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# A Cross-Sectional Survey of UK General Practitioners of Awareness of Human Papillomavirus-associated Oropharyngeal Cancers

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Gilson, Richard; University College London, Department of Infection and Population Health |
| Keywords: | General Practice, Primary Health Care, Human papillomavirus, HPV Vaccines, Oropharyngeal Neoplasms, HPV |
A Cross-Sectional Survey of UK General Practitioners of Awareness of Human Papillomavirus-associated Oropharyngeal Cancers

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Keywords (5 MeSH headings): General Practice, Primary Health Care, HPV, Human papillomavirus, HPV Vaccines, Oropharyngeal Neoplasms

Word count: 1573

Data sharing agreement: The raw dataset, statistical analysis spreadsheet and response rate calculations are available online alongside this article as supplementary files.
Abstract:

Objectives: To examine the level of awareness of the link between human papillomavirus (HPV) and oropharyngeal cancer (OPC) and epidemiological trends in HPV-related OPC amongst UK General Practitioners.

Design: Cross-sectional survey

Participants: 384 General Practitioners from England, Scotland, Wales and Northern Ireland.

Setting: General Practitioners attending training courses.

Primary and secondary outcome measures: Proportion of respondents aware of the link between HPV and OPC; respondents' self-rated knowledge of OPC; proportion of participants aware of the epidemiological trends of HPV-associated OPC.

Results: 384 questionnaires were completed giving an overall response rate of 72.9%. 74.0% of participants were aware of the association between HPV and OPC (with 19.4% and 62.7% rating their knowledge of OPC as very good/good and average, respectively). 71.9% were aware of the increase in rates of HPV-associated OPC. Less than half (41.5%) of participants correctly associated male predominance and 41.2% did not correctly associate younger age with HPV-associated OPC.

Conclusions: The association of HPV infection with OPC is a relatively recent discovery. Although the level of awareness of HPV and OPC among General Practitioners was high, the characteristics of HPV-associated OPC were less well recognised, indicating the need for further education.
Article Summary:

Strengths and limitations of this study

- This study is the first to report on awareness of HPV-associated OPC in a sample of UK General Practitioners.
- This study involved a cross-section of participants from a variety of geographical regions and General Practitioners of varying levels of experience.
- This study demonstrates that further education on the epidemiological trends and patient demographics of HPV-associated OPC may be needed to ensure early detection of disease. We provide a learning module in the supplementary material.
- Limitations of the study include participation of a self-selecting group of GPs and trainees attending training updates.

Funding Statement: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests: Nil declared.
**Introduction**

Head and neck cancer (HNC) is a significant cause of morbidity and mortality with over 11,000 new cases diagnosed in the UK each year\(^1\). The most common anatomical sites are the oral cavity, pharynx and larynx, with over 90% of tumours diagnosed being squamous cell carcinomas\(^2\). Survival rates of HNC are related to histological type, primary tumour site, disease stage at time of diagnosis and aetiology. Knowledge of the risk factors and epidemiology is key to primary prevention and earlier diagnosis\(^3\). HPV-positive OPC is much more responsive to chemotherapy and radiotherapy (82% vs 55%) and has better overall survival rates at 2 years (95% vs 62%)\(^4\). The increasing rates of head and neck cancers and the fact that their outcome depends on early diagnosis, has been recognised in the GP Curriculum of the Royal College of General Practitioners \(^5\).

Research in the past decade has revealed the increasing importance of human papillomavirus (HPV) infection as a major risk factor for the development of HNC, in particular oropharyngeal cancer (OPC)\(^6\)\(^7\). Whilst rates of tobacco-related disