV vaccine with their patients. A possible explanation for this result is the difference in age of the subjects. Also, cultural differences between the Netherlands and the USA may contribute to the difference in results. Furthermore, the American data were obtained in 2011 and 2013. Recent epidemiological findings about HPV and oral cancer may have contributed to dental students' willingness in discussing HPV with patients. For example, the British Dental Association launched a campaign in April 2015 to increase knowledge of the relation between HPV and supported gender-neutral HPV vaccination. A similar change in readiness of dentists to inform patients about tobacco and alcohol as risk factors for oral cancer, has also been reported [36]. Dentists in America reported liability concerns and discomfort in having sexual health-related discussions with patients as a barrier for discussing HPV with patients [23,29].

Research has shown that cultural background and religion could influence discomfort in having sexual health-related discussions [37,38]. However, our study did not find differences in discussing this topic between students with a western and a non-western ethnicity.

The study design in the previous study among dentists in Florida was guided by the Transtheoretical Model, to construct the Stages of Change to assess behavioural readiness of dentists to discuss HPV with patients for primary prevention of cancers [23]. As dental students are not yet treating patients independently, the outcome variable of this study was to assess the opinion of dental students about discussing HPV with patients. Therefore, it was not possible to segment them into stages of behavioural adaptation.

Another limitation of the present study is the potential risk of selection bias; since the participation was on a voluntary base, the study may have attracted students with a baseline level of knowledge that differs from that of their non-participating peers. However the participation of female students in this study of 68% resembles the participation of female students at the Academic Centre for Dentistry Amsterdam of approximately 65%. Moreover the relatively low response rate limits the generalizability of study results, although the response rate (14%) was higher than the response of dentists in Florida in a similar study (8%). Finally, as there are three Dental Schools in the Netherlands, these results only resemble the students' opinions in Amsterdam, which may differ from their peers' at universities in other parts of the country.

CONCLUSION

Findings from the present study highlight that future dentists are willing to play a role in preventing HPV-related oral cancer. They might play this preventative role by 1) informing patients about HPV to reduce the risk of getting infected; 2) discussing HPV-vaccination and 3) early detection of (pre) malignant lesions, which improves the prognosis of patients with oral cancer. To prepare dental students for this future professional role, dental schools should include more training on this topic in their curricula.

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3

Dutch dental hygiene students' knowledge of HPV-related oropharyngeal squamous cell carcinoma and HPV vaccination

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ABSTRACT

Introduction: The incidence of human papillomavirus (HPV) related oropharyngeal cancer is rising thus the understanding of HPV-infection and vaccination amongst oral healthcare professionals is becoming increasingly important. This study aimed to investigate the knowledge of Dutch dental hygiene students on HPV-infection and vaccination and assessed various aspects of HPV-related oropharyngeal cancer.

Methods: This descriptive cross-sectional study invited the entire Dutch dental hygiene student population registered in September 2016 to complete an online questionnaire concerning the knowledge of HPV-infection and vaccination, including aspects of HPV-related Oropharyngeal Squamous Cell Carcinoma (OPSCC). Data were analysed using t-tests, Mann Whitney U tests and Chi-square tests.

Results: Invited were all 1248 Dutch dental hygiene students and 232 (18.6%) students completed the questionnaire. More than 95% of students indicated HPV-infection as a risk factor for OPSCC and 48.7% was aware of the availability of HPV vaccination. Additionally, students considered it important to discuss HPV as a risk factor for oropharyngeal cancer with their patients. In general, the students scored highest on the questions about risk factors for OPSCC and poorest on the questions about general HPV knowledge and HPV vaccination. Although the mean overall knowledge score was significantly higher in senior compared to junior students, knowledge scores of senior students remained insufficient.

Conclusion: This study identified deficits in knowledge of HPV and HPV-vaccination amongst Dutch dental hygiene students. Future research should focus on improving the content of dental hygiene curricula and development of ongoing educational tools for dental hygienists.

INTRODUCTION

The incidence of head and neck cancer is overall rising worldwide however, there is a significant variation in across the globe.[1–3,4] It has been reported that the occurrence of oropharyngeal squamous cell carcinoma (OPSCC) is elevated in the USA and Europe, which is caused by a persistent infection with high-risk human papillomavirus (HPV) types.[2,5]

In contrast to patients diagnosed with oral squamous cell carcinoma, only 4% of oral cancers are actually associated with HPV infections.[6] However, in 2012 in Europe and the USA approximately 40% and 71% of OPSCCs were HPV-positive respectively and these cases are continuously rising.[2,5,7] In The Netherlands, there has also been an slight increase of OPSCC incidence, however the percentage of HPV-positive OPSCC is rising considerably over time. [8, 9] Nowadays HPV is associated with half of the patients diagnosed with OPSCC in The Netherlands and these cancers may be preventable or detected early. [9,10] HPV-infection is usually transmitted sexually, the infection is asymptomatic in most cases and tends to resolve spontaneously within 2 years.

There are more than 200 different types of HPV; low risk HPV-types may cause anogenital warts and a persistent infection, whilst high risk HPV-types may progress to cancer. [11] There are about 14 high-risk types which include; HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 66 and 68. HPV 16 and 18 were the first types to be classified as having a carcinogenic potential for cervical cancer and a persistent infection with one of these types is responsible for most cases of cervical SCC, OPSCC and anal cancer and a smaller portion of vulvar, vaginal and penile cancer. [12]

Patients diagnosed with HPV-positive OPSCCs have different demographic characteristics compared to patients with HPV-negative OPSCCs. HPV-positive OPSCC's tend to originate within the tonsils and base of the tongue and are more frequently diagnosed in middle-aged white men who use tobacco and alcohol less frequently, have a more affluent socioeconomic status and have more sexual partners. HPV-positive OPSCCs appear to have better response to standard therapy than HPV-negative OPSCCs, and therefore have better survival rates.[13,14] As of 2020, more than 100 countries have introduced HPV-vaccination for girls with the aim of protecting against cervical cancer.[15] Since 2010, thirteen-year-old girls receive an invitation for this vaccination in The Netherlands and the vaccination uptake rose from 52% in 2011 to 63% in 2020 [16], which is relatively high compared to other European countries and the USA.[17]

Recent research shows that HPV-vaccination is also effective in prevention of oropharyngeal and anogenital cancer and that introduction of pan-gender vaccination would constitute a significant decrease of these cancers and would benefit girls and boys.[15,18] Therefore, the USA, Australia and most European countries introduced the HPV-vaccination also for boys, which has been available in The Netherlands since 2022.[18,19,20]

Besides public health interventions to reduce HPV-related OPSCC incidence, such as providing HPV-vaccination and information, multiple types of healthcare professionals could be included and there may be a role for oral healthcare professionals as well. In addition to this, patients should be able to approach their oral healthcare professional with questions about the HPV or may even present with symptoms of OPSCC during their regular check-up or assessment appointments. For these reasons, dental hygienists should have sufficient knowledge about HPV related OPSCC and be aware of the clinical presentation of OPSCC.

The aim of this study was to investigate knowledge of dental hygiene students on HPV-infection and vaccination. Based on information from media coverage and/or information provided at the time of vaccination invitation, a certain basic level of knowledge can be expected from Dutch junior hygienist students. Furthermore, we assessed opinions and attitudes towards various aspects of HPV-related OPSSC. Additionally, because dental hygiene students' knowledge and self-confidence may increase during their studies, we compared mean knowledge and self-confidence levels of junior and senior students.

METHODS AND MATERIALS

Study design and setting

This descriptive cross-sectional study was conducted in The Netherlands from November 21th to December 5th 2016. There are four dental hygiene schools in The Netherlands, and these are in the cities of Amsterdam, Groningen, Arnhem/Nijmegen and Utrecht. In November 2016, a total number of 1,248 students were registered to participate in one of the four baccalaureate years of the dental hygiene curriculum.

Study population

The study population consisted of alle dental hygiene students in The Netherlands, and we invited the total dental hygiene student population who were registered to participate in our survey. We included all dental hygiene students that were registered for participation in the curriculum at one of the four Dental Hygiene Schools in the Netherlands, at the 1th of September 2016. Via the National coordination centre for dental hygiene schools (Landelijk overleg Opleidingen Mondzorgkunde), all four dental hygiene schools in The Netherlands were approached to participate in the study and they all consented. No sample size calculation for this study was performed because of the descriptive character of the study and the fact that we have approached the entire population of dental hygiene students in the Netherlands. Participants were recruited depending on the preference of the dental hygiene schools. Students registered in Utrecht and Arnhem/Nijmegen received an invitation by e-mail and students registered in Amsterdam or Groningen received an invitation via their digital learning platform.

Data collection tools and procedures

Data were collected using a web-based self-administered structured questionnaire. The survey was a modified version of a questionnaire that was developed and validated by Daley et al. [21, 22] A panel of five faculty members of two different dental hygiene schools in the Netherlands and two dental hygiene students, pilot tested the questionnaire and minor revisions were made upon feedback.

The questionnaire was entered in an online Dutch-language survey tool (http://www.enquetesmaken.com). An invitation letter with a web link to the online survey was sent to all 1248 Dutch dental hygiene students, followed by a reminder to non-responders one week after the initial mailing. The survey was open for a period of two weeks and participants completed the survey anonymously and on a voluntary basis. The invitation letter included a description about; 1) the purpose of the study, 2) the estimated time required to complete the questionnaire, 3) the anonymous processing of the data and, 4) obtainment of informed consent by completion of the survey. The order of questions was fixed, the number of screens was 21 and every screen included one item. The range of questions per item varied between 1 and 17. Data were stored in the protected digital database of The Academic Centre of Dentistry in Amsterdam.

To prevent students from participating multiple times we used cookies. Using a unique server link for each student would have been the preference, but this was technically not possible at the participating dental hygiene schools.

Researchers used Facebook pages for dental hygiene students and dental hygienists to advertise for the survey. These messages explained that students received an invitation by e-mail or digital learning platform and asked them to participate in the survey. These messages did not contain a link to the survey, as the design was 'closed'. As an incentive for students to participate, eight cinema vouchers were raffled among participants.

Study variables

Knowledge of HPV and HPV-vaccination were the main outcome variables of this study. Independent variables were year of study and vaccination status. Students in year 1 or 2 were considered junior students and students in year 3 or 4 were considered senior hygiene students. Additionally, we aimed to investigate several HPV-related aspects, including dental hygiene students' opinions and attitudes regarding some HPV-related prevention practices and their confidence in clinical examination for oral and oropharyngeal cancer.

Measurements

Knowledge: This was assessed by 31 items about HPV and HPV-vaccination. These questions required responding 'correct', 'incorrect' or 'I don't know'. The option 'I don't know' was added so students that did not have the knowledge to answer the question were not forced to choose an answer. One multiple choice question required selecting risk factors for oral and/or oropharyngeal cancer. This was the first question in the

questionnaire and the aim was to assess whether students were aware of HPV-infection as a risk factor for development of cancer.

Several HPV-related aspects: Four-point Likert scales were used to assess students' 1) confidence in clinical examination for oral and oropharyngeal cancer, 2) need for professional guidelines, 3) comfort in discussing sexually transmitted infections with patients and 4) role for dental hygienists regarding primary prevention of HPV-related OPSCC. Multiple-choice questions were used to obtain information about 1) current education on HPV, 2) barriers students experience for discussing the role of HPV as a communicable sexual disease with special attention for the etiological contribution for the development of OPSCC, 3) advantages and disadvantages of vaccination, 4) their source of information about various aspects of HPV-infection and, 5) counselling patients about the consequences of HPV-infection in the head and neck region.

Demographic information: This included age, gender, ethnicity, study year, dental hygiene school and HPV-vaccination status.

Data processing and analysis

The collected data were entered into SPSS 23 (IBM Corp., Armonk, NY, USA) for data management and statistical analysis.

Descriptive statistics were used to report respondents' knowledge and subgroups based on demographic variables. Unpaired t-tests and Chi-square goodness of fit tests were used to compare results between junior and senior students and between vaccinated and unvaccinated students. When the requirement of a minimum of 5 or more expected frequencies in each category was not met, a Fisher's exact test was used. Mann-Whitney U tests were used to compare differences in responses from subgroups, on questions with categorical data. A post hoc power analysis was performed using G*Power software, version 3.1.9.4 (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany); with a medium effect size (0.5) and a power of 80%, subgroups of 53 participants were needed. For all questions, significance level was set at a p-value of 0.05 or lower.

RESULTS

Of the 1,248 Dutch dental hygiene students that were invited to participate in the survey, 232 students completed questionnaire, representing a response rate of 18.6%. Participants' demographic characteristics are presented in table 1.

Table 1. Characteristics of participants (n= 232)

Mean age (range):	**21.5 (17-48)**
Study year	n (%)
Year 1	42 (18.1)
Year 2	59 (25.4)
Year 3	67 (28.9)
Year 4	64 (27.6)
Sex	n (%)
Male	13 (5.6)
Female	219 (94.4)
Vaccination status:	n (%)
Vaccinated	90 (38.8)
Not-vaccinated	142 (61.2)
Migration background	n (%)
Parents born in EU	176 (75.9)
At least one parent not born in EU	53 (22.8)
Insufficient information	3 (1.3)
Location dental school	n (%)
Amsterdam	27 (11.6)
Groningen	48 (20.7)
Arnhem/Nijmegen	45 (19.4)
Utrecht	112 (48.3)

Knowledge

Correct responses of all dental hygiene students per knowledge question, with a stratification for subgroups vaccinated/unvaccinated students and study junior students (year 1+2) and senior students (year 3+4), are shown in table 2.

The mean percentage of correct responses for all 31 knowledge items was 54.3% (SD=15.9). Vaccinated students had a significantly better overall mean score for all 31 knowledge items than unvaccinated students (59.8±13.0% vs. 51.1±16.5%, $t(230)=4.20$, $p<0.001$). Similar differences in the overall knowledge score were found between junior and senior students; seniors scored significantly better than juniors (58.7±13.9% vs. 48.6±16.5%, $t(230)=-5.07$, $p<0.001$).

Table 2. HPV-related knowledge questions with the correct answers to the questions, responses of dental hygiene students to the questions and differences between subgroups vaccinated/unvaccinated and study year 1+2 and year 3+4 (N=232). Abbreviation: Vacc: vaccinated; Unvacc: unvaccinated

		Correct Answers	Vaccination statusCorrect answers			Study yearCorrect answers		
	Answer	All (n=232)	Vacc (n=85)	Unvacc (n=147)		Y1+2 (n=101)	Y3+4 (n=131)	
Which patients have an increased risk for developing OSCC and/or OPSCC?		N (%)	N (%)	N (%)	P[a]X²	N (%)	N (%)	P[a]X²
A. Smokers	correct	229 (98.7)	85 (100)	144 (97.9)	0.19	99 (98.0)	130 (99.2)	0.42
B. Patients with a high alcohol consumption	correct	211 (90.9)	78 (91.7)	133 (90.5)	0.74	86 (85.1)	125 (95.4)	0.01
C. Men	correct	23 (9.9)	9 (10.6)	14 (9.5)	0.79	4(4.0)	19 (14.5)	0.01
D. Women	incorrect	212 (91.4)	78 (91.8)	134 (91.2)	0.87	95 (94.1)	117 (89.3)	0.20
E. Patients older than 40 years old	correct	206 (88.8)	77 (90.6)	129 (87.8)	0.51	87 (86.1)	119 (90.8)	0.26
F. Patients younger than 40 years old	incorrect	211 (90.9)	79 (92.9)	132 (89.8)	0.42	93 (92.1)	118 (90.1)	0.60
G. Patients with a previous OSCC and/or OPSCC	correct	226 (97.4)	81 (95.3)	145 (98.6)	0.12	101 (100)	125 (95.4)	*0.03*
H. Patients who are infected with HPV	correct	221 (95.3)	82 (96.5)	139 (94.6)	0.51	94 (93.1)	127 (96.9)	0.17
General HPV knowledge questions								
A. Approximately 50% of patients with OSCC and/or OPSCC will die from this disease	incorrect	65 (28.0)	27 (31.8)	38 (25.6)	0.36	24 (23.8)	41 (31.3)	0.21
B. Some types of HPV can cause OSCC and OPSCC	incorrect	157 (67.7)	62 (72.9)	95 (64.6)	0.32	56 (55.4)	101 (77.1)	>0.01
C. OSCC is often preceded by the presence of a clinically identifiable lesion	correct	167 (72.0)	60 (70.6)	107 (72.8)	0.63	63 (62.4)	104 (79.4)	>0.01
D. An increasing number of patients diagnosed with OPSCC lack risk factors as tobacco and alcohol use	correct	61 (26.3)	23 (27.1)	38 (25.9)	0.95	25 (24.8)	36 (27.5)	0.64
E. The average age of patients diagnosed with OPSCC is decreasing	correct	20 (8.6)	7 (8.2)	13 (8.8)	0.12	9 (8.9)	11 (8.4)	0.89
F. The majority of OPSCC are diagnosed in an advanced stage	correct	126 (54.3)	49 (57.6)	77 (52.3)	0.56	46 (45.5)	80 (61.1)	0.02
G. There are more than 100 types of HPV	correct	59 (25.4)	25 (29.4)	34 (23.1)	0.55	21 (20.8)	30 (29.0)	0.15

		Correct Answers	Vaccination status Correct answers			Study year Correct answers		
	Answer	All (n=232)	Vacc (n=85)	Unvacc (n=147)		Y1+2 (n=101)	Y3+4 (n=131)	
H. A person can have HPV without knowing it	correct	185 (79.7)	71 (83.5)	114 (77.6)	0.30	78 (77.2)	107 (81.7)	0.40
I. Most HPV infections resolve within a short time	correct	28 (12.1)	10 (11.8)	18 (12.2)	0.15	11 (10.9)	17 (13.0)	0.63
J. Some types of HPV can cause cervical cancer	correct	152 (65.5)	66 (77.6)	86 (58.5)	0.01	53 (52.5)	99 (75.6)	>0.01
K. HPV causes herpes and cold sore	incorrect	59 (25.4)	25 (29.4)	34 (23.1)	0.02	20 (19.8)	39 (29.8)	0.08
L. HPV causes HIV	incorrect	96 (41.4)	39 (45.9)	57 (38.8)	0.27	28 (27.7)	68 (51.9)	>0.01
M. HPV is a sexually transmitted virus	correct	122 (52.6)	54 (63.5)	68 (46.3)	0.03	38 (37.6)	84 (64.1)	>0.01
N. Antibiotics can cure an HPV infection	incorrect	114 (49.1)	49 (57.6)	65 (44.2)	0.14	38 (37.6)	76 (58.0)	>0.01
O. There is a vaccine that prevents against certain types of HPV	correct	122 (52.6)	58 (68.2)	64 (43.5)	<0.01	44 (43.6)	78 (59.5)	0.02
P. Using a condom decreases the chance of transmitting HPV	correct	110 (47.4)	45 (52.9)	65 (44.2)	0.27	39 (38.6)	71 (54.2)	0.02
Q. HPV causes AIDS	incorrect	94 (40.5)	43 (50.6)	51 (34.7)	0.06	31 (30.7)	63 (48.1)	<0.01
HPV vaccination knowledge questions								
A. HPV-vaccination prevents transmission of some types of HPV	correct	87 (37.5)	38 (44.7)	49 (33.3)	<0.01	36 (35.6)	51 (38.9)	0.61
B. HPV-vaccination protects women against cervical cancer	correct	143 (61.6)	69 (81.2)	74 (50.3)	<0.01	50 (49.5)	93 (71.0)	<0.01
C. Individuals vaccinated against HPV do not have to practice safe sex (e.g. using condoms)	incorrect	163 (70.3)	74 (87.1)	89 (60.5)	<0.01	62 (61.4)	101 (77.1)	<0.01
D. In the national immunization programme the HPV-vaccination is only available for females	correct	103 (44.4)	54 (63.5)	49 (33.3)	<0.01	35 (34.7)	68 (51.9)	<0.01
E. Men can request their general practitioner for HPV-vaccination, however this is not covered financially	correct	52 (22.4)	21 (24.7)	31 (21.0)	0.19	26 (25.7)	26 (19.8)	0.29
F. The HPV-vaccination is only effective for individuals who have never had sex before	incorrect	79 (34.1)	37 (43.5)	42 (28.6)	0.03	28 (27.7)	51 (38.9)	0.07

Students generally performed best on the item about risk factors for Oral Squamous Cell Carcinoma (OSCC) and/or OPSCC; the mean percentage of correct responses on the 8 questions was 82.9% (SD=8.6). This was the only knowledge item where no statistically significant difference was found in mean score between vaccinated and unvaccinated students (83.7±8.2% vs. 82.5±8.9%, t(230)=1.02, p=0.31).

The mean percentage of correct responses was 44.0% (SD=20.5) for 17 questions testing general HPV knowledge. For the 6 knowledge questions testing HPV vaccination knowledge, mean percentage of correct answers was 45.0% (SD=29.9). For all knowledge questions, students responded more often with 'I don't know' than the correct response. To the question 'were you aware of the availability of an HPV vaccination before participation in this study', 48.7% responded with 'yes'.

The main source of information about OSCCC, OPSCC and HPV was theoretical education in the dental hygiene curriculum (45.3%). Clinical education was not an important source of information (13.4 %).

One third (37.2%) of dental hygiene students reported they did not receive any information at all about this topic. Internet or social media and professional literature were sources of information for respectively 20.7% and 21.1% of respondents. Fellow students (4.7%) and patients (1.7%) were least reported as sources of information. Vaccinated students reported significantly more frequent to have acquired their information by a newspaper or magazine than unvaccinated students (11.8% vs. 4.8%, $X^2(1)=3.82$, p=0.05).

Examination for oral and oropharyngeal cancer

Dental hygiene students did not feel confident about performing an examination of the oral and oropharyngeal region during a regular check-up appointment. On a 4-point Likert scale (1 = very confident, 4 = very unconfident) students rated their confidence in visual inspection at 2.4 (SD = 0.7) and manual palpation at 2.6 (SD = 0.7). Senior students had significantly more confidence in performing a visual inspection than juniors (*mean*=2.4 SD=0.6 vs. *mean*=2.5 SD=0.8, U=5701.00, z=-1.99, p=0.046). Furthermore, to stimulate dental hygiene students to examine all patients for OSCC and/or OPSCC they would like to have more scientific evidence, more common knowledge among patients about performing this examination and additional training in their dental hygiene curriculum (respectively, *mean*=3.0, SD=0.6; *mean*=3.1, SD= 0.7; *mean*=3.4, SD=0.7 on a 4-point Likert scale (1 = don't agree, 4 = fully agree)). Students in study year 3+4 considered availability of scientific evidence as less important than their fellow students in year 1+2 on a 4-point Likert-scale (1= very important 4= not important) (*mean*=2.9 SD=0.7 vs. *mean*=3.1 SD=0.5, U=5427.00, z=-2.84, p=0.01). Respondents considered availability of a protocol for OSCC and/or OPSCC examination as very important (*mean* = 1.3, SD = 0.6) on a 4-point Likert-scale (1 = very important 4 = not important). There were no differences between subgroups based on vaccination status for these questions.

Counselling patients

Discussing personal topics with patients such as the impact of lifestyle on general health, was considered 'easy'. Sensitive topics such as domestic violence, sexually transmitted infections and eating disorders were considered 'less easy' to discuss (Table 3). Students with a non-EU migration background felt more comfortable about discussing the topics lifestyle, eating disorders and sexually transmitted viruses compared to their peers with both parents from the EU, however this difference was only significant for eating disorders.

According to dental hygiene students, dental hygienists should discuss HPV as a risk factor for OPSCC with their patients (*mean* = 1.5, SD = 0.6 (on a 4-point Likert-scale of 1 = very important to 4 = not important)).

The best way to start a conversation about HPV with patients, according to dental hygiene students, was to present it as a risk factor for OPSCC (62.9%). Presenting it as a viral infection or adding a question about sexual behaviour in the patient medical history form were both preferred by 18.5% of students. The main reason to refrain from informing patients about the availability of an HPV vaccination was insufficient education about this topic in the dental hygienist curriculum (82.3%). Other reasons were feeling uncomfortable about discussing this topic (29.3%) and lack of knowledge among patients about the vaccination preventing HPV-related OPSCC (28.4%). 28.0% of respondents had the opinion that it is not a dental hygienist's responsibility to inform patients about HPV-vaccination and questioning the safety of the vaccination was a reason to refrain from informing patients for 18.5%.

Table 3. Response of dental hygiene students to five questions assessing how comfortable they feel about discussing personal topics with patients reported on a 4-point Likert scale (from 1 = not easy to 4 = very easy) and differences between subgroups based on vaccination status, migration background and study year. Mean scores ± SD are provided. Abbreviation: Vacc: vaccinated; Unvacc: unvaccinated; EU: European Union.

Question		Vaccination status (n=232)			Migration background (n=229)			Study year (n=232)		
	All (n=232)	Vacc (n=85)	Unvacc (n=147)	p	Yes (n=176)	No (n=53)	p	Y1+Y2 (n=101)	Y3+Y4 (n=131)	p
1. Lifestyle	3.2(0.6)	3.2(0.6)	3.2(0.6)	0.99	3.2(0.6)	3.4(0.6)	0.07	3.2(0.6)	3.3(0.6)	0.18
2. Domestic violence	1.7(0.6)	1.7(0.6)	1.7(0.6)	0.92	1.7(0.6)	1.7(0.7)	0.92	1.8(0.6)	1.7(0.6)	0.57
3. Eating disorders	2.0(0.7)	2.0(0.7)	2.1(0.7)	0.37	2.0(0.6)	2.3(0.7)	<0.01	2.1(0.7)	2.0(0.6)	0.17
4. Sexually transmitted infections	2.1(0.7)	2.1(0.7)	2.1(0.7)	0.98	2.1(0.7)	2.3(0.7)	0.10	2.2(0.8)	2.1(0.6)	0.12
5. Substance abuse	3.0(0.6)	3.1(0.6)	3.0(0.7)	0.34	3.0(0.6)	3.0(0.7)	0.53	2.9(0.7)	3.1(0.6)	0.11

Comment data presentation: To favour the visual data presentation of table 3, we presented the non-parametrical Likert-scale scores as continuous data but we did use the non-parametrical Mann Whitney U test to calculate differences between groups.

DISCUSSION

Since the number of patients diagnosed with HPV-related OPSCC is rising and public awareness about HPV-infection as a risk factor for OPSCC is increasing, it is likely that patients will approach their oral healthcare professional with questions. [16] Because of the relation between knowledge and patient interaction, a sufficient knowledge level among dental health care providers is essential. [23] In this study we aimed to evaluate dental hygiene students' knowledge of HPV.

We identified knowledge deficits on topics such as transmission, vaccination, and curability. Students did not know that men are at higher risk of development of OSCC and/or OPSCC than women, only 9.9% answered this question correctly. In the Netherlands this difference in incidence has been considerable over the past decades; with men more than twice as likely to be affected than women.[24] Subsequently, they did not know that an infection with HPV usually resolves spontaneously within a short time and that there are more than 100 types of HPV. They were not aware of the different biological and epidemiological features of patients diagnosed with HPV-related OPSCC; only 9% reported that the average age is declining, 12% correctly responded that most HPV infections will resolve spontaneously within a short time and 26% knew that an increasing number of patients diagnosed with OSCC and/or OPSCC lack traditional risk factors as tobacco and alcohol use. On the item 'HPV causes herpes and cold sore' more students incorrectly agreed on this statement (32%) than correctly disagreed (24%), herpes and cold sore are caused by infection with the Herpes Simplex Virus (HSV), which indicates they do not only lack knowledge about HPV, but also have incorrect knowledge about other viruses.[25]

A study among American dental hygienists in 2016 showed comparable knowledge deficits, however they scored better on several knowledge items than students in The Netherlands. For example, they had a better response on the statements; HPV cannot cause HIV/AIDS (83% vs. 41%) or herpes (51% vs. 25%), HPV is a sexually transmitted virus (97% vs. 53%), antibiotics cannot cure HPV (80% vs 49%), HPV can cause oropharyngeal (92% vs 68%) and cervical cancer (99% vs 66%).[23] These differences could be explained by the fact that our study included dental hygiene students from all study years, who did not complete the curriculum yet, and a possible difference in content of dental curricula.

Significantly higher knowledge levels of senior students compared with juniors indicate that they acquired knowledge via the dental curriculum. However, the education provided in the current curriculum may not be sufficient because knowledge levels among senior students remained insufficient; the mean percentage of correct responses for all knowledge items was only 58.7 (SD=13.9). Students reported that theoretical education in the dental curriculum was their main source of information. Which indicated that the content of the dental curriculum may not fully prepare students to answer patients' HPV related questions.

In our study 41% of female students were vaccinated and so the vaccine coverage of our study population is in line with the coverage in The Netherlands.[16] The mean age of the participants was 21.5 years with a range of 17-48 years, which indicates that some students were not included in the national immunization programme because they were too old at the time of introduction of the vaccination. The fact that vaccinated students had significantly more knowledge about HPV could be explained by the association between vaccination uptake and vaccination related knowledge.[26] Probably these students did not acquire their knowledge through the dental curriculum. Results showed that they significantly more often acquired their information by a newspaper or magazine, however this was a source for only 11.8% of vaccinated students. It is more plausible they acquired their knowledge as teenagers by information provided by the national immunization programme.

To prevent HPV-related cancer, prevention efforts of multiple types of healthcare providers is necessary. Opinions about the role of oral healthcare providers in reducing the incidence of HPV-related OPSCC vary worldwide. The American Dental Association encourages oral health professionals to educate patients about the relation between HPV and oropharyngeal cancer and counsel patients about HPV-vaccination.[27] Dutch oral health professional organizations do not encourage oral healthcare professionals to engage in HPV-related prevention practices. Counselling patients about HPV and vaccination is covered by the government as part of the National Immunization Programme. Recently the government launched campaigns about the HPV vaccination not only protecting against cervical cancer, but a broader range of cancer, including OPSCC.[16]

Results of our study indicate that future dental hygienists are willing to engage in primary prevention. Primary prevention involves reducing high risk behaviour in patients such as alcohol and tobacco use and is effective in reducing the incidence of oral cancer.[28] To reduce the risk for HPV-related OPSCC, providing patients with information about transmission of HPV, including high risk sexual behaviour, and the HPV-vaccination is necessary. Identification of risk factors in patients and counselling skills to encourage them to cease high-risk behaviour are also necessary. Results of our study showed that dental hygiene students considered informing patients about HPV-infection as a risk for OPSCC as important. However, they do not seem prepared to inform patients about HPV vaccination; most students reported that they did not have sufficient education about this topic to counsel their patients. Besides a lack of knowledge about the topic, students may also not know how to discuss the topic with their patients ('lack of perceived control'). Practical exercises in discussing difficult topics with patients should therefore be part of the curriculum of dental hygiene schools.

Secondary prevention involves clinical examination for the early detection of oral cancer. Detecting a primary oropharyngeal tumour during this examination is difficult. Primary tumours are relatively small, and it is impossible to visually inspect the tonsils

and base or the tongue during oral examination. A comprehensive examination includes visual inspection and palpation of the lymph nodes in the neck, so it is possible to detect cancer at a more advanced stage when a first symptom is a metastasis of a lymph node in the neck.[13,29] Other symptoms for OPSCC include a persistent sore throat, pain when swallowing, one-sided ear pain, hoarseness or a persistent lump in the throat.[13] Lack of scientific evidence is often mentioned as a reason for oral healthcare professionals to refrain from performing an examination for oral cancer in all their patients.[30,31]

It is remarkable that availability of scientific evidence for oral cancer examination is considered less important for senior oral hygiene students than for junior students. A possible explanation is that senior students tend to rely more on their clinical experience, have more experience and more confidence in performing this examination, and therefore consider clinical experience more important than scientific evidence.[32]

A recent evaluation of the content of head and neck cancer curricula of European dental schools showed that education about HPV-related OPSCC was included in 94% of curricula and 87% also contained education about strategies to discuss HPV infection with patients [33]. Despite inclusion of these topics in most curricula, a study among Dutch dental students showed knowledge deficits on HPV related knowledge.[22] These deficits were comparable to those of Dutch dental hygiene students in this study, however dental students performed slightly better on almost all knowledge questions. Similar results in lack of knowledge about HPV among dental students were found in non-EU countries such as the US and Jordan.[34,35] A systematic review from 2020 Parsel et al. revealed that these deficits were also present among dental healthcare providers worldwide.[36] These findings suggest that education in dental curricula may not fully prepare dentists and dental hygienists to counsel their patients about HPV.

To increase HPV-knowledge levels about HPV among dental hygienists, future research should focus on adapting the dental hygiene curricula. Assessing opinions of dental educators about the content of the curriculum and research about best practices to teach students about HPV could be beneficial. As well as exploring patterns of students understanding as they move through the curriculum. Consensus about the role of oral healthcare professionals is essential for adaptation of dental curricula. The European Dental Hygiene Federation developed a common European curriculum as basis for educational curricula in the 24 countries represented by this association. There is a considerable variation regarding what constitutes the practise of dental hygiene across EDHF member states, but prevention and examination for oral cancer are core activities in all countries.[37] A profile with a brief description of competences for dental hygienists in Europe was presented by the European Dental Hygienist Federation to aid in development of dental hygiene education in Europe. A document with a more precise description about the content of curricula, including education about HPV, could be valuable for dental hygiene schools. Another effective method for increasing HPV-related knowledge among dental hygienists is postgraduate education.[38]

A drawback of our questionnaire was that it contained two slightly different questions about students' knowledge about HPV infection as a risk factor for oral and/or oropharyngeal cancer. The first question required students to point out risk factors for oral and/or oropharyngeal cancer and 95.3% correctly identified HPV. The second question was part of the item containing general HPV knowledge questions and was 'some types of HPV can cause oral and oropharyngeal cancer'. It was answered correctly by 67.7% of respondents. The aim of this question was to obtain information whether students knew only certain high-risk types of HPV are related with cancer while most types are not carcinogenic. The formulation of these questions was quite overlapping, and it would have been better to make the second statement a bit more specific, for example 'only high-risk types of HPV can cause oral and/or oropharyngeal cancer'.

Another limitation of this study was the possible self-reporting bias related to the cross-sectional survey method. Also, a positive selection bias should also be pointed out because students with higher interest and consequentially a higher knowledge are more likely to participate in this study. Therefore, knowledge levels of dental hygiene students might be even lower than reported. However, current knowledge levels of students might be higher than those of students in 2016, when we conducted this study. Recently the Dutch ministry of health launched campaigns informing the public that HPV vaccination not only protects against cervical cancer, but also against a broader range of cancers including OPSCC, which may have attributed to knowledge levels among dental hygienists, as well as among patients.[16] The relative low response rate of 18% may have been affected by the fact that the study was open for only two weeks and participation was voluntarily. Differences in number of participants between the four dental hygiene schools could be related to differences in the way the questionnaire was distributed at the schools, and to the fact that the study originated from the dental hygiene school in Utrecht.

A considerable period of time has passed since the collection of the data for this, during which the topic has received attention in various ways. Also, the HPV vaccination strategy in the Netherlands had changed. Therefore, it seems urgently warranted to conduct a follow-up study soon, in which the content of the educational programmes of the dental schools is also examined in detail.

CONCLUSION

This study among Dutch dental hygiene students identified specific knowledge deficits on various aspects of HPV-infection and vaccination. Results showed that senior students had better knowledge levels than junior students, however, their knowledge remained insufficient. This indicates that more attention should be paid to this topic in the Dutch dental hygiene curriculum.

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4

Knowledge and attitudes of dentists in The Netherlands regarding HPV-related cancer of the oropharynx

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ABSTRACT

Objective: To explore dentists' knowledge of human papillomavirus (HPV)-related oropharyngeal squamous cell carcinoma (OPSCC) and their willingness to play a role in prevention.

Methods: A web-based questionnaire that included questions about (1) HPV knowledge, (2) OPSCC knowledge, (3) perceived role in prevention, and a measure of confidence in clinical screening, was sent to 7364 dental healthcare providers in the Netherlands.

Results: Six hundred and seven (n=607) dentists completed the questionnaire. 48% of knowledge questions were answered correctly by more than half of the respondents. Significantly more female than male dentists were aware of the relationship between HPV and OPSCC and the availability of an HPV vaccine. Respondents considered it important that the relationship between HPV and OPSCC is discussed with patients and that a protocol is developed that is useful in screening for oral and oropharyngeal cancer.

Conclusions: Although dentists had specific HPV-related knowledge deficits, the majority was aware of the association between HPV and OPSCC, and were willing to play a role in prevention.

INTRODUCTION

Worldwide there is an increasing incidence of head and neck cancer. In 2012, 690.000 patients were diagnosed with head and neck cancer and this number rose to 931.931 patients in 2020 [1,2]. Also, in The Netherlands the incidence is increasing; from 1.936 patients in 1989 to 3.017 patients in 2020 [3]. Approximately 30% of these cancers is diagnosed in the oral cavity and these are mainly squamous cell carcinoma that develop in the oral mucosa. The incidence of oropharyngeal cancer has also increased in this period; from 214 patients in 1989 to 673 patients in 2020 and was diagnosed twice as often in men than in women. While the worldwide number of patients diagnosed with OPSCC is increasing marginally, the incidence of HPV-associated OPSCC is increasing significantly [4-6]. In 2012, approximately 30% of OPSCC was related to HPV and this percentage has been increasing ever since. In more developed countries this percentage is higher; in the United States 71% of OPSCC was related to HPV and in Europa 40% on average [6-9]. The Dutch Cancer Registration (NKR) collects data about the presence of HPV in oropharyngeal cancer. A recent analysis reveals that between 2015 and 2018 46% of OPSCC was related to HPV [10]. In contrast with the oropharyngeal region, a persistent infection with HPV is not related to cancer in the oral cavity [11].

Previously, patients diagnosed with OPSCC were usually older men with traditional risk factors such as high tobacco and alcohol consumption. Nowadays, patients diagnosed with OPSCC are more likely to be middle-aged men who lack these risk factors. One of the explanations for the increased prevalence rates may be a change in sexual behaviour. As HPV is transmitted sexually, engaging in orogenital sex with multiple sex partners will increase the risk of infection [7,8]. Persistent infection with a high-risk type of HPV is an important risk factor for development of OPSCC [9]. Regardless of the anatomic site, most of these cancers are associated with HPV types 16 and 18 [9]. HPV vaccination for young women is included in immunization programs of countries worldwide, with the aim to provide protection against cervical cancer[10]. This vaccination also protects against HPV-associated OPSCCs [7]. However, the current uptake of HPV vaccination is relatively low [12]. Misconceptions and lack of knowledge about the vaccine might be related to the poor quality of online information [13,14].

Dental providers are among the most frequently visited health care professionals and they could play a role in primary prevention of OPSCC by providing patients with information about HPV transmission and the vaccine. Previous research has shown that dental professionals are willing to provide their patients with information about HPV, but they lack knowledge and skills to sufficiently counsel their patients [16-19]. They reported barriers such as discomfort in discussing the sexual transmission of the virus, low self-efficacy for communicating efficiently and practice related barriers [18,20]. Some dental professional organizations responded to the need of education about HPV, for example, the American Head and Neck Cancer Society provided guidance for dentists

to answer patients' questions about HPV infection and HPV-related head and neck cancer [21]. Researchers attempted to develop educational interventions that could help professionals to feel more comfortable about discussing HPV [17,22,23].

In addition to counselling patients about HPV, dental healthcare professionals could also play a role in early detection of OPSCC. Early detection of clinical symptoms of OPSCC is important, because detection of cancer at an early stage reduces mortality, burden of disease and costs for society [24]. It is generally agreed that patients, especially those in high-risk groups, should be clinically screened for signs of oral and oropharyngeal cancer as part of their routine dental care [24]. OPSCCs may be difficult to detect clinically and along with the change in patient profile, this often results in diagnosis of HPV-associated OPSCC at a more advanced stage [25]. Because OPSCCs are likely to develop as primary disease in the crypts of the tonsil and base of the tongue, it is difficult to detect them by examining the intra-oral tissues only. The first symptom is often a swollen lymph node in the neck as clinical sign of a metastasis [26]. Dental healthcare providers should be aware of this and refer patients to secondary care accordingly. Patients with OPSCC could experience other symptoms such as pharyngitis, dysphagia, trismus, earache, a lump in the back of the mouth or throat or weight loss. These symptoms should be included in the medical history.

With the increasing incidence of HPV associated OPSCC, it is important that dentists have sufficient knowledge of HPV and skills to counsel their patients about HPV. Therefore, we conducted this study among dentists in The Netherlands to explore their knowledge and attitudes regarding HPV-related oropharyngeal cancer. The aims of this study were: a) to evaluate the current knowledge level of HPV related OPSCC and HPV vaccination of dentists; b) evaluate their confidence in performing a screening for OPSCC; and c) determine their perceived role in prevention and need for additional education.

METHODS

The survey instrument was a questionnaire that was adapted from a former survey among dental students in The Netherlands [20]. An online survey software program was used (Qualtrics, Provo, UT, USA). The Ethics Review Committee of the Vrije Universiteit Amsterdam confirmed that the Dutch Medical Research Involving Human Subjects Act (WMO) did not apply to this study.

A total of 7,364 dental healthcare professionals were invited to complete a web-based questionnaire and up to two reminder emails were sent at a 3-week interval. The invitation e-mail was sent to all professionals that had referred a patient to the Centers of Special Care Dentistry in Amsterdam and Groningen and to the members of the Scientific Dentistry United (SDU). Therefore, the 7,364 dental healthcare providers that received an

invitation consisted of a variety of dentists, dental hygienists, dental healthcare students, prosthodontists, and oral surgeons. Only dentists were allowed to participate in the survey.

The questionnaire contained 24 items, which included a total of 78 questions. The first questions were about current practice as a dental health care professional. To assess dentists' knowledge about HPV, HPV vaccination and risk for oral and oropharyngeal cancer, we included statements that required one of the following responses: 'correct', 'incorrect', or 'I don't know'. The questionnaire included dichotomous questions about the knowledge of a relation between HPV and oropharyngeal cancer, perceived responsibility in discussing the relation between HPV and OPSCC with patients, and knowledge about the availability of an HPV vaccination. Multiple-choice questions were used to obtain data about their sources of information about HPV, need for postgraduate education, barriers to refrain from discussing HPV with patients and factors that would stimulate them to discuss HPV with patients.

Five-point Likert scales were used to assess participants' confidence in discussing different topics with their patients such as lifestyle, domestic violence and sexually transmitted diseases. These scales were also used to rate the quality of education in dental school, the importance to develop professional guidelines and their perceived role in prevention of HPV-related OPSCC. Finally, background and demographic information was obtained.

Data were analyzed with SPSS, version 26.0 (IBM Corp SPSS statistics) using unpaired t-tests and Chi-square goodness of fit test to investigate the difference in responses between male and female dentists and between age groups. Differences in responses between subgroups on questions with categorical data were assessed using the Mann-Whitney *U* test. A p-value of 0.05 or lower was considered statistically significant.

RESULTS

Sample description

Of the 7,364 dental healthcare professionals that were invited, 885 responded to the survey. Six hundred and seven of these respondents were practicing dentists and their data were included for statistical analysis. The participants were primarily male (66.4%), between 30-59 years of age (73.1%) and worked in a general dental practice (96.6%). They worked on average 32.5 hours a week (SD=7.2) and saw 92 (SD=46.5) patients on average in a week. They worked in dental practices that were located in all regions of The Netherlands, with the greatest proportion in the western provinces (46.8%). The majority had completed their dental studies in Amsterdam (38.7%).

Table 1. Sixteen questions assessing dentists' knowledge about HPV, stratified for gender. The correct answers for each item are indicated with an asterisk. Data are expressed as percentages.

	Male n = 403			Female n = 204				Overall N = 607		
	Correct	Incorrect	I don't know	Correct	Incorrect	I don't know	X^2 (1, N = 607)	Correct	Incorrect	I don't know
1. Approximately 50% of patients who get oral and oropharyngeal cancer will die from this disease	32.8	48.4*	18.9	34.8	34.8*	30.4	13.80, p = 0.001	33.4	43.8	22.7
3. Oral cancer is often preceded by the presence of clinically identifiable premalignant changes	77.7*	17.1	5.2	78.9*	14.2	6.9	1.38, p = 0.50	78.1*	16.1	5.8
4. An increasing number of patients diagnosed with oral and oropharyngeal cancer lack risk factors as tobacco and alcohol use	48.6*	23.3	28	48.5*	19.1	32.4	1.95, p = 0.38	48.6*	21.9	29.5
5. The average age of patients diagnosed with oropharyngeal cancer is declining	50.1*	4.7	45.2	44.1*	5.4	50.5	1.96, p = 0.38	48.1*	4.9	47
6. The majority of malignant lesions in the oral and oropharyngeal region is diagnosed in an advanced stage of progression.	60.3*	21.8	17.9	65.7*	15.7	18.6	3.27, p = 0.20	62.1*	19.8	18.1
7. There are more than 100 types of HPV	22.3*	6.9	70.7	23.3*	8.8	68.1	0.79, p = 0.67	22.6*	7.6	69.9
8. A person can have HPV without knowing it	93.5*	0.5	6.0	94.1*	0.5	5.4	0.80, p = 0.96	93.7*	0.5	5.8
9. Most HPV infections resolve within a short time	20.6*	52.4	27.0	25*	46.4	28.4	2.19, p = 0.34	22.1*	50.4	27.5
10. Some types of HPV cause cervical cancer	86.1*	0.7	13.2	94.1*	0.0	5.9	0.18, p = 0.01	88.8*	0.5	10.7
11. HPV causes herpes and cold sore	17.9	58.8*	23.3	25	57.4*	17.6	5.49, p = 0.06	20.3	58.3*	21.4
12. HPV causes HIV/aids	8.4	74.2*	17.4	7.8	75*	17.2	0.07, p = 0.96	8.2	74.5*	17.3
13. HPV is a sexually transmitted virus	84.4*	5.5	10.2	86.8*	3.9	9.3	0.84, p = 0.66	85.2*	4.9	9.9
14. Antibiotics can cure a HPV infection	4.5	81.1*	14.4	5.9	74.5*	19.6	3.59, p = 0.17	4.9	78.9*	16.1
15. There is a vaccine that prevents against certain types of HPV	78.7*	6.2	15.1	84.3*	3.4	12.3	3.31, p = 0.19	80.6*	5.3	14.2
16. Using a condom decreases the chance of transmitting HPV	81.4*	6.7	11.9	82.4*	6.4	11.3	0.048, p = 0.96	81.7*	6.6	11.7

Knowledge

Of the participating dentists, 67% was aware of the relation between infection with HPV and oropharyngeal cancer. Female dentists were significantly more often aware of this relation than their male colleagues (75.0% vs. 54.3%; $\chi^2(2, N=607) = 3.95$, $p=0.047$)) (Table 1).

They acquired their HPV-related knowledge from professional literature (65.2%), continuous education (45.1%) and internet and (social) media (20.8%). Female dentists were significantly more often aware of the availability of HPV vaccination (respectively 88.2% vs. 80.4%; $\chi^2(2, N=607) = 5.91$, $p=0.02$). Females were also more aware of the fact that in the Netherlands HPV vaccination was only available for girls (81.9% vs. 74.7% for males), but this difference did not reach statistical significance ($\chi^2(2, N=607) = 5.47$, $p=0.07$).

A large majority of the dentists was aware of the risk factors for oral and oropharyngeal cancer; 98.7% correctly identified tobacco, 95.2% identified alcohol consumption and 86% identified previous cancer as risk factors (Figure 1).

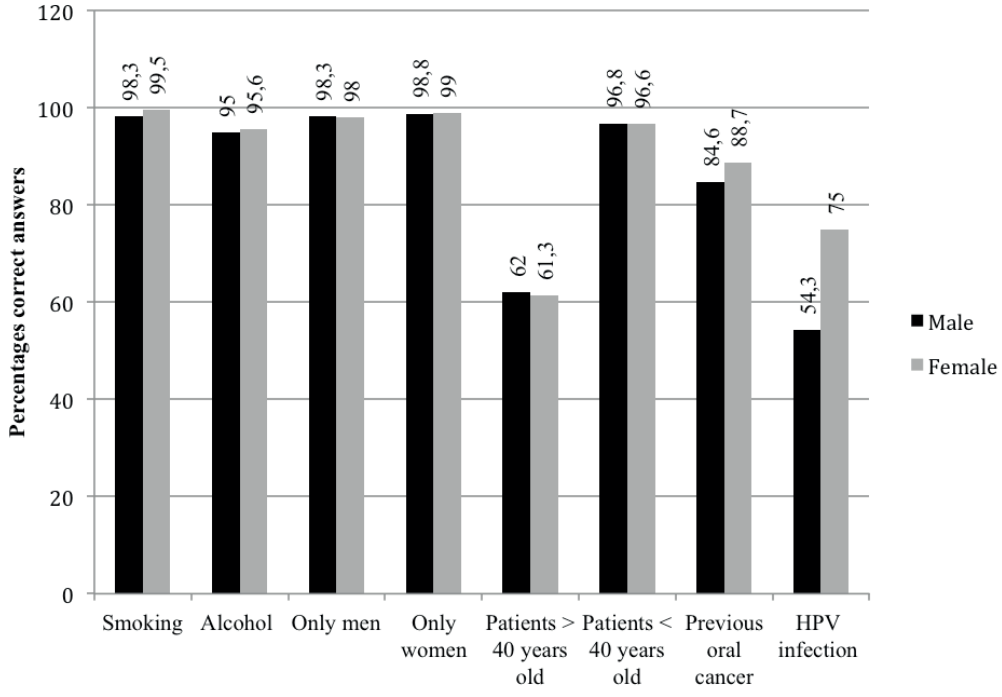

Figure 1. Percentages of correct answers, stratified for gender, to questions on potential risk factors of oral cancer.

Of the 15 questions assessing dentists' knowledge about HPV, 7 (46,7%) were answered correctly by more than half of the respondents (Table 2). Male dentists knew significantly more often that patients diagnosed with OPSCC have a 5-year survival rate of more than 50% (48.4% vs. 34.8%; $\chi^2(2, N=607) = 13.80$, p=0.001). Female dentists were more aware of the fact that HPV infection is a risk for cervical cancer (94.1% vs. 86.1%; ($\chi^2(2, N=607) = 0.18$, p=0.01) (Table 2). Of the 6 questions exploring the knowledge about HPV vaccination, 4 (66.6%) were answered correctly by more than half of the respondents (Tab. 1) To acquire more knowledge about HPV, dentists reported to desire courses and educational events (69.9%) and professional literature (50.1%) about HPV.

Table 2. Six questions assessing dentists' knowledge about HPV vaccination, stratified for gender. The correct answers for each item are indicated with an asterisk. Data are expressed as percentages.

	Male N = 403			Female N = 204				Overall N = 607		
	Correct	Incorrect	I don't know	Correct	Incorrect	I don't know	χ^2 (1, N = 607)	Correct	Incorrect	I don't know
1 The vaccine prevents transmission of some types of HPV	**60.5***	20.1	19.4	**57.4***	23.5	19.1	0.99, p = 0.61	**59.5***	21.3	19.3
2. The HPV-vaccine protects women against cervical cancer	**79.7***	6.0	14.4	**84.8***	5.9	9.3	3.20, p = 0.20	**81.4***	5.9	12.7
3. Individuals vaccinated against HPV do not have to practice safe sex (e.g. using condoms)	0.5	**92.3***	7.2	0.5	**94.1***	5.4	0.72, p = 0.70	0.5	**92.9***	6.6
4. In the national immunization programme the HPV-vaccine is only available for females	74.7*	5.5	19.9	**81.9***	5.9	12.3	5.47, p = 0.07	**77.1***	5.6	17.3
5. Men can request their general practitioner for HPV-vaccination, however this is not covered financially	**31.5***	4.0	64.5	**34.8***	4.4	60.8	0.81, p = 0.66	**32.6***	4.1	63.3
6. The HPV-vaccine is only effective for individuals who have never had sex before	16.6	**56.1***	27.3	30.4	**37.7***	31.9	**22.18, p < 0.001**	21.3	**49.9***	28.8

Examination for oral and oropharyngeal cancer

The majority of dentists (86.8%) reported to perform an examination for oral and oropharyngeal cancer during routine dental check-up. They performed this examination by visual inspection (97.5%) and palpation of the intra- and extra-oral tissues (42.3%). Only a few dentists were familiar with other examination techniques, such as light sources (N=2) and biopsy (N=3). Dentists reported a low level of confidence in performing this examination. On a 5-point Likert scale (1=not confident, 5=very confident) they rated their confidence in visual inspection on average as 2.5 (SD=0.7) and manual palpation as 2.7 (SD=0.7).

To stimulate dentists to perform an examination for oral and oropharyngeal cancer in all patients, almost all dentists would like to receive more scientific evidence for the health benefits (96.9%), additional training (94.6%), more time and financial compensation to perform a screening (94.6%), the availability of reliable screening devices (93.9%) and enhancement of knowledge about HPV and OPSCC in the general public (92.6%). On a 5-point Likert scale (1=very satisfied, 5=very unsatisfied) dentists rated the quality of training in performing an examination in dental school as 2.8 (SD=1.0). Dentists considered a protocol for oral and oropharyngeal cancer examination important (*mean*=1.95, SD=0.9) on a 5-point Likert-scale of 1=very important 5=not important. Development of a protocol was considered significantly more important by females (*mean*=1.77, SD=0.9) than by males (*mean*=2.03, SD=0.8) (U=35028, p=0.001, r=-0.13).

Communication and prevention

According to 69.5% of respondents, it is important for dentists to discuss HPV as a risk factor for OPSCC with patients. To facilitate them in counseling patients about HPV, they would like to use information material provided by dental professional organizations or the health authorities (57.2%), the possibility to attend continuing education events about HPV (54.5%). Public awareness campaigns to improve HPV-related knowledge of the general population was desired by 53.9%. Skill-building education in patient provider communication was desired by 9.9%.

Of responding dentists, 2.6% reported to discuss HPV vaccination with their patients, 56% considered starting this conversation and 41.4% did not intend to discuss HPV vaccination in the future. Arguments for not discussing HPV vaccination were limited knowledge about the vaccination (68.7%) and not feeling responsible as a dentist to discuss HPV vaccination (50.7%). Dentists who were willing to discuss HPV vaccination did not score significantly better on knowledge questions about HPV vaccination compared to dentists who were not prepared to discuss HPV vaccination ($p>0.05$).

Discussing personal topics with the patient, such as lifestyle and the relationship between general health and oral health, were considered ‘easy’ (*mean*=1.8, SD=0.8) and *mean*=1.5 (SD=0.7) respectively (Table 3). Topics as domestic violence, sexually transmitted infections and eating disorders were considered ‘less easy’ to talk about

(respectively *mean*=3.7 (SD=0.9); *mean*=2.8 (SD=0.9); *mean*=2.4 (SD=1.0). Female dentists reported significantly more discomfort in discussing lifestyle and the relationship between general health and oral health than male dentists ($p<0.05$; Table 3).

Table 3. Opinion of dentists how easy it is to discuss personal topics with patients, stratified according to gender. Data are presented as mean score ± SD of 5-point Likert scales (ranging from 1 = very easy to 5 = very difficult).

Question	Men	Women	Mann Whitney U-test	
			U	P
1. Lifestyle	1.4 (± 0.6)	1.6 (± 0.7)	35665	0.02
2. Domestic violence	3.8 (± 0.9)	3.6 (± 0.8)	318	0.42
3. Eating disorders	2.4 (± 0.9)	2.5 (± 1.0)	18175	0.48
4. Sexually transmitted infections	2.8 (± 0.9)	2.7 (± 0.9)	502	0.72
5. Substance abuse	1.8 (± 0.7)	1.9 (± 0.8)	33240	0.04

DISCUSSION

It is important that dentists are aware of the increasing incidence of HPV-related OPSCC and the fact that these tumors have specific biological and epidemiological features distinct from HPV-negative OPSCC. This study shows that dentists are willing to play a role in prevention of HPV-related OPSCC and early detection of these tumors by counseling their patients about HPV and performing clinical examinations during check-up appointments. However, dentists were not fully prepared for this role.

Although scientific evidence for a population-based head and neck cancer screening programme is lacking, most dentists perform an opportunistic examination during regular check-up appointments [27]. Results in this study showed that dentists did not feel comfortable about their competences in performing this examination. Also, palpation of the head and neck region, as part of this routine examination, was performed by less than half of the respondents. It is debatable whether this is a problem or not. It seems defendable to perform a palpation when there is a specific indication, for example an abnormality of the oral mucosa. Additionally, dentists in The Netherlands are used to refer patients to a head and neck surgeon when they are in doubt of the diagnosis of an abnormality in the head and neck region. However, when palpation is indicated, dentists need to be competent in performing it. A possible explanation for their lack of comfort in performing an oral and oropharyngeal cancer examination is insufficient clinical training in dental school. Responding dentists in our study were marginally satisfied with the quality of clinical training in dental school. The fact that there were no differences in satisfaction between dentists of different age groups indicates that education on

this subject has not changed over the years. In a former study, dental students in The Netherlands reported that they would like to have additional clinical training for oral and oropharyngeal cancer screening in their curricula [20]. To improve oral and oropharyngeal cancer examination competences among oral healthcare professionals, future research should focus on evaluating the clinical training in performing this cancer examination and developing strategies to effectively educate students. Additionally, the organization of clinical workshops could contribute, this was desired by 94.6% of respondents. Development of clinical practice guidelines could function as a fundament for these workshops and for campaigns to improve oral and oropharyngeal cancer knowledge among the general population.

When counseling patients about HPV, the sexual transmission of the virus is part of the conversation. Respondents in our study did not feel comfortable about discussing HPV with their patients. However, to facilitate them in counseling their patients about HPV, they did not desire training to strengthen their skills in communication with patients. They did want to acquire more theoretical knowledge of HPV by attending postgraduate courses and availability of information material provided by professional organizations. This suggests that when dentists have sufficient knowledge of HPV, they feel comfortable about discussing HPV with their patients. More knowledge of HPV among the general population could also contribute. Recently, the National Institute for Public Health and Environment (RIVM) in The Netherlands launched campaigns to inform the public about HPV because of the introduction of HPV-vaccination for boys in the national immunization program [28]. This could contribute to increased knowledge levels of the general public and to patients approaching their oral healthcare professional with questions about the relation between HPV and oral and oropharyngeal cancer.

Results revealed specific HPV-related knowledge deficits. Only 11 of the 23 statements about HPV and HPV vaccination were answered correctly by more than half of the respondents. Responding dentists were aware of the traditional risk factors for oral and oropharyngeal cancer such as tobacco, excessive alcohol use and previous head and neck cancer. Less than half of the respondents knew that the number of patients diagnosed with OPSCC without those risk factors is growing and that the average age is declining. The question we used in the questionnaire, to test knowledge of risk factors for cancer, only included patient characteristics and did not include clinical symptoms of oral and oropharyngeal cancer such as abnormalities of the oral mucosa, pharyngitis, dysphagia, trismus, earache, a lump in the back of the mouth or throat or weight loss. Patients with a potential malignancy often do not experience any symptoms at an early stage, which is one of the reasons that these cancers are often diagnosed at a late stage [29]. The European profile for graduating dentists describes that dentists need to be aware of the risk factors for oral and oropharyngeal cancer and refer patients to secondary care when necessary [30]. The fact that significantly more female dentists were aware of the relation between HPV and cervical cancer can be explained by the fact that

an HPV vaccination was available only for girls at the time we conducted our research. Mothers could have been more concerned about their daughters' vaccination uptake. Furthermore, they could have obtained HPV-related knowledge by information provided by the cervical cancer screening program. Although female dentists were more often aware of the availability of an HPV vaccination, they did not have more knowledge of the vaccination; of the six questions about the HPV vaccine only one question was answered correctly by significantly more female dentists (Table 2). So, both male and female dentists have knowledge deficits on this topic.

Sixty-seven percent of respondents was aware of the relation between HPV and oropharyngeal cancer, which is comparable with the knowledge of Dutch dental students [20]. Respondents acquired their knowledge by professional literature; social media and internet were not a source of information. For dental students consulting professional literature was as important as consulting social media and the internet. This difference may be age-related; only 3% of the participating dentists were between 18-29 years of age. For patients, online information is the second most popular source, after healthcare providers, of information regarding HPV. The role of internet is becoming more and more important in exchange of medical information, but unfortunately the quality of this information about HPV is often inaccurate and incomplete [31]. The dental community needs to adapt accordingly by providing reliable sources of information about HPV for dentists and patients. In the Netherlands, the National Institute for Public Health and Environment (RIVM) provides evidence-based information on their website. Dentists could refer to this information when patients approach them with questions about HPV and vaccination.

Demographic characteristics of responding dentists in our study closely resemble those of dentists in The Netherlands; 59% of dentists is male (vs. 66% of respondents) and 48% is between 40- and 59 years old (vs. 61% of respondents) [32]. Respondents worked in dental practices that were equally divided across the Netherlands. However, there is a possibility of selection bias; since the participation was voluntary and the response rate was relatively low, our survey may have attracted dentists with different baseline knowledge. Because the data are self-reported there may also be a social desirability bias in the questions about examination practices and communication with patients. Another drawback of this study is that it was not possible to calculate a response rate. The questionnaire was sent to different types of dental healthcare professionals, and we do not know what the number of dentists was amongst them. Finally, it could have been possible that some professionals received the invitation multiple times; for example, when they are member of the SDU and have referred a patient to the Centers of Special Care Dentistry in Amsterdam and/or Groningen.

CONCLUSION

Findings from the present study show that dentists in The Netherlands are willing to play a role in prevention of HPV-related OPSCC and early detection of these tumors by counseling their patients about HPV and performing clinical examinations during check-up appointments. However, dentists are not fully prepared for this role. We have identified deficits in knowledge about the changed biological and epidemiological features of HPV-positive OPSCC compared to HPV-negative ones. Data have also revealed that dentists have a lack of confidence and skills in performing an examination for oral and oropharyngeal cancer. Development of evidence-based clinical guidelines, professional literature, patient information materials and postgraduate education courses is recommended.

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5

Evaluation of head and neck cancer education at European dental schools

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ABSTRACT

Aim: In Europe approximately 150.000 patients are diagnosed with head and neck cancer annually. Dentists play an important role in prevention and detection at an early stage when survival rates are best. This study aims to evaluate content of head and neck cancer education curricula of European dental schools.

Materials and Methods: A questionnaire, comprising 23 questions about content of curricula and teaching methods, was distributed to the deans of all 234 members of the Association for Dental Education in Europe.

Results: The response rate was 24%. All dental schools included head and neck cancer screening practices in their curricula, two-thirds had their students perform this screening on all patients routinely and education was mostly divided over various courses (65%). A variation in content of education in screening practices and counselling patients about various risk factors was reported. Alcohol and tobacco use were included in most curricula as risk factors for head and neck cancer (98%), gastro-oesophageal reflux was a less frequently included (41%). The human papillomavirus (HPV) as a risk factor for oropharyngeal cancer was included in 94% of curricula and 87% also contained education about strategies to discuss prevention of HPV-related cancer. No association was found between curricula containing strategies about discussing HPV-related cancer and inclusion of the HPV vaccine in national immunisation programmes.

Conclusion: Variation in head and neck cancer education results in differences of specific knowledge and competences of graduating European dentists. Dental schools can use these findings to improve their curricula.

INTRODUCTION

The incidence of head and neck cancer in Europe is high; in 2020 an estimated 151,000 patients will be diagnosed, and 60,000 of these patients will be death within 5 years. Although survival rates are rising, more than half of patients are diagnosed at a late stage and already have regional or metastatic disease which reduces their chance of survival [1,2,3]. Early diagnosis and timely start of treatment is crucial for further improving success of treatment.

Oral cavity and laryngeal cancers are the most common head and neck cancers. Overall numbers of these cancers are rising marginally, but due to the human papillomavirus (HPV) the incidence of oropharyngeal cancer is increasing gradually [4,5]. Lifestyle is considered an important factor in developing head and neck cancer. The most well recognized risk factors are the use of tobacco and alcohol. Approximately one in four oral cancers is related to use of tobacco, and 7-19% is attributable to use of alcohol [6]. Recent research shows that HPV infection is also an important risk factor, which is transmitted through sexual contact [7]. Due to the human papillomavirus there is a shift in characteristics of patients diagnosed with head and neck cancer. They used to be older men, who have a history of alcohol and tobacco use. Nowadays they are more likely to be younger men (40-69 year old), without these traditional risk factors or other health problems, but they have the risk factor of having multiple lifetime sex partners [8,9]. Persistent infection with high-risks types HPV 16 and 18 is an important risk factor for development of cancer at various anatomic sites as the cervix, anus, penis and oropharynx [10]. Therefore, a vaccine is included in all European national immunisation programmes for teenage girls, several programmes include boys as well [11]. Due to misconceptions and lack of information vaccine uptake dropped dramatically the last few years [12]. European dentists see their patients on regular basis and have a great opportunity to provide their patients with information about the vaccine and contribute to increase vaccine uptake.

The General Assembly of the Association for Dental Education in Europe presented a profile with competences for European Dentists with the aim of harmonising curricula of dental schools throughout Europe. According to competences 4.13 and 6.59 a dentist should be competent at recognize neoplasms and refer patients when needed [13]. However, recent research shows dentists and dental students have deficits in knowledge about risk factors for head and neck cancer, they do not feel confident about discussing HPV prevention with their patients and performing a screening for head and neck cancer [14,15,16]. This suggests that head and neck cancer education of dental curricula may not be sufficient to fully prepare dentists for the above-mentioned competences. Therefore, the aim of this study was to compare content of head and neck cancer education programmes at European dental schools, which might help to improve their curricula.

MATERIALS AND METHODS

This study used a cross-sectional descriptive survey research design and was approved by the internal Ethical Review Board of the Academic Centre of Dentistry Amsterdam. The study population consisted of all 234 members of the Association for Dental Education in Europe (ADEE). Membership consists primarily of dental schools in Europe, except for a few in the Middle East. The survey instrument was a 20-item questionnaire and contained questions about background information on each dental school and their curricula, teaching methods used, clinical screening practices and theoretical education about head and neck cancer (Supplement 1).

In March 2018 a letter was sent to all deans of the 234 ADEE registered dental schools, requesting to invite the appropriate faculty member to fill out the questionnaire. A reminder was sent in July. The questionnaire could be returned by ordinary mail, e-mail or online via Formdesk. When dental schools returned multiple questionnaires instead of one, only the online questionnaire was included. If dental schools returned multiple questionnaires completed by different faculty members, they were merged into one based on mean outcomes. Data analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) using Chi-square and Fishers' exact tests to explore associations several subgroups and the independent variables. P values <0,05 were considered statically significant.

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

RESULTS

Fifty-five dental schools responded to the survey, one dental school could not be invited because of insufficient address information, resulting in a response rate of 24% (Table 1). Fourteen questionnaires were returned by ordinary mail, 10 by e-mail and 31 were completed online. One dental school was excluded because it only offered a postgraduate dental programme. Dental schools were equally divided over Europe and two were located in Lebanon (Table 1). Half of the schools (52%) had more than 100 enrolled students for the academic year 2017-2018 and most curricula required 5 years (69%). Differences were reported in approach of head and neck cancer education. Only one-third of curricula (35%) had a specific course covering head and neck cancer education. At larger dental schools the head and neck cancer education was significantly more often divided over various courses (X^2 (1, N=49) =4.4, p=0.035). In two-third (65%) of curricula students performed an examination for head and neck cancer routinely on all patients. In the remaining curricula students were trained to perform an examination in all high-risk

patients or when the clinician decides it is necessary for a specific patient. Patients were examined mostly during all visits (32%) or during the initial visit (30%). All curricula taught students to recognize lesions that are suspicious for oral cancer, but irregularities in the skin of the head and neck were only included in 73% of curricula (Table 2). Variation was also reported in examination practices of other regions of the head and neck. Clinical intra- and extra oral examination for head and neck cancer included the oral cavity in all curricula, but palpating the tonsils and thyroid gland was only included in one-third (Tables 3 and 4).

Variation was reported in content about risk assessment (Tables 5 and 6). Almost all curricula taught students to counsel patients about tobacco and alcohol use as risk factors. Sexual practices was recognised as a risk factor by 69%, but only 37% of the dental schools taught students to discuss this topic with their patients. Most dental schools did not identify male patients from 40 years old and oesophageal reflux as risk factors.

Most curricula included specific education about HPV as a risk factor for oropharyngeal cancer (94%) and counselling patients about prevention of HPV-related cancer (87%). In 2018, when the survey was conducted, only 35 of the 55 responding dental schools were located in a country that included a HPV vaccine in the national immunisation programme. No association was found between availability of the HPV vaccine in 2018 and education about HPV (Fisher exact test (1, N=54) = 0.702, P=0.506).

Table 1. Number responding dental schools per geographical location and country.

Northern Europe (n=13)	Eastern Europe (n=10)	Southern Europe (n=13)	Western Europe (n=17)	Middle East (n=2)	Total (n=55*)
Finland (2)	Bulgaria (1)	Albania (1)	Belgium (2)	Lebanon (2)	
Ireland (1)	Czech Republic (1)	Italy (4)	France (4)		
Lithuania (1)	Hungary (2)	Portugal (2)	Germany (7)		
Norway (2)	Poland (3)	Serbia (1)	Netherlands (2)		
United Kingdom (7)*	Romania (2)	Slovenia (1)	Switzerland (2)		
	Ukraine (1)	Spain (1)			
		Turkey (3)			

*One of the 55 dental schools is excluded because it only provides postgraduate education

Table 2. Potentially (pre)cancerous lesions included in the curricula of European dental schools, stratified according to their geographical location#.

Potentially (pre)cancerous lesions	Positive response (%) n=54	Northern Europe (%) n=12	Eastern Europe (%) n=10	Southern Europe (%) n=13	Western Europe (%) n=17	p-value X^2
Epithelial discolorations	96	100	90	92	100	0.44
Irregular textural changes in the epithelium	89	100	80	92	82	0.38
Swellings and bumps in the epithelium	85	100	90	85	77	0.32
Ulcerations	98	100	90	100	100	0.23
Asymmetry in the face	83	100	70	85	77	0.25
Swollen glands or lymph nodes	96	100	90	100	94	0.53
Irregularities in the skin of the head and neck	73	83	80	77	59	0.43
Other*	13	17	30	8	0	0.11

The two dental schools in Lebanon were not included in the comparison of the dental schools based on geographical location.
*"Other" i.e. specified as: white lesions, orbital tumours, leukoplakia, erosive lichen planus, modified fluorescence in Velscope evaluation.

Table 3. Topics of intraoral examination included in the curriculum of European schools, stratified according to their geographical location#.

Intraoral examination	Positive response (%) n=54	Northern Europe (%) n=12	Eastern Europe (%) n=10	Southern Europe (%) n=13	Western Europe (%) n=17	p-value X^2
Visually assess the oral cavity	100	100	100	100	100	-
Visually assess the lateral borders of the tongue	100	100	100	100	100	-
Visually assess the base of the tongue	93	92	100	92	88	0.74
Visually assess the alveolar mucosa	100	100	100	100	100	-
Visually assess the hard palate	100	100	100	100	100	-
Visually assess the soft palate	100	100	100	100	100	-
Visually assess the oropharynx	89	100	90	92	77	0.24
Palpate the tongue	89	83	100	92	82	0.49
Palpate the palate	78	75	90	85	65	0.42
Palpate the floor of the mouth	89	83	90	92	88	0.91
Palpate the buccal and vestibule mucosa	83	75	90	92	77	0.54
Palpate the tonsils and the tonsillar pillars	32	33	20	54	24	0.26
Other	7	25	10	0	0	0.05

The two dental schools in Lebanon were not included in the comparison of the dental schools based on geographical location.
*"Other" i.e. specified as: lip mucosa, visually assess the ventral part of the tongue.

Table 4. Topics of extraoral examination included in the curricula of European dental schools, stratified according to their geographical location#.

Extraoral examination	Positive response (%) n=54	Northern Europe (%) n=12	Eastern Europe (%) n=10	Southern Europe (%) n=13	Western Europe (%) n=17	p-value x^2
Visually assess the lips	98	100	100	100	94	0.55
Visually assess the eyes	59	58	80	69	35	0.10
Visually assess the facial skin	89	92	100	100	71	0.04
Visually assess the facial symmetry	91	92	90	92	88	0.98
Visually assess the posture or gait	54	42	50	69	29	0.18
Palpate the (cervical) lymph nodes	94	100	100	92	88	0.47
Palpate the temporomandibular joint	83	92	90	77	82	0.72
Palpate the musculature	76	75	90	77	71	0.71
Palpate the submandibular gland	85	75	100	85	82	0.43
Palpate the parotid gland	82	67	100	85	77	0.24
Palpate the thyroid gland	30	42	30	31	18	0.57

The two dental schools in Lebanon were not included in the comparison of the dental schools based on geographical location.

Table 5. Risk factors for oral cancer that students are taught to assess in patients, included in the curricula of European dental schools, stratified according to their geographical location#.

Risk factors	Positive response (%) n=54	Northern Europe (%) n=12	Eastern Europe (%) n=10	Southern Europe (%) n=13	Western Europe (%) n=17	p-value x^2
Tobacco use	98	92	100	100	100	0.33
Alcohol use	98	92	100	100	100	0.33
Sexual practices	69	42	70	85	77	0.11
Nutrition/diet	74	83	70	77	65	0.71
Previous head and neck cancer	91	92	80	100	88	0.43
Familial occurrence of head and neck cancer	72	75	100	77	53	0.06
(Male) patients over 40 years old	30	33	10	46	29	0.32
Prolonged sun exposure/solar radiation	82	75	80	85	82	0.94
Gastro-oesophageal reflux	41	50	40	62	12	0.03
Oral conditions (e.g. leukoplakia)	100	100	100	100	100	-
Other	11	33	10	8	0	0.05

The two dental schools in Lebanon were not included in the comparison of the dental schools based on geographical location.
*"Other" i.e. specified as: any previous malignancies, immunosuppression, lichen planus, radiotherapy in head or neck region, betelnut/paan, any lesion that after ten days of causal treatment doesn't modify its appearance.

Table 6. Risk factors students are taught to counsel patients, included in the curricula of European dental schools, stratified according to their geographical location#.

Risk factors	Positive response (%) n=54	Northern Europe (%) n=12	Eastern Europe (%) n=10	Southern Europe (%) n=13	Western Europe (%) n=17	p-value x^2
Tobacco use	98	100	100	92	100	0.38
Alcohol use	85	83	90	77	88	0.80
Sexual practices	37	25	50	46	29	0.50
Nutrition/diet	57	75	90	46	35	0.02
Previous head and neck cancer	65	50	90	54	71	0.18
Familial occurrence of head and neck cancer	57	42	90	69	41	0.04
(Male) patients over 40 years old	20	25	20	23	12	0.80
Prolonged sun exposure/solar radiation	70	75	90	69	53	0.23
Gastro-oesophageal reflux	30	42	30	39	6	0.12
Oral conditions (e.g. leukoplakia)	85	83	90	85	82	0.96
Other	7	25	0	8	0	0.63

The two dental schools in Lebanon were not included in the comparison of the dental schools based on geographical location.

DISCUSSION

This study shows a variation in content of head and neck cancer education at European dental schools. Several risk factors for head and neck cancer have been identified and some are greater threats than others. Alcohol and tobacco use are the strongest risk factors and are modifiable by lifestyle changes. Other modifiable risk factors are HPV infection and nutrition. Almost all dental schools reported identification of alcohol and tobacco use and trained their students in counselling skills to motivate patients to change their lifestyle. Prevention of HPV infection can be achieved by use of the HPV vaccine or change in sexual behaviour. The majority of dental schools taught their students about HPV as a risk factor for oropharyngeal cancer and strategies for prevention. These strategies are educating patients about risks of HPV transmission, instructing about changes in sexual behaviour and encourage patients to participate in HPV vaccination programmes. Remarkably, only one third of the curricula addressed sexual behaviour counselling. Former research has shown dental students and dentists feel discomfort in having sexual-health related discussions with patients and dental curricula do not include sufficient training on this topic [14,17]. Due to HPV the risk profile for head and neck cancer changed, younger men are more likely to get diagnosed. However, most dental schools did not indicate male patients from 40 years old a being at risk for head and neck cancer. Therefore, most curricula do not seem to be adapting fully to changing risk profiles in the population and provide their students with sufficient competences to play a role in prevention of HPV related oropharyngeal cancer.

Gastro-oesophageal reflux (GORD) was the least frequently included risk factor reported to discuss with patients. This may be explained by the fact that symptoms of GORD are interpreted in different ways by various cultures and languages, which could explain the geographical differences in this study [18].

Early (pre) cancerous lesions often do not cause malfunction, pain or other discomfort, which often results in detection in a late stage when chances of survival are less. It is important for clinicians to be aware of these signs and symptoms and refer patients accordingly [13]. Almost half of the curricula did not have their students examine patients for head and neck cancer routinely. A possible explanation is that European dental schools focus on self-reported information about general health, obtained by a written medical history. These general health forms are used by 94% of European dental schools and they report to be satisfied with this approach to identify possible health problems [19].

Methods of examination (visualization and palpation) taught were not consistent across curricula, but several did not include the base of the tongue. One dental school replied they did not include this part because it is not possible to visualize the base of the

tongue. To visually examine as much of the tongue as possible, it is advised to use gaze to grasp the tongue and withdraw the tongue as far as possible [20]. Only one third of dental schools included palpation of the tonsils and tonsil pillars in their examination practices. Examination of parts of the oropharynx (tonsils, soft palate, base of tongue and lateral/ posterior pharyngeal walls) was least frequently taught. Given the tendency of HPV related cancers to develop in these parts, this may be viewed as a significant deficiency.

It is remarkable that visual inspection of the skin of the face was not included in almost one third of the curricula in Western Europe although the incidence of melanoma skin cancer is highest in this part of Europe [21]. The majority of these cancers is diagnosed in the head and neck region. Since skin cancer is associated with exposure to UV rays, it is largely preventable [22]. However, 20% of dental curricula in Northern and Western Europe did not include prolonged sun exposure as a risk factor.

Gaps in theoretical knowledge and lack of confidence in performing an examination for head and neck cancer have been reported in former research among Dutch dental students in 2017 [14]. Dutch dental students suggested including more clinical training in their curricula and suggested implementation of clear clinical guidelines for examination.

Variation in content of dental curricula in Europe has been showed for other topics, for example on local anaesthesia education [23]. These variations are reported despite the availability of a profile of competences for graduating European dentists by the General Assembly of the Association or Dental Education in Europe (ADEE). This can be explained by the fact that most competences have not been described in great detail [13]. Another explanation for the variation in head and neck cancer education could be the fact that the content of clinical practice guidelines for oral cancer is not uniform in European countries. The quality of these guidelines is 'moderate' and they are in need for improvement on methodological aspects and applicability [24]. Adding the use of a high-quality clinical guideline in the profile of competences of the ADEE may lead to more uniformity in European dental curricula and optimization of clinical practice.

This study has several limitations. The relatively low response rate of 24% could by explained by the fact that the questionnaire was written in English and this is not the native language of most European countries. This could also have caused uncertainties, misinterpretations or misunderstanding of the questions. Moreover, results may be biased because respondents may be more interested in teaching of head and neck cancer and have more content on this topic in their curricula.

Further research should explore more details about the content of the curricula, for example on teaching in communication skills. Site visits to European dental schools and discussion with local focus groups could also contribute to obtain more detailed information. To improve education in head and neck cancer, it might be useful to investigate opinions of dental students too.

CONCLUSION

Head and neck cancer education at European dental schools is common, but variation is reported in theoretical content and methods of examination. Examination techniques taught in dental curricula need to be more thorough because detecting of (pre) cancerous lesions at an early stage improves survival rates for patients. Most European dental schools taught their students skills to counsel patients about traditional risk factors as alcohol and tobacco use, but most curricula did not seem to be adapting fully to the changing risk profiles in the population. Therefore, further research to improve head and neck cancer education at European dental schools seems warrant.

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SUPPLEMENT 1

QUESTIONNAIRE

Survey Questionnaire – An Oral Cancer Assessment of Dentistry Courses in Europe

(4 pages)

1. What is the name of your dental school?

.....

2. Where is your dental school located?

.....

3. What is your title/position in the dental school?

.....

4. How many students are enrolled in your program for the 2017-2018 academic year?

.....

5. Of the last five years what is your average number of students graduating per year?

.....

6. What is the duration of the dentistry course?
   - o 4 years
   - o 5 years
   - o 6 years
   - o Other (please specify) .....

7. Does your program have a specific, required curriculum component or components covering head and neck cancer or is head and neck cancer something which is covered at teachers' discretion as part of other courses' content?
   - o Specific, required curricular component
   - o Learned as part of various courses
   - o No specific curriculum or content covering head and neck cancer

8. In the clinic, do students perform head and neck cancer examinations on all patients?
   - o Yes (go to question 9)
   - o No (go to question 8a)

8a. Which of the following patients receive head and neck cancer examinations routinely?
- o All patients
- o All adults starting at age .....
- o All high risk patients
- o It is left to the clinician's discretion
- o No patients
- o Other (please specify) .....

9. During which of the following visits are head and neck cancer examinations performed?
- o Initial visit
- o Recall visits
- o Prophy visits
- o Annually
- o All visits
- o Never
- o Other (please specify) .....

10. Do students in your program perform head and neck cancer examinations in community settings as well as in the clinic?
- o Yes
- o No

11. On average, how many patients does a student in your program see in clinic annually?

.....

12. By the time your students graduate from your program, approximately how many head and neck cancer examinations will they have performed on average?

.....

13. Are your students taught to recognize potentially cancerous or precancerous lesions in the head and neck region?
- o Yes (go to 13a)
- o No (go to 14)

13a. Which of the following will your graduates recognize as potentially cancerous or precancerous lesions? Mark all that apply.
- o Epithelial discolorations
- o Irregular textural changes in the epithelium
- o Swellings and bumps in the epithelium
- o Ulcerations
- o Asymmetry in the face

- o Swollen glands or lymph nodes
- o Irregularities in the skin of the head and neck
- o Other (please specify) .....

14. Which of the following are your students taught to do as part of the **intraoral** examination for potential head and neck cancers? Mark all that apply.
    - o Visually assess the oral cavity
    - o Visually assess the lateral borders of the tongue
    - o Visually assess the base of the tongue
    - o Visually assess the alveolar mucosa
    - o Visually assess the hard palate
    - o Visually assess the soft palate
    - o Visually assess the oropharynx
    - o Palpate the tongue
    - o Palpate the palate
    - o Palpate the floor of the mouth
    - o Palpate the buccal and vestibule mucosa
    - o Palpate the tonsils and the tonsillar pillars
    - o Other (please specify).....

15. Which of the following are your students taught to do as part of the **extraoral** examination for potential head and neck cancers? Mark all that apply.
    - o Visually assess the lips
    - o Visually assess the eyes
    - o Visually assess the facial skin
    - o Visually assess facial symmetry
    - o Visually assess the posture or gait
    - o Palpate the cervical lymph nodes or other lymph nodes
    - o Palpate the temporomandibular joint
    - o Palpate the musculature
    - o Palpate the submandibular gland
    - o Palpate the parotid gland
    - o Palpate the thyroid gland
    - o Other (please specify) .....

16. Which of the following head and neck cancer risk factors are your students taught to assess in their patients? Mark all that apply.
    - o Tobacco use
    - o Alcohol use
    - o Sexual practices
    - o Nutrition/diet

- o Previous head and neck cancer
- o Familial occurrence of head and neck cancer (heredity)
- o (Male) patients over 40 years old
- o Prolonged sun exposure/solar radiation
- o Gastro-oesophageal reflux
- o Oral conditions (for example leukoplakia and erythroplakia)
- o Other (please specify) .....

17. For which of the following risk factors are your graduating students taught to counsel patients? Mark all that apply.
    - o Tobacco use
    - o Alcohol use
    - o Sexual practices
    - o Nutrition/diet
    - o Previous head and neck cancer
    - o Familial occurrence of head and neck cancer (heredity)
    - o (Male) patients over 40 years old
    - o Prolonged sun exposure/solar radiation
    - o Gastro-oesophageal reflux
    - o Oral conditions (for example leukoplakia and erythroplakia)
    - o Other (please specify) .....

18. Are your students specifically taught and made aware of the fact that the human papillomavirus (HPV) has emerged as a big risk factor for oropharyngeal cancer?
    - o Yes
    - o No

19. Are your students taught about any strategies for prevention of human papillomavirus-related cancer?
    - o Yes
    - o No

20. If you have any other information about your head and neck cancer program or curriculum you would like to share, please specify below:

.....

.....

.....

.....

End of the questionnaire. Thank you for participating.

6

Knowledge of Diagnosis and Management of Selected Oral Mucosal Lesions among dentists in The Netherlands

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ABSTRACT

Background: Knowledge of oral mucosal lesions (OMLs) among dentists is relevant in diagnosing potentially malignant diseases and oral cancer at an early stage. The aim of this survey was to explore dentists' knowledge about OMLs.
Material and Methods: Respondents to a web-based questionnaire, containing 11 clinical vignettes representing patients with various OMLs, provided a (differential) diagnosis and management for each. Information about demographics and clinical experience of the participants was acquired as well. Descriptive statistics were performed and T-tests were used to test for significant ($p<0.05$) differences in mean scores for correct diagnosis and management between subgroups based on demographic variables.
Results: Forty-four of 500 invited dentists completed the questionnaire. For (potentially) malignant OMLs, the number of correct diagnoses ranged from 14 to 93%, whilst the number of correct management decisions ranged from 43 to 86%. For benign OMLs, the number of correct diagnoses and management decisions ranged from 32 to 100% and 9 to 48%, respectively. For 11 clinical vignettes, mean scores for correct diagnosis, correct management and correct diagnosis and management were respectively 7.2 (±1.8), 5.7 (±1.5), and 3.8 (±1.7).
Conclusions: The results show that dentists in the Netherlands do not have sufficient knowledge to accurately diagnose some OMLs and to select a correct management. This may result in over-referral of benign OMLs and under-referral for (potentially) malignant OMLs. Clinical guidelines, that include standardized criteria for referral, and continuing education, may improve dentists' ability to correctly diagnose and accurately manage OMLs.

INTRODUCTION

Knowledge of oral mucosal lesions (OMLs) among dental practitioners is relevant in diagnosing relatively harmless lesions but also oral cancer at an early stage and their potentially malignant precursors. In case of malignant disease, early detection reduces mortality and morbidity[1]. OMLs prevalence, defined as an abnormal change in the oral mucosa such as the colour of surface, swelling or loss of integrity [2], varies significantly across different studies, ranging from 5% to 65% [3]. The variability arises from differences in methodology employed in studies and from sociodemographic differences between countries [4].

OMLs include developmental defects, benign lesions, oral potential malignant disease (OPMD) and malignant disease. These various diseases may cause symptoms such as a burning sensation, swelling, irritation or pain, but often do not cause any symptoms [2,5-7]. Especially in oral squamous cell carcinoma (OSCC), accounting for over 90% of oral cancers, symptoms are limited or lacking at an early stage of the disease, often causing patients to seek late care with cancer at an advanced stage [5,7,8].

Screening patients for oral cancer during dental check-up appointments using visual oral examination is a cost-effective strategy in oral cancer detection [9]. Since dental practitioners see many patients on a regular basis, they have the opportunity to detect OPMD and early stage OSCC, and to determine which lesions with a provisional diagnosis can be closely observed versus referral as cancer is suspected. A recent systematic review about delay in diagnosis of oral cancer indicated that lack of ability to correctly diagnose OMLs among healthcare professionals is related to delay in diagnosis [10]. Various studies explored oral cancer knowledge, attitudes and screening practices of dental practitioners, with only a few focusing on referral decisions [11-14]. One approach that has proved very effective in teaching examining diagnostic and referral decisions has been the use of clinical vignettes [15,16]. These simulate clinical situations by describing a patients' visit by using clinical pictures, a description of the complaint, and a patients' history. Using these, it was found that the number of correct referral decisions by dental practitioners in England was higher than the number of accurate diagnoses. There also appeared to be a lack of discrimination between risk factors in the process of making a referral decision [16]. It was suggested that when dentists are in doubt about the diagnosis of OMLs, their default position is to refer. The latter and other studies on this topic, mainly focussed on OPMDs and OSCCs whereas some benign OMLs may have the potential to negatively influence the quality of life through impact on mastication, swallowing, aesthetics, and speech [5,12,16,17]. Some OPMDs or OSCC at an early stage mimic benign OMLs, such as small tumours or ulcerative lesions that are diagnosed as traumata, which causes a delay in diagnosis [10]. So, ability to distinguish between these types of OMLs is important.

To explore dentists' knowledge about OMLs, we conducted this survey among dentists in the Netherlands, using a questionnaire containing 11 clinical vignettes, which

represented various OMLs and required respondents to provide a (differential) diagnosis and accurate management for each.

MATERIAL AND METHODS

Data collection

By means of its Data Stations Project, the Royal Dutch Dental Association (KNMT) periodically collects data on delivery of oral health care, practice management and dentists' opinions and views regarding current issues in dentistry in the Netherlands (18). In January 2019, an invitation e-mail was sent to 500 dentists (243 males; 257 females), randomly selected from the dentists who participate in the Data Stations Project periodic surveys. The e-mail included a link to the 25-item web questionnaire. Reminders were sent after 2 and 4 weeks; data collection ended 6 weeks after the first invitation.

Instrument

The 25-item self-constructed questionnaire (Supplement 1) in Dutch consisted of two sections and was developed for this study in cooperation with the department of Oral and Maxillofacial Surgery of the Amsterdam University Medical Centers in Amsterdam. The first section consisted of 11 clinical vignettes, representing patients with various OMLs including a clinical picture of a lesion and a brief textual description of a simulated clinical history. The description contained typical characteristics for each OML (for an example of a clinical vignette, see Fig. 1). These pictures and descriptions were provided by a maxillofacial surgeon and selected from medical records of referrals to the outpatient clinic. The selected cases represented a wide range of benign and (potentially) malignant OMLs; white lesions (2), red lesions (2), pigmentations (2), ulcerated lesions (2), soft tissue enlargements (2) and one skin lesion (Tab. 2). In the first section of the questionnaire three multiple choice questions for each case required participants to select the correct diagnosis, differential diagnosis, and management. While for the diagnosis and management one option could be selected, for the differential diagnosis, multiple options could be selected. The multiple-choice questions were constructed using information the guidelines of the Dutch Association of Oral and Maxillofacial Surgeons. The second section contained 7 questions and included demographic characteristics, participants' current oral examination practices, referral practices, and postgraduate education courses. A panel of fifteen dental students, eight residents of the department of Oral and Maxillofacial Surgery and three maxillofacial surgeons of the department of Oral and Maxillofacial Surgery, pilot tested the questionnaire and minor revisions were made upon their feedback.

Case VII	
A 67-year-old man, ASA: 2. Smoking: pipe smoking 2 to 3 times daily Health: TIA, artificial knee (R) Med: Ascal	
While inspecting the mucosa, you notice an abnormality on the right edge of the tongue. The area feels somewhat solid. The patient indicates that the abnormality has existed for 2 months, is not aware that it is a lesion and does not suffer from it.	

Q7A: Most likely diagnosis

- ○ Squamous cell carcinoma
- ○ Pigmented nevus
- ○ Erythroplakia
- o Morsicatio linguarum
- o Lichen planus
- o Leukoplakia

Q7B: Likely differential diagnosis (Multiple options are possible)

- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Squamous cell carcinoma
- ☐ Pigmented nevus
- ☐ Erythroplakia
- □ Morsicatio linguarum
- □ Lichen planus
- □ Leukoplakia

Q7C: Policy

- ○ No policy required
- ○ A check-up appointment after 2 or 3 weeks
- ○ A check-up appointment after 1 or 2 months
- ○ A follow-up appointment after 6 months
- ○ Referral to an OMF Surgery

Figure 1: Example of a vignette used in the questionnaire

Statistical analysis

Data were analysed using Statistical Package for Social Sciences (SPSS), version 26 (IBM Inc., New York, USA). Figures were made using GraphPad Prism version 9.3.1 for Windows, GraphPad Software, San Diego, California USA, www.graphpad.com. Frequencies and means (SD) were used for data description. To grade knowledge, participants were awarded one point for each correct answer: correct diagnosis (CD), correct management (CM) and the combination of correct diagnosis and management (CD+M). To test whether there were significant ($p<0.05$) differences in mean scores of CD, CM and CD+M between subgroups based on the variables sex, years of graduation, and participants that did and did not want to attend a course on various aspects of OMLs, unpaired t-tests were used.

Ethics statement

The invitation e-mail mentioned that participation was voluntary. Participants consented to the survey by answering the questionnaire, which was distributed by an independent data collection institute that was responsible for confidential processing of the data. Data were anonymised before they were sent to the researchers. The Medical Ethical Review Committee of the VU University confirmed that the Medical Research Involving Human Subjects Act did not apply to this study, so an institutional review board approval was not necessary.

RESULTS

A number of 500 questionnaires was distributed among dentists, and completed by 63 participants. After screening for incomplete data, 19 were removed and data of the remaining 44 participants were used for analysis, resulting in a response rate of 8.8%. The complete demographic dataset is summarised in Table 1.

Table 1: Demographics of the study population. Continuous variables are depicted as mean±SD and categorical variables as N(%).

Demographics	Total Population (N=44)
Age in years	41.5±11.6
Female/Male	29 (66%) / 15 (34%)
Years of practice	16.2±11.3
	Range: 1 - 36
University of graduation	
Amsterdam	22 (50%)
Groningen	7 (16%)
Nijmegen	8 (18%)
Elsewhere	7 (16%)
Dentist/specialization	
General practitioner	41 (93%)
Specialization:	
Dentist-teacher	5 (11%)
Periodontology	0
Implantology	2 (5%)
Pedodontology	0
Endodontology	2 (5%)
Gnathology	0
Average working hours per week	32.8±7.9
Working hours per week ≥ 32 hours	28 (64%)
Year of graduation ≥ 2010	14 (32%)

In the benign group, vignette 8 (aphthous stomatitis) had the highest percentage (100%) of correct diagnosis, whilst the lowest (32%) was case 6 (melanotic macule). For vignette 9 (fibroma), the correct management, a follow-up appointment after 6 months, was selected by 48% of participants. Only 9% of participants correctly reported that there was no follow-up up appointment necessary for vignettes 3 (amalgam tattoo) and 5 (median rhomboid glossitis), respectively) (Table 2).

Table 2: Numbers and percentages of participants that selected the correct diagnosis, follow-up management and diagnosis+management and the most commonly selected misdiagnosis and incorrect management, for 11 clinical vignettes.

Vignette	Correct diagnosis N (%)	Correct management N (%)	Correct diagnosis + management N (%)	Most commonly selected incorrect diagnosis N (%)	Most commonly selected incorrect management N (%)
Benign OML					
3	MRG 34 (77%)	No follow-up 4 (9%)	2 (4.5%)	Geographic tongue 4 (9%)	Referral 19 (43%)
5	Amalgam tattoo 21 (48%)	No follow-up 4 (9%)	2 (4.5%)	Nevus pigmentosus 10 (23%)	Referral 19 (43%) Check-up 6 months 17 (39%)
6	Melanotic macule 14 (32%)	Referral 17 (39%)	7 (16%)	Nevus pigmentosus 26 (59%)	Check-up 6 months 13 (30%)
8	Aphthous stomatitis 44 (100%)	No follow-up 18 (41%)	18 (41%)		Check-up 2-3 weeks 15 (34%)
9	Fibroma 41 (93%)	Follow-up 6 months 21 (48%)	21 (48%)	Lipoma 2 (4.5%)	Referral 15 (34%)
(potentially) malignant OML					
1	Leukoplakia 39 (89%)	Referral 32 (73%)	29 (66%)	Morsicatio buccarum 2 (4.5%)	Check-up 2-3 weeks 8 (18%)
2	Oral Lichen Planus 41 (93%)	Follow-up 6 months 19 (43%)	18 (41%)	Leukoplakia 1 (2%) Erythroplakia 1 (2%) Morsicatio 1 (2%)	Referral 17 (39%)
4	Erythroplakia 24 (55%)	Referral 26 (59%)	17 (39%)	Erosive lichen planus 12 (27%)	Check-up 2-3 weeks 13 (30%)
7	Oral SCC 30 (68%)	Referral 38 (86%)	28 (64%)	Erythroplakia 5 (11%) Morsicatio linguarum 5 (11%)	Check-up 2-3 weeks 5 (11%)
10	Salivary gland tumour 23 (52%)	Referral 33 (75%)	22 (50%)	Fibroma 7 (16%) Traumatic ulcer 7 (16%)	Check-up 2-3 weeks 11 (25%)
11	Cutaneous SCC 6 (14%)	Referral 38 (86%)	6 (14%)	Basal cell carcinoma 14 (32%)	Check-up 2-3 weeks 3 (7%)

Abbrevations: MRG: median rhomboid glossitis; SCC: squamous cell carcinoma.

* indicates a statistically significant difference ($P<0.05$).

In the (potentially) malignant group, the most frequently correct diagnosed was vignette 2 (oral lichen planus; 93% correct), whilst vignette 11 (cutaneous SCC), was diagnosed correctly by 14%. Except for oral lichen planus, all (potentially) malignant OMLs required referral, which was selected for 73-86% of the vignettes (Table 2).

For vignettes that represented patients who should be referred to specialist care, the correct management varied from 59 to 86%. Almost all dentists would directly refer the

patients in vignette 7 and 11, which represented OSCC and cutaneous SCC (both 86%), or make a check-up appointment after 2-3 weeks (11% and 14%). For vignettes that did not need referral, the most commonly selected incorrect management was direct referral to specialist care; except for aphthous stomatitis (Table 2).

Mean scores for correct diagnosis (CD), correct management (CM) and correct diagnosis and management (CM+P) were respectively; 7.2 (±1.8), 5.7 (±1.5) and 3.8 (±1.7) of 11 vignettes. This means that on average participants identified the CD for 7.2 of 11 vignettes, the CM for 5.7 vignettes and the CD+M for 3.8 vignettes. For the mean score for CM, a significant difference was found between dentists that graduated after 2010 and before 2010; the latter more often selected the correct management ($t(42) = -2.11$, $p=0.04$). There were no statistical significant relationships between the CD, CM and CD+M scores and sex, and between dentists that did and did not express a need for continuing education (Fig. 2).

Of the participants, 65.9% reported inspecting the oral mucosa in every patient visiting for a check-up appointment, 27.3% in most patients and 6.8% in some patients. Sixty-three percent reported taking a clinical photograph when observing an

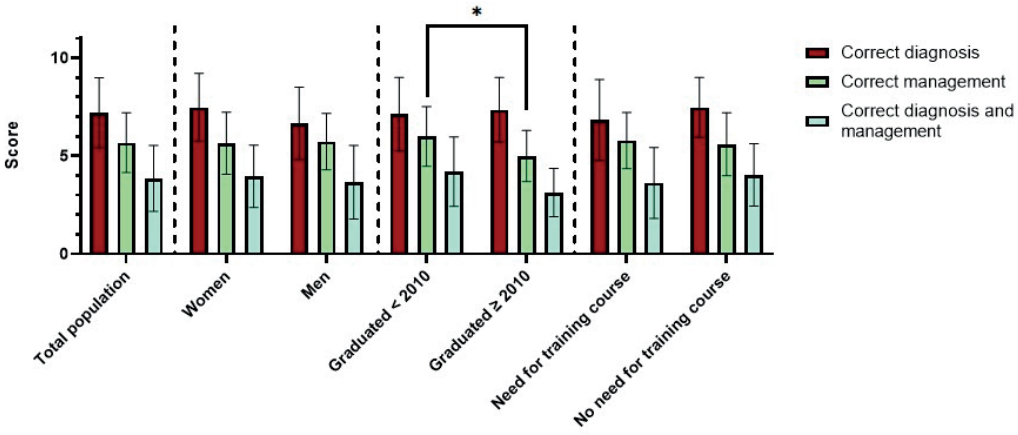

Figure 2: Mean number of correct diagnosis, correct management and correct diagnosis and management, stratified for sex, year of graduation and expressed need of education (data expressed as mean±SD). * indicates a statistically significant difference.

OML in their patients. Most participants (72.7%) mentioned that to help them making a diagnosis they sometimes use clinical images from various sources especially the internet (38.6%) and textbooks (40.9%). Two thirds (63.6%) of participants referred one to five patients a year to specialist care and 20.5% referred six to ten patients per year. The main reason for referring a patient was confirmation of a diagnosis (90.9%).

At the moment of the survey, 84.1% of respondents expressed no need for continuing education about OMLs, and 77% completed a postgraduate education about this topic in the past (Table 3).

Table 3: Current approach for oral mucosal lesions.

Current approach for oral mucosal lesions		N(%)
1. Do you inspect the oral mucosa during each semi-annual inspection?		
In all patients.		29 (66%)
In most patients.		12 (27%)
In some patients.		3 (7%)
In (virtually) no patients.		0
2. Do you take clinical pictures when you observe oral mucosal lesions?		
Yes		28 (64%)
No		16 (36%)
3. Do you compare an abnormality in a patient with an image from a textbook or the internet and/or discuss it with a colleague to arrive at a diagnosis?		
I have no time for comparison; I refer the patient directly to OMFS.		1 (2%)
No, I use my own developed knowledge.		2 (5%)
No, I ask my colleague for help.		8 (18%)
Sometimes, it depends on the lesion.		32 (73%)
Yes, pictures from books.		18 (41%)
Yes, pictures from the Internet.		17 (39%)
4. How often per year do you refer patients with OML to OMFS?		
Not a single patient so far		0
1-5	per year	28 (64%)
6-10	per year	9 (21%)
11-15	per year	4 (9%)
16-20	per year	0
>20	per year	3 (7%)
5. Reason(s) for referrals to OMFS *		
I feel insecure about the image.		23 (52%)
I would like confirmation of a diagnosis		40 (91%)
I do not know how to help my patient further.		15 (34%)
The patient requests a referral.		7 (16%)
Other.		7 (16%)

6. Did you complete a course in detecting oral mucosal lesions since graduation?*	
No.	10 (23%)
Yes, I attended a lecture/symposium.	31 (71%)
Yes, I completed a course.	5 (11%)
Yes, I completed an e-learning course.	4 (9%)
Yes, other.	3 (7%)
7. Do you need a course in detecting oral mucosal lesions?*	
No.	37 (84%)
Yes, I would like to attend a lecture/symposium.	22 (50%)
Yes, I would like to attend a training course.	19 (43%)
Yes, through e-learning.	26 (59%)
Yes, other.	1 (2%)

* For questions 5, 6 and 7 multiple options could be selected.

DISCUSSION

The aim of this survey was to explore whether dentists' knowledge about OMLs is sufficient to correctly diagnose and manage various OMLs in patients. Therefore, we conducted this survey among dentists in the Netherlands, using a questionnaire containing 11 clinical vignettes, which represented selected OMLs and required respondents to provide a (differential) diagnosis and accurate management for each. In summary, the results revealed a lack of ability to correctly diagnose some OMLs and a tendency to refer to a specialist when in doubt. This tendency was evident from the fact that there were more correct referrals for malignant OMLs than correct diagnoses. For three vignettes representing malignant OMLs, 14 to 68% of participants selected a correct diagnosis, whereas 75 to 86% selected the correct management of direct referral. So, although participants lacked knowledge to provide a correct diagnosis, they selected the correct management. For benign OMLs, the opposite was observed; regardless of a correct diagnosis, many respondents reported referring a patient with a benign OMLs to a specialist. Remarkably, this tendency was not present for the vignette representing oral lichen planus, which we categorised as a potentially malignant lesion, which is arguable, as the overall malignant transformation rate is low and varies from 0.5-1% [19]. Many respondents probably had this knowledge since the majority selected the correct management of a check-up appointment after 6 months, instead of direct referral. In addition, respondents reported that the main reason for referral to a specialist was confirmation of their diagnosis (91%), which suggests that they do not feel confident about their diagnosis.

The lack of ability in diagnosing some OMLs was evident as the range of correct diagnoses was 14 to 100% and the fact that on average only 7.2 out of 11 cases were diagnosed correctly. The most common benign OMLs, aphthous stomatitis [20], was diagnosed correctly by all participants. The lowest percentage for correct diagnosis (14%), was for the vignette representing a cutaneous squamous cell carcinoma. This vignette was included to increase awareness among dentists about including examination of the skin of patients as part of their routine extra oral examination. Cutaneous SCC is the second most common cancer with an increasing incidence and it frequently occurs on the head and neck skin [21].

While most benign OMLs can be diagnosed based on clinical features only, for (potentially) malignant OML a biopsy for histopathological assessment is required [11]. In some countries dentists are encouraged to take such biopsies. However, this is not the case in The Netherlands, so timely referral of (potentially) malignant lesions is even more important than providing an initial correct diagnosis.

Comparing results for specific OML to previous research is difficult, as results of this study are vignette specific; each lesion is a separate entity with a unique combination of characteristics. Comparable research is scarce, as studies that investigated dentists' ability in diagnosing OMLs used questionnaires that did not include patients' history and clinical presentation [22-25]. We found one comparable study among dentists in England and our study confirms their findings that dentists have a tendency to refer to a specialist when in doubt about their diagnosis [16]. It was not possible to compare results for specific OMLs because they only reported whether the diagnosis was correct or not and did not show the actual diagnosis for the clinical vignettes.

Our study contributes to the aim of diagnosing early-stage oral cancer in patients in two ways. First, it creates awareness among Dutch dentists about their limited ability to correctly diagnose and refer OMLs. Second, specification of deficits in diagnostic ability and management of OMLs among dentists is likely to be beneficial for adapting curricula of dental schools, as there is a wide variety in theoretical content and examination techniques taught in European dental schools [26]. Results may also provide a background for development of clinical guidelines to be used by healthcare professionals to diagnose and manage OMLs and improvement of postgraduate education. Most respondents reported that they already had attended a postgraduate course about OMLs and did not need additional education. Considering the relatively low percentages of correct diagnosis and patient management, attending these courses more frequently might be beneficial to refresh knowledge about OMLs. Further research into the most appropriate content and forms of education, and frequency of postgraduate education is desirable. This study showed a tendency of over-referral, so evaluation whether providing dentists with clinical guidelines, that include standardized criteria for referral, could be beneficial. Research in the United Kingdom has showed that availability of a national referral guideline improves the cancer detection rate and reduces over-referral. However,

compliance with guidelines is required and needs to be improved [27]. Availability of an electronic consultation tool for dentists, with the possibility to consult an oral surgeon, is also an option [22,23].

Although the questionnaire in our study contained a limited number of 11 OMLs, to limit the time investment for participants, it still provides information about a wide range of OMLs that dentists are faced with in their daily practice.

For selection of a correct management each vignette, we consulted existing guidelines of the Dutch Association of Oral and Maxillofacial Surgeons. Management and referral guidelines are sometimes not unanimous and may be interpreted differently. For example, for the vignette representing a salivary gland tumour, we decided that direct referral was the correct management. This is arguable because the textual description revealed that the lesion was present for only 1.5 weeks in this patient with complete dentures, so an alternative policy could be removal of a possible traumatic cause and making a follow-up appointment after 2-3 weeks. When considering this second option also correct, all participants selected a correct management for this vignette. A similar discussion regarding selection of the correct management applies to the vignettes representing leukoplakia and erythroplakia; the provided patients' history did not mention how long these lesions were present. So, if we considered removal of possible traumatic causes, followed by an appointment after 2 to 3 weeks also correct, ability to select a correct management for these vignettes was excellent. Therefore, the mean scores for correct management for several OMLs should be interpreted with some caution.

In addition, bias may have occurred in this survey, as participation was voluntarily, and dentists with an interest in this topic may have been more likely to participate, results may present a more optimistic picture. Only one statistically significant relationship was found for mean scores for CD, CM and CD+M between subgroups based on demographic characteristics, this may be due to the small sample size and low response rate. A postal survey may increase the response rate [28].

CONCLUSIONS

In conclusion, this study shows that dentists in the Netherlands do not have sufficient knowledge of some OMLs in order to provide an accurate diagnose and management. On average, only 7.2 out of 11 clinical vignettes representing OML were diagnosed correctly. The percentage of correct diagnosis for (potentially) malignant OML ranged from 14 to 68%, and for benign OML from 32 to 100%. Participants tended to refer when in doubt about the diagnosis. Further research should focus on exploring whether providing dentists with clinical guidelines that include standardized criteria for referral and continuing education could improve their ability to correctly diagnose OMLs and accurately manage these lesions.

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SUPPLEMENT 1

QUESTIONNAIRE

Case I

A 36-year-old man, ASA: 2.
Smokes tobacco: 1 packet per day
Health: Hypertension
Med: Acenocoumarol

The patient is new to your practice. You notice a sharply bounded, non-wipeable, white discoloration of the right cheek mucosa. On palpation, the lesion feels slightly rough.

Q1A: Most likely diagnosis

- o Leukoplakia
- o Erythroplakia
- o Squamous cell carcinoma
- o Aspirine burn
- o Contact lesion
- o Morsicatio buccarum

Q1B: Likely differential diagnosis (Multiple options are possible)

- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Leukoplakia
- ☐ Erythroplakia
- ☐ Squamous cell carcinoma
- ☐ Aspirine burn
- ☐ Contact lesion
- ☐ Morsicatio buccarum

Q1C: Policy

- o No policy required
- o A check-up appointment after 2 or 3 weeks
- o A check-up appointment after 1 or 2 months
- o A follow-up appointment after 6 months
- o Referral to OMF Surgery

Case II

A 49-year-old woman, ASA: 2.
Health: Diabetes Mellitus I
Med: Insuline (Novomix)

The patient has white, non-wipeable fine reticular lines on her the right and left buccal mucosa for a number of months. Occasionally there is a slight painful or burning sensation.

Q2A: Most likely diagnosis

- o Leukoplakia
- o Oral lichen planus
- o Erythroplakia
- o Erythema Multiforme
- o Squamous cell carcinoma
- o Aspirine burn
- o Contact lesion
- o Morsicatio buccarum

Q2B: Likely differential diagnosis (Multiple options are possible)

- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Leukoplakia
- ☐ Oral lichen planus
- ☐ Erythroplakia
- ☐ Erythema Multiforme
- ☐ Squamous cell carcinoma
- ☐ Aspirine burn
- ☐ Contact lesion
- ☐ Morsicatio buccarum

Q2C: Policy

- o No policy required
- o A check-up appointment after 2 or 3 weeks
- o A check-up appointment after 1 or 2 months
- o A follow-up appointment after 6 months
- o Referral to OMF Surgery

Case III

A 36-year-old woman, ASA: 2.
Smokes tobacco: half packet per day
Alcohol: 2 cans (33cl) of beer per day
Health: Asthma
Med: Ventolin

During a semi-annual inspection, you find a slightly elevated, partly red and partly white lesion on the dorsum of the tongue. It does not bother the patient. It has been present for a few years.

Q3A: Most likely diagnosis

- o Leukoplakia
- o Erythroplakia
- o Fissured tongue
- o Geographic tongue
- o Median Romboid Glossitis
- o Foliate Papillitis
- o Squamous cell carcinoma
- o Struma of tongue

Q3B: Likely differential diagnosis (Multiple options are possible)

- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Leukoplakia
- ☐ Erythroplakia
- ☐ Fissured tongue
- ☐ Geographic tongue
- ☐ Median Romboid Glossitis
- ☐ Foliate Papillitis
- ☐ Squamous cell carcinoma
- ☐ Struma of tongue

Q3C: Policy

- o No policy required
- o A check-up appointment after 2 or 3 weeks
- o A check-up appointment after 1 or 2 months
- o A follow-up appointment after 6 months
- o Referral to OMF Surgery

Case IV

A 39-year-old woman, ASA: 2.
Health: Kidney failure
Med: Hydrochloorthiazide

During an endodontic treatment in tooth number 26, you notice that there is a red mucosal lesion on the left side of her tongue, anterior tonsillar pillar and soft palate. She experiences occasionally a burning sensation. No other oral abnormalities are present.

Q4A: Most likely diagnosis

- o Erythroplakia
- o Leukoplakia
- o Erosive lichen planus
- o Geographic tongue
- o Squamous cell carcinoma
- o Contact lesion
- o Frictional trauma
- o Morsicatio

Q4B: Likely differential diagnosis (Multiple options are possible)

- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Erythroplakia
- ☐ Leukoplakia
- ☐ Erosive lichen planus
- ☐ Geographic tongue
- ☐ Squamous cell carcinoma
- ☐ Contact lesion
- ☐ Frictional trauma
- ☐ Morsicatio

Q4C: Policy

- o No policy required
- o A check-up appointment after 2 or 3 weeks
- o A check-up appointment after 1 or 2 months
- o A follow-up appointment after 6 months
- o Referral to OMF Surgery

Case V

A 35-year-old man, ASA: 2.
Health: Asthma
Med: Ventolin

During the intake of this new patient, you notice a blue discoloration of the gingiva between 42 and 44. He was not aware of this and is not bothered by it.

Q5A: Most likely diagnosis

- o Smokers melanosis
- o Squamous cell carcinoma
- o Melanoma
- o Melanin pigmentation
- o Nevus pigmentosus
- o Amalgam tattoo

Q5B: Likely differential diagnosis (Multiple options are possible)

- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Smokers melanosis
- ☐ Squamous cell carcinoma
- ☐ Melanoma
- ☐ Melanin pigmentation
- ☐ Nevus pigmentosus
- ☐ Amalgam tattoo

Q5C: Policy

- o No policy required
- o A check-up appointment after 2 or 3 weeks
- o A check-up appointment after 1 or 2 months
- o A follow-up appointment after 6 months
- o Referral to OMF Surgery

Case VI

A 46-year-old woman, ASA: 2.
Alcohol: 1 glass of wine (25cl) per day
Health: Allergic to kiwi fruit
Med: -

During a check-up, you notice a brown lesion on the lower lip. The patient is not bothered by it, has had the lesion for several years and does not know whether it has changed in size during the past year.

Q6A: Most likely diagnosis

- o Squamous cell carcinoma
- o Amalgam tattoo
- o Melanotic macule
- o Smokers melanosis
- o Pigmented nevus
- o Melanoma

Q6B: Likely differential diagnosis (Multiple options are possible)

- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Squamous cell carcinoma
- ☐ Amalgam tattoo
- ☐ Melanotic macule
- ☐ Smokers melanosis
- ☐ Pigmented nevus
- ☐ Melanoma

Q6C: Policy

- o No policy required
- o A check-up appointment after 2 or 3 weeks
- o A check-up appointment after 1 or 2 months
- o A follow-up appointment after 6 months
- o Referral to OMF Surgery

Case VII

A 67-year-old man, ASA: 2.
Smokes a pipe 2 or 3 times per day
Health: TIA, artificial knee (right)
Med: Ascal

While inspecting the mucous, you notice a lesion of the right lateral border of his tongue. On palpation, the area feels somewhat solid. The patient indicates that the lesion does not cause complaints, but that the lesion was there for 2 months.

Q7A: Most likely diagnosis

- o Squamous cell carcinoma
- o Pigmented nevus
- o Erythroplakia
- o Morsicatio linguarum
- o Lichen planus
- o Leukoplakia

Q7B: Likely differential diagnosis (Multiple options are possible)

- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Squamous cell carcinoma
- ☐ Pigmented nevus
- ☐ Erythroplakia
- ☐ Morsicatio linguarum
- ☐ Lichen planus
- ☐ Leukoplakia

Q7C: Policy

- o No policy required
- o A check-up appointment after 2 or 3 weeks
- o A check-up appointment after 1 or 2 months
- o A follow-up appointment after 6 months
- o Referral to OMF Surgery

Case VIII

A 26-years-old man, ASA: 2.
Health: Allergic to nickel
Med: no details

In between regular semi-annual inspections, a patient presents with a lesion in his mouth that is sensitive when eating, drinking and talking. Clinically, you notice a gray-white, 3 mm diameter, spot surrounded by a red area on the inside of the upper lip.

Q8A: Most likely diagnosis

- o Aphthous stomatitis
- o Erythema Multiforme
- o Crohn's disease
- o Squamous cell carcinoma
- o Contact lesion
- o Behçet's disease

Q8B: Likely differential diagnosis (Multiple options are possible)

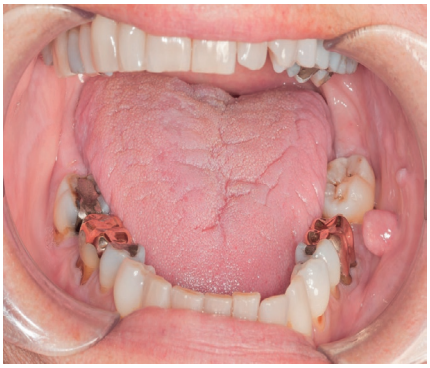
- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Aphthous stomatitis
- ☐ Erythema Multiforme
- ☐ Crohn's disease
- ☐ Squamous cell carcinoma
- ☐ Contact lesion
- ☐ Behçet's disease

Q8C: Policy

- o No policy required
- o A check-up appointment after 2 or 3 weeks
- o A check-up appointment after 1 or 2 months
- o A follow-up appointment after 6 months
- o Referral to OMF Surgery

Case IX

A 50-year-old man, ASA: 2.
Health: TIA, Hypertension
Med: Anticoagulant



During intake of a new patient, you notice a 0.9 mm large deviation near tooth number 36. He tells you it has been present for 2 years and causes no complaints. The swelling feels firm on palpation.

Q9A: Most likely diagnosis

- o Fibroma
- o Melanoma
- o Lipoma
- o Cowden syndrome
- o Crohn's disease
- o Foliate papillae
- o Squamous cell carcinoma
- o Morsicatio buccarum

Q9B: Likely differential diagnosis (Multiple options are possible)

- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Fibroma
- ☐ Melanoma
- ☐ Lipoma
- ☐ Cowden syndrome
- ☐ Crohn's disease
- ☐ Foliate papillae
- ☐ Squamous cell carcinoma
- ☐ Morsicatio buccarum

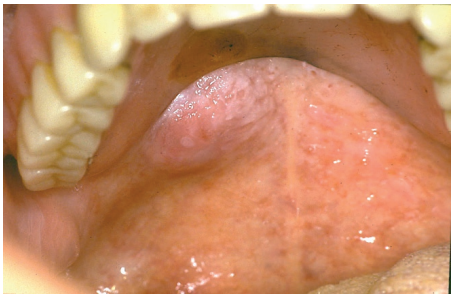
Q9C: Policy

- o No policy required
- o A check-up appointment after 2 or 3 weeks
- o A check-up appointment after 1 or 2 months
- o A follow-up appointment after 6 months
- o Referral to OMF Surgery

Case X

A 67-year-old man, ASA: 2.
Health: Diabetes Mellitus II
Med: Metformine

During control of an upper prosthesis, you notice a palatal swelling. The patient indicates that he has had it for about a week and a half and does not cause any complains .



Q10A: Most likely diagnosis

- o Salivary gland tumor
- o Osteosarcoma
- o Fibroma carcinoma
- o Pressure point
- o Torus palatinus
- o Squamous cell carcinoma

Q10B: Likely differential diagnosis (Multiple options are possible)

- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Salivary gland tumor
- ☐ Osteosarcoma
- ☐ Fibroma carcinoma
- ☐ Pressure point
- ☐ Torus palatinus
- ☐ Squamous cell carcinoma

Q10C: Policy

- o No policy required
- o A check-up appointment after 2 or 3 weeks
- o A check-up appointment after 1 or 2 months
- o A follow-up appointment after 6 months
- o Referral to OMF Surgery

Case XI

A 71-year-old man, ASA: 2.
Health: TIA
Med: Clopidogrel

During the extra-oral examination, you notice a red, slightly elevated swelling in the left temporal area . The patient indicates that the swelling has been present for several months and that it may have increased slightly in size. On palpation, the swelling feels firm.

Q11A: Most likely diagnosis

- o Squamous cell carcinoma
- o Merkel-cell carcinoma
- o Seborrheic keratosis
- o Basal-cell carcinoma
- o Melanoma
- o Folliculitis

Q11B: Likely differential diagnosis (Multiple options are possible)

- ☐ No differential diagnosis required; the clinical aspect is so clear that no other diagnosis qualifies.
- ☐ Squamous cell carcinoma
- ☐ Merkel-cell carcinoma
- ☐ Seborrheic keratosis
- ☐ Basal-cell carcinoma
- ☐ Melanoma
- ☐ Folliculitis

Q11C: Policy

- o No policy required
- o A check-up appointment after 2 or 3 weeks
- o A check-up appointment after 1 or 2 months
- o A follow-up appointment after 6 months
- o Referral to OMF Surgery

QNr.	
12	**Gender**
	Male
	Female
13	**Age (years)**
	21-35
	36-50
	51-65
14	**Year of graduation**
	1981-1985
	1986-1990
	1991-1995
	1996-2000
	2001-2005
	2006-2010
	2011-2015
	2016-2019
15	**University of graduation**
	Amsterdam
	Groningen
	Nijmegen
	Utrecht
	Elsewhere
16	**Dentist/Specialization**
	General dental practitioner
	Dentist-teacher
	Periodontology
	Implantology
	Endodontology
	Pedodontology
	Gnathology
	Different…
17	**Years of practice**
	0-10
	11-20

	21-30	
	31-40	
18	**Average working hours per week**	
	≤32	
	≥33	
19	**Do you inspect the oral mucosa during each semi-annual inspection?**	
	In all patients.	
	In most patients.	
	In some patients.	
	In (virtually) no patients.	
20	**Do you take clinical pictures when you observe oral mucosal lesions?**	
	Yes	
	No	
21	**Do you compare an abnormality in a patient with an image from a textbook or the internet and/or discuss it with a colleague to arrive at a diagnosis?**	
	I have no time for comparison; I refer the patient directly to OMFS.	
	No, I use my own developed knowledge.	
	No, I ask my colleague for help.	
	Sometimes, it depends on the lesion.	
	Yes, pictures from books.	
	Yes, pictures from the Internet.	
22	**How often per year do you refer patients with OML to OMFS?**	
	Not a single patient so far	
	1-5	per year
	6-10	per year
	11-15 year	per
	16-20 year	per
	>20 year	per

23	Reason(s) for referrals to OMFS
	I feel insecure about the image.
	I would like confirmation of a diagnosis?
	I do not know how to help my patient further.
	The patient requests a referral.
	Other.
24	Did you complete a course in detecting oral mucosal lesions since graduation?
	No.
	Yes, I attended a lecture/symposium.
	Yes, I completed a course.
	Yes, I completed an e-learning course.
	Yes, other.
25	Do you need a course in detecting oral mucosal lesions?
	No.
	Yes, I would like to attend a lecture/symposium.
	Yes, I would like to attend a training course.
	Yes, through e-learning.
	Yes, other.

7

General discussion

The rising incidence of HPV-related oropharyngeal squamous cell carcinoma (OPSCC) necessitates the understanding of various clinical aspects of HPV-infection among oral healthcare professionals. The knowledge about this subject of (future) oral health professionals in The Netherlands was assessed by means of surveys among dental students (**chapter 2**)**,** dental hygiene students (**chapter 3**) and dentists (**chapter 4**). Deficits were identified, which indicated a need of additional education. Furthermore, their attitudes towards carrying out HPV-related prevention practices were explored and confidence in successfully performing these different tasks in their daily practice. They considered informing patients about HPV as a risk factor for OPSCC as important but were less prepared to counsel their patients about HPV-vaccination. These findings contribute to the discussion about oral healthcare providers' role in providing information on various aspects of preventive measures of HPV-related OPSCC.

The next part of this thesis elucidates the efforts of oral healthcare providers in the early diagnosis of head and neck cancer. In general, more than two-thirds of the patients with oral squamous cell carcinoma (OSCC) are diagnosed at an advanced stage [1]. Early diagnosis of OSCC is essential since it is the most effective means of influencing prognosis and reducing treatment related disfigurement and sequelae [2]. The awareness and sufficient knowledge about various aspects of head and neck cancer is crucial and therefore the head and neck cancer-related content of dental curricula across Europe was evaluated in **chapter 5**. The knowledge, diagnosis and management of selected oral mucosal lesions, including potential malignant lesions and OSCC, among dentists in The Netherlands was explored in **chapter 6**.

KNOWLEDGE ABOUT HPV-RELATED OROPHARYNGEAL SQUAMOUS CELL CARCINOMA AMONG ORAL HEALTHCARE PROFESSIONALS

Until a few decades ago, the main cause for OPSCC was the use of tobacco, but despite the decrease in tobacco consumption, the prevalence rates of OPSCC are still rising in the US and Europe. This is due to the increasing proportion of OPSCC that are related to infection with a high-risk type of HPV [3]. These HPV-positive tumours are often diagnosed at an advanced stage when regional lymph node metastasis are present [4-6]. The majority of cases of cervical and anogenital cancer is also related to HPV-infection and therefore the need for public health information and interventions to reduce the burden of HPV-related cancers is of importance. Besides the introduction of HPV-vaccination in many national immunization programmes, with the aim of preventing HPV-related cancers, efforts of primary healthcare professionals are required in providing patients with information about clinical aspects and prevention of HPV infection, and signs and signals of early

malignant disease. Healthcare professionals with a wide variety of specialization could be included, including a role for oral healthcare professionals [7-10].

In The Netherlands, almost 80% of the population visits a dentist at least once a year [11]. The chances that an oral health professional is confronted with a patient with a potential OPSCC during a regular dental check-up appointment are limited. The incidence of OPSCC in a Dutch population of 17 million people was 723 in 2021 [12,13]. The incidence of OPSCC is less than the incidence of OSCC; which was 913 patients in 2021[13]. Early detection of OPSCC is important because early diagnosis of malignant disease results in more favourable treatment outcomes and less treatment related side effects. Therefore, knowledge and awareness of signs and symptoms, patients' characteristics, clinical aspects of OPSCC, and potential precursor lesions among oral health professionals, is important. It is encouraging that 87% of the dentists in The Netherlands indicate to be alert of possible signs and symptoms for head and neck cancer in all patients during routine check-up appointments (**chapter 4)**. However, during periodic dental check-ups, it is almost impossible to examine the oropharyngeal region with the aim of detecting an OPSCC at an early stage [1]. So, despite the oral healthcare professionals' willingness to screen for head and neck cancer, their role in early detection of OPSCC during dental check-ups will be limited in contrast to oral cancer which is easier to detect by visual inspection. They should, however, be aware of symptoms of OPSCC such as an abnormal neck mass, persistent sore throat, pain when swallowing and one-sided ear pain or hoarseness. When such symptoms are present, dentists should refer the patient immediately for further investigations [14].

Characteristics and demographics of patients diagnosed with HPV-positive OPSCC differ from those with HPV-negative OPSCC and oral health professionals need to be aware of these differences. Patients that are at risk for development of HPV-negative OPSCC are older males, usually with heavy tobacco and alcohol consumption habits [5]. HPV-positive OPSCC are especially diagnosed in young male patients and possible risk factors are related to sexual behaviour such as oro-genital sex and multiple partners at an early age [15]. The results of the presented surveys that are described in **chapter 2, 3 and 4** show knowledge deficits among oral health professionals on these specific patient characteristics, whereby about only half of the dentists (48.1%) were aware of the young age of OPSCC patients and 48.6% knew that an increasing number of OPSCC patients lack classical risk factors such as tobacco and alcohol use. For senior dental students these percentages were 46.4% and 41.1%, and for senior dental hygiene students 8.4% and 27.5%, respectively.

Data presented in **chapter 4** show that 79.6% of dentists was aware of the association between HPV-infection and oral/oropharyngeal cancer before participation in the study and for dental students this percentage was 63.5% (**chapter 2)**. Recent studies, conducted in 2021 in the Netherlands, reported a comparable awareness rate for

general practitioners (72.0%) and a very low awareness rate for the general population (11.0%) [7,16]. A systematic review, investigating the awareness among medical and dental professionals worldwide, showed rates varying from 26% to 91% [17]. However, direct comparison of these awareness percentages with the results described in this thesis is not quite possible, because the studies included in the systematic review used slightly different questions. Moreover, most studies asked for the association between HPV and oral cancer, whereas the association between HPV and the risk of developing oral cancer is negligible [18]. The systematic review was performed more than 5 years ago and at that moment a distinction between the oral and oropharyngeal region with respect to a possible relationship of cancer in these regions and HPV infection was not commonly made in the professional literature. In the questionnaire of our study, the term 'oral and oropharyngeal cancer' was used, but in retrospect, it would have been better to eliminate the term 'oral cancer' and only use the term 'oropharyngeal cancer'.

Oral healthcare providers could play a role in prevention of HPV-related OPSCC by educating their patients about various aspects of HPV infection. The American Dental Association encourages oral health professionals to educate patients about the relation between HPV and oropharyngeal cancer and counsel them about HPV-vaccination [19]. Until now, Dutch oral health professional organizations, such as The Royal Dutch Dental Association (**Koninklijke** Nederlandse Maatschappij tot bevordering der Tandheelkunde (KNMT), do not actively encourage oral healthcare professionals to engage in HPV-related prevention practices. Counselling patients about HPV and vaccination is a responsibility of general practitioners and the municipal public healthcare services (GGD; Gemeentelijke Gezondheidsdienst). The Dutch National Immunisation Programme is organized by the National Institute for Public Health and the Environment (RijksInstituut voor Volksgezondheid en Milieu (RIVM)). Results in chapter 4 show that dentists in the Netherlands are prepared to engage in prevention practices to some extent; according to 69.5% it is important to discuss the role of HPV as a risk factor for cancer with patients. However, they were less prepared to counsel their patients about HPV-vaccination; 41.1% of the dentists did not to consider discussing this. The fact that they preferred passive information tools, such as leaflets provided by professional organizations, to facilitate counselling patients about HPV may be explained by the fact that they do not feel comfortable in discussing the transmission of HPV through sexual contact.

Actively engaging in primary prevention practices to prevent HPV transmission and encouraging the uptake of HPV-vaccination, is different from answering patients' HPV-related questions. This requires sufficient HPV-related knowledge levels among oral health professionals. Recently, the RIVM launched a campaign about HPV vaccination for the general public in which they clearly stated that HPV vaccination not only protects against cervical cancer, but also against a broader range of cancers, including oropharyngeal cancer [20]. The information provided by the RIVM explains the anatomy of the oropharyngeal region for the general public as 'the region of the mouth and

throat'. This may lead to the incorrect assumption that HPV-infection is a risk factor for the development of oral cancer [18], resulting in patients approaching their oral healthcare providers with questions about HPV and oral cancer. Therefore, sufficient knowledge among these professionals is essential. In **chapter 2, 3 and 4** we explored HPV-related knowledge among oral healthcare professionals and the results showed that their knowledge is limited. They had insufficient knowledge on several items: 1) only 22.6% of dentists knew that there are more than 100 types of HPV; 2) 22.1% knew that most HPV infections resolve spontaneously within a short time; and 3) 58.3% knew that HPV does not cause herpes or cold sore. Results for knowledge items were slightly worse for senior dental students than for dentists, and were the least among senior dental hygiene students. However, on some items senior students scored better than dentists. For example, 74.5% of dentists reported that the statement 'HPV can cause HIV/aids' was incorrect, versus 89.3% of dental students. Also 78.1% of dentists reported that the statement 'oral cancer is often preceded by clinically identifiable changes' was correct, versus 94.6% of dental students, and 79.4% of dental hygiene students. A possible explanation of the difference in knowledge levels among dentists and students is that most dentists acquired their knowledge by professional literature and postgraduate education, as described in **chapter 4**. Most students reported in **chapter 2 and 3** that they acquired their knowledge by theoretical education in the curriculum.

HEAD AND NECK CANCER EDUCATION IN DENTAL CURRICULA

In **chapter 2, 3 and 4** we identified deficits in oral healthcare providers' knowledge of risk factors for oral and oropharyngeal cancer and lack of confidence in performing routine examination practices, such as visual inspection and palpation for abnormalities for head and neck cancer, This is not exceptional, because deficits in knowledge on oral cancer, lack of confidence in performing an examination for head and neck cancer and lack of skills in counselling patients about cessation of high-risk behaviour, have been reported in surveys performed among oral health professionals everywhere in Europe [21-24]. This suggests that head and neck cancer education in European dental curricula might not be sufficient to fully prepare dentists for the early detection and information of their patients on prevention of head and neck cancer.

In **chapter 5** we aimed to examine the content of head and neck cancer curricula at European dental schools and the results may possibly contribute to improvements. Results showed a variation in theoretical content and methods for clinical practice in head and neck cancer examination. Only 55% of dental curricula taught their dental students to conduct an examination for oral cancer in all patients. When this figure is compared to figures reported by dentists in Europe, it shows that most dentists perform this

examination on a regular basis; ranging from 78-88% in the UK, 87% in The Netherlands (**chapter 4**), 58% in Italy and 90% in Spain [22-24]. Possible explanations for the relatively low number of dental schools teaching dental students to conduct an examination for the possible presence of oral cancer in all patients are the lack of scientific evidence for opportunistic screening of patients for head and neck cancer and the reliability on patient-reported symptoms for indicating an examination, obtained by a written medical history; almost all dental schools reported to use written medical history forms. However, (potentially) malignancies often do not cause any symptoms at an early stage and therefore it is advised to perform a clinical oral examination during a regular dental check-up appointment [25].

Furthermore, methods of head and neck cancer examination were not consistent in the dental curricula; some curricula did include examination of the oropharyngeal region and base of the tongue. Visual inspection of the complete oropharyngeal region is not possible without using adjunctive devices. However, the cranial part of the tonsils, the anterior and posterior pharyngeal arches and uvula can be inspected by direct vision. The base of the tongue could be inspected using a gaze to grasp the tongue and withdraw it as far as possible [26,27]. When asymmetries in the oropharyngeal region are present or when patients report other symptoms of OPSCC, the tonsils and base of the tongue could be palpated with a gloved finger; 32% of the dental curricula included training in performing this palpation [26,27]. Remarkably, although 94% of dental curricula included training in palpation of the neck for possible enlarged cervical lymph nodes or a neoplasm, dentists across Europe report moderate confidence in performing this part of head and neck cancer examination [1,22,24]. To be able to differentiate between normal and abnormal tissue requires a lot of experience and advanced knowledge.

In Northern and Western Europe, 8% to 29% of the dental curricula did not include visual inspection of the facial skin in the examination for head and neck cancer. This is worrying, as the incidence rates of skin cancer have been rapidly increasing during the last decades in these areas and the vast majority of skin cancers, especially basal cell carcinoma and squamous cell carcinoma, are diagnosed in the head and neck region [28,29]. The most common type is basal cell carcinoma, which is the most common cancer affecting white-skinned individuals [30]. Although the mortality rate is relatively low, it can cause significant disfigurement due to local extension and infiltration of underlying structures, when left untreated. Oral healthcare providers who visually inspect the facial skin can detect skin abnormalities or skin cancer at an early stage and refer appropriately to secondary care for a definitive diagnosis and treatment.

Almost all European dental schools, that responded to the survey in **chapter 5**, included tobacco and alcohol use as risk factors for head and neck cancer in their curricula and taught their students to counsel patients about cessation. Patients with gastro-oesophageal reflux disease (GERD) were less frequently reported as being at risk for head and neck cancer. GERD and obesity are the two main risk factors for oesophageal

adenocarcinoma and the incidence of these carcinoma is rising in European countries, with the highest incidence rates in the UK and the Netherlands [31]. These carcinomas are relatively aggressive and have a low survival rate. Counselling patients about GERD includes changing lifestyle such as cessation of tobacco use and losing weight; 70% of curricula reported that they did not educate students in counselling patients about GERD [32]. Male patients over 40 years old were least frequently reported as being at risk for head and neck cancer. As mentioned above, this is one of the characteristics of patients that are at risk for HPV-related OPSCC. HPV is transmitted sexually, and 31% of curricula did not include sexual practices as a risk factor. Taken together, these data suggest that most dental curricula are not fully adapted to the changed risk profile of patients diagnosed with OPSCC.

Variation in content of dental curricula across Europe has been described for other topics, for example on local anaesthesia education [33]. These variations are reported, despite the availability of a profile of competences for graduating European dentists by the General Assembly of the Association of Dental Education in Europe (ADEE). However, the description of the required competences with regard to oncology lacks detail, illustrated by competences 4.13 and 6.59, which indicates that dentists should be competent at recognizing neoplasms and refer patients when needed [34]. The fact that the current profile of competences for graduating European dentists lacks information on education about HPV-related diseases underlines the urgency of an update.

KNOWLEDGE OF DIAGNOSIS AND MANAGEMENT OF ORAL MUCOSAL LESIONS AMONG DENTISTS

In the Netherlands, most people visit their oral healthcare professional on a regular basis and during this visit their oral cavity is examined. Benign lesions and malignant or potentially malignant disease of the oral mucosa or the jaw bones may be detected during these examinations, without the patient heaving any complaints. In case of a squamous cell carcinoma, early diagnosis is important since a small tumour size and absence of regional lymph node metastasis, is associated with a better survival, less sequela of treatment and thus better quality of life [35]. Since the incidence of various oral lesions is low, it is difficult for healthcare professionals to make an estimate on the diagnosis which sometimes results to a delayed diagnosis of oral cancer or oral potentially malignant disorders (OPMDs) [36]. In **chapter 6,** by means of a survey, the knowledge, diagnosis and management of some selected oral mucosal lesions (OMLs) among dentists in The Netherlands was explored. The results revealed that in some OML cases dentists found it difficult to make a correct diagnosis and to choose the best way to manage the lesion. Because the incidence of most oral lesions, including malignant diseases, is low, it is difficult for oral healthcare providers to estimate the clinical character of a lesion, despite the education they received

during their dental studies about clinical signs and symptoms of OPMDs, and specifically symptoms where one should be suspicious of early oral cancer.

Oral leukoplakia (OL) is the most common OPMD and is defined as a predominantly white plaque of questionable risk after having excluded (other) known diseases or disorders that carry no increased risk for cancer, and it is the most common potentially malignant disorder in the oral cavity [37]. When a clinical diagnosis of OL is made, a biopsy should be taken to determine the histopathological diagnosis which ranges from hyperkeratosis, various degrees of epithelial dysplasia to squamous cell carcinoma (SCC). When epithelial dysplasia is present, there is an increased risk for malignant transformation, however, malignant transformation may also occur in OLs without epithelial dysplasia [38]. It is encouraging that 89% of responding dentists correctly diagnosed the clinical case description representing a patient with oral leukoplakia. Most dentists (73%) selected the correct management of direct referral to a specialist and 18% reported to make a check-up appointment after 2 to 3 weeks, which could also be considered 'correct' because the patients' history did not mention how long the lesion was present. Frictional keratosis is a frequently raised differential diagnosis for oral leukoplakia and usually appears in areas of frequent rubbing such as the lips, tongue and buccal mucosa [35]. This explains the fact that the most commonly selected misdiagnosis for leukoplakia was morsicatio buccarum. Frictional keratosis slowly disappears several months after elimination of the cause. Elimination of the suspected cause may take several months and in case of an uncertain clinical diagnosis it is wise to take a biopsy [35].

Deficits in knowledge of the clinical diagnosis erythroplakia were also identified. Oral erythroplakia is a rare clinical diagnosis and histopathology commonly shows epithelial changes ranging from severe dysplasia to invasive SCC. It is concerning that only 55% of responding dentists correctly diagnosed the vignette representing a patient with erythroplakia and 59% reported to refer this patient to secondary care. An oral squamous cell carcinoma at the lateral margin of the tongue was correctly diagnosed in 68% of the cases, a salivary gland tumour was correctly diagnosed in 52% and cutaneous squamous cell carcinoma was only correctly diagnosed in 14%.

These results revealed a tendency among dentists to refer a patient to a specialist when they are in doubt of the diagnosis. Additionally, 91% reported that the main reason for referral was confirmation of their clinical diagnosis by a specialist. So, these results suggest that when dentists detect an OML, and are in doubt about the diagnosis, their default action is to refer to a specialist. This may result in over-referral for benign OML, but it can also contribute to early diagnosis of a (potentially) malignant OML. The factors contributing to early diagnosis of cancer are complex and varied and to understand these factors several theoretical models have been developed to describe the events and processes to describe the pathway to diagnosis [39,40]. The Aarhus statement defined seven time points that are relevant in the total time interval between the first symptom and start of treatment [39]. Factors that influence these time points are related to the patient,

the type of disease (size, growth rate), the doctor and the system. The first time point of this model is when the first symptoms are noticed and in **chapter 6** we developed clinical case descriptions representing patients at this point in time; either the patient reported symptoms and/or these were clinically visible in the oral mucosa. Results suggest that the time interval between the detection of a (potentially) malignant OML by an oral healthcare provider and referral to secondary care seems to be relatively short. This finding is made based on the assumption that dentists that reported to make a check-up appointment after 2 to 3 weeks, would refer the patient when the lesion was still present during this follow up.

This study did not investigate whether dentists would have detected the OML in the first place, because we presented them descriptions of patients that reported symptoms or mentioned visual abnormalities of the oral mucosa. Most patients with early malignant OML do not have symptoms, or perceive symptoms as abnormal, and often refrain from seeking help, which are patient related factors that influence delay in diagnosis [39]. Oral health professionals see their patients on a regular basis and have the opportunity to detect potential malignant lesions or malignant tumours at an early stage. Therefore, an opportunistic examination for head and neck cancer during regular dental check-up appointments is essential. It is concerning that, although 87% of dentists reported to be aware of symptoms for head and neck cancer in every patient (chapter 4), only 66% of dentists reported inspecting the oral mucosa in every patient (chapter 6).

FUTURE PERSPECTIVES

Results in this thesis create awareness among oral health professionals about their deficits in knowledge of various aspects on HPV infection and diagnosis and management of some OML, and stresses the need for more emphasis on head and neck cancer education. Research into the most appropriate forms of education, content of dental curricula, and content and frequency of postgraduate education is desirable. Availability of professional literature about this topic is desired, and therefore the authors published two articles about HPV in a Dutch language journal for oral health professionals [1,41]. Oral health providers reported positive attitudes towards counselling patients about HPV as a risk factor for OPSCC, however, they were less enthusiastic about counselling patients about HPV vaccination. These results contribute to the discussion about oral healthcare providers' engagement in prevention of HPV-positive OPSCC in The Netherlands. To facilitate the conversation about HPV in the dental practice setting, passive information tools, such as leaflets and posters, are desired. Government health authorities and professional organisations could provide these tools. They could also implement information programs to increase public awareness of the symptoms of head and neck cancer and examination by oral health professionals during regular check-up appointments.

Results in this thesis indicate that oral health providers do not feel confident about their head and neck cancer examination skills and have a tendency to refer a patient to a specialist when in doubt about their diagnosis. Over-referral of benign lesions has been identified in former research as a problem of oral cancer screening programmes [35]. This results in an unnecessary burden for public health services and stress for the patient. Development of evidence-based clinical guidelines that include a protocol for head and neck cancer examination practices and standardized criteria for referral to reduce both under and over-referral [42, 43]. Additionally, an electronic consultation tool, with the possibility to consult a specialist using clinical photographs, could be beneficial [44].

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8

Summary
Samenvatting

SUMMARY

Infection with a high-risk type of the human papillomavirus (HPV) is associated with an increasing percentage of oropharyngeal squamous cell carcinoma (OPSCC), particularly tonsillar and basal tongue carcinomas. Patients diagnosed with HPV-related OPSCC are younger and often lack classical risk factors such as alcohol and tobacco use. Many countries included an HPV vaccination in their national immunization programmes for boys and girls that protects against six kinds of HPV-related cancer, including OPSCC. Besides malignancies, infection with HPV can cause benign lesions of the skin and the mucosa of the orogenital region. Oral healthcare professionals could play a role in counselling patients about HPV and early diagnosis of HPV-related diseases. Therefore, they need to have sufficient knowledge about this topic. In this thesis we explored HPV-related knowledge of oral healthcare students and professionals and their attitudes towards counselling patients about HPV. In **chapter 2, 3 and 4** we identified specific deficits in HPV-related knowledge. For example, participants showed a lack of knowledge about patient characteristics for HPV-positive OPSCC. This is concerning as HPV-related OPSCC are generally present in younger patients and classical risk factors are lacking. Therefore, OPSCC may be less well recognized in these patients. Oral healthcare professionals considered counselling patients about HPV as a risk factor for OPSCC as important but were more reluctant about discussing HPV vaccination with patients. They reported barriers such as a lack of knowledge and the sensitive aspect of sexual transmission of the virus. Furthermore, it was reported that it is not the responsibility of the oral healthcare professionals to inform patients about HPV vaccination.

Results of chapters **2, 3 and 4** showed that oral healthcare professionals did not feel confident about their head and neck cancer examination skills. Dentists reported a relatively low level of confidence in performing a visual inspection and palpation of the head and neck region. Levels of confidence reported by oral health students were comparable, however, dental students reported to be slightly more confident than dental hygiene students. Although visual examination of the complete oropharyngeal region is not possible, oral healthcare professionals could be aware of symptoms of OPSCC during examination of the head and neck region.

The incidence of head and neck cancer is increasing, and almost half of these cancers are diagnosed at advanced stages. Sufficient knowledge of head and neck cancer among oral healthcare providers is relevant for diagnosing potentially malignant diseases and oral cancer at an early stage. Lack of confidence in head and neck cancer examination and deficits in knowledge among oral healthcare professionals might contribute to a delay in diagnosis. The content of head and neck cancer education of dental curricula might not be sufficient to fully prepare dentists for early detection and prevention of head and neck cancer. Therefore, the objective of **chapter 5** was to evaluate the content of head and

neck cancer education in curricula of European dental schools. We found a wide variation in the content of these curricula. Regarding clinical examination, one-third of dental schools did not educate their students to examine the skin of the head and neck region for suspicious lesions and two-third did not include palpation of the neck region. Results also indicated a variation in theoretical content, for example in risk assessment; sexual behaviour was recognised as a risk factor by 69% and gastro-oesophageal reflux by 41%. This variation in content results in differences of specific knowledge and competences of graduating European dentists.

In **chapter 6**, we aimed to explore dentists' knowledge about selected oral mucosal lesions (OMLs). Results showed that dentists did not have sufficient knowledge to accurately diagnose some OMLs and to determine a correct management. This may result in over-referral of benign OMLs and under-referral for (potentially) malignant OMLs. Clinical guidelines, that include standardized criteria for referral, postgraduate education and adaptation of dental curricula may improve dentists' ability to correctly diagnose and accurately manage OMLs.

SAMENVATTING

Wereldwijd en ook in Nederland is er een toename van de incidentie van humaan papillomavirus (HPV) geassocieerde orofarynxkanker. Deze kanker komt op jongere leeftijd voor dan de klassieke orofarynxkanker, die meestal wordt veroorzaakt door roken en overmatig alcoholgebruik. Keelkanker komt vooral voor in de tonsillen en de tongbasis. Sinds kort is er een HPV-vaccinatie vanuit het Rijksvaccinatieprogramma beschikbaar die beschermt tegen een langdurige infectie met HPV, die kan leiden tot kanker van de baarmoederhals, de anogenitale regio en de orofarynx. Naast maligne aandoeningen kan een HPV-infectie leiden tot benigne aandoeningen van de huid en het slijmvlies van het anogenitale gebied en de mondholte. Mondzorgverleners kunnen een rol spelen in het counselen van hun patiënten over HPV en vroegtijdige diagnostiek van HPV-gerelateerde aandoeningen in het hoofdhalsgebied. Daarom is het belangrijk dat zij voldoende basale kennis hebben over dit onderwerp. In dit proefschrift werd het kennisniveau over HPV en vaccinatie van Nederlandse (toekomstige) mondzorgverleners onderzocht en hun bereidheid om patiënten hierover te informeren. In **hoofdstukken 2, 3 en 4** hebben we aangetoond dat er een gebrek aan kennis is over specifieke HPV-gerelateerde onderwerpen. Er was bijvoorbeeld onvoldoende kennis over het verschil tussen patiënten met HPV-positieve en met HPV-negatieve tumoren. Het is belangrijk dat mondzorgverleners op de hoogte zijn van het feit dat HPV-positieve orofarynxtumoren vaker voorkomen bij relatief jongere patiënten, die vaak niet roken en geen overmatig alcohol gebruiken in tegen stelling tot HPV-negatieve patiënten die voorkomen bij oudere patiënten die veel roken en alcohol drinken. Respondenten vonden het belangrijk dat de relatie tussen humaan papillomavirus en orofarynxkanker met patiënten wordt besproken en wensten een protocol dat bruikbaar is bij het onderzoeken van patiënten met mogelijke klinische symptomen van mondholte- of keelkanker. Ze waren minder enthousiast over het bespreken van HPV-vaccinatie met hun patiënten. Redenen waren een gebrek aan kennis, ongemak bij het bespreken van de wijze van overdracht van het virus door seksueel contact en de mening dat het niet de taak van een mondzorgverlener is om de voor- en nadelen van HPV-vaccinatie met hun patiënten te bespreken.

Uit de resultaten in **hoofdstukken 2, 3, en 4** bleek dat mondzorgverleners zich relatief onzeker voelden over hun kennis en vaardigheden in het signaleren van de mogelijke aanwezigheid van mond- of keelkanker. Tandartsen rapporteerden dat zij onzeker waren over het de zorgvuldigheid bij het uitvoeren van klinische visuele inspectie en het palpatie/manueel onderzoek. Voor tandheelkunde- en mondzorgkundestudenten waren de resultaten vergelijkbaar waarbij tandheelkundestudenten iets waren zekerder over hun vaardigheden dan mondzorgkundestudenten. Het detecteren van een orofarynxcarcinoom tijdens visuele inspectie van de mondholte is sowieso lastig omdat het meestal ontstaat in de crypten van de tonsillen en in de tongbasis. Het is niet ongebruikelijk dat het eerste symptoom een zwelling in de hals is als gevolg van een

regionale lymfekliermetastase . Het is belangrijk dat mondzorgverleners hiervan op de hoogte zijn en hun patiënt doorverwijzen indien zij een zwelling in de hals opmerken. Die zwelling kan overigens ook door andere aandoeningen worden veroorzaakt.

Er is wereldwijd en ook in Nederland een toename van de incidentie van hoofd-halskanker en bijna in de helft van de gevallen wordt de tumor in een laat stadium gediagnostiseerd. Het is belangrijk dat mondzorgverleners over voldoende kennis beschikken over diverse aspecten van hoofd-halskanker zodat ze potentieel maligne en maligne mondafwijkingen in een vroegtijdig stadium kunnen herkennen. Bij een vroegtijdig diagnose is de kanker klein en daardoor meestal behandelbaar, is de kans op genezing groot en zijn de bezwaren en bijwerkingen door de behandeling(en) in het algemeen beperkt. Onderzoek toont aan dat gebrek aan kennis van de klachten en symptomen van mondkanker en onzekerheid over voldoende klinische vaardigheden bij het uitvoeren van onderzoek naar de mogelijke aanwezigheid van mondkanker bij mondzorgverleners factoren die kunnen bijdragen aan een late diagnose van de ziekte. Een mogelijke oorzaak hiervan is onvoldoende theoretisch en klinisch onderwijs over hoofd-halskanker tijdens de opleiding Tandheelkunde. In **hoofdstuk 5** hebben we daarom de mate en omvang van onderwijs over hoofd-halskanker in de curricula van de opleidingen Tandheelkunde in geselecteerde landen in Europa geïnventariseerd. Hierbij bleek dat er een grote variatie over dit onderwerp was in de verschillende curricula. Een derde van de opleidingen rapporteerde dat ze studenten geen onderwijs gaven over het klinisch onderzoek van de huid in de hoofd-halsgebied en twee derde bood geen onderwijs aan over het palperen van de hoofd-halsgebied. Over het theoretisch onderwijs werden variaties gerapporteerd over bijvoorbeeld risicofactoren; seksueel contact werd door meer dan twee derde als risicofactor voor het krijgen van een orofarynxcarcinoom aangeduid. Counseling van patiënten over dit onderwerp werd maar door een derde van de instellingen onderwezen. De variatie in de curricula over inhoud en de omvang van diverse aspecten van hoofd-halskanker resulteert in verschillen in het kennisniveau en de competenties tussen de afgestudeerde tandartsen van de verschillende Tandheelkunde opleidingen in landen in Europa.

Tot slot werd in **hoofdstuk 6** de kennis van tandartsen in Nederland over geselecteerde mondslijmvliesafwijkingen onderzocht. Er werd een vragenlijst opgesteld waarin 11 verschillende casussen werden beschreven bestaande uit goedaardige, potentieel maligne en maligne slijmvliesafwijkingen. Tandartsen werd gevraagd om voor elke casus een diagnose, differentiaaldiagnose en een beleid te bepalen . De resultaten toonden grote variatie in de kennis en het kennisniveau van de verschillende afwijkingen. Zo werden goedaardige afwijkingen zoals een afte of een fibroom door de meeste tandartsen juist gediagnostiseerd. Een melanotische macula werd echter door slechts een derde van de deelnemers juist gediagnostiseerd. Een speekselkliertumor en een plaveiselcelcarcinoom werden respectievelijk door 52% en 63% van de tandartsen juist gediagnostiseerd. Bij het klinisch vermoeden van een maligniteit is directe verwijzing

naar een MKA-chirurg het juiste beleid. De resultaten suggereren dat een gebrek aan kennis kan leiden tot bovenmatig veel verwijzingen van goedaardige afwijkingen en juist een late verwijzingen van (potentieel) maligne afwijkingen. Om tandartsen te ondersteunen in hun klinische besluitvorming, zou een richtlijn van de beroepsgroep over diverse aspecten van mondholtekanker, met daarin ook aanbevelingen over de wijze van verwijzen van patiënten naar de MKA-chirurg, wenselijk zijn. Het regelmatig volgen van bij- en nascholing en het optimaliseren van onderwijs over hoofd-halskanker tijdens de studie Tandheelkunde, kunnen het kennisniveau van tandartsen onderhouden en vergroten en daarmee bijdragen aan de vroegtijdige diagnostiek van patiënten met (potentieel) maligne mondafwijking.

9

Author contributions
Dankwoord
Curriculum vitae

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Chapter 2

Prevention of HPV-related oral cancer by dentists: assessing the opinion of Dutch dental students

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Chapter 3

Dutch dental hygiene students' knowledge of HPV-related oropharyngeal squamous cell carcinoma and HPV vaccination

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Chapter 4

Knowledge of Dutch dentists regarding HPV associated cancer of the oropharynx

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Chapter 5

Evaluation of head and neck cancer education at European dental schools

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Chapter 6

Knowledge of Diagnosis and Management of Selected Oral Mucosal Lesions among Dentists in The Netherlands

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NWT Nederlandse Wetenschappelijke Vereniging van Tandartsen

NVVRT
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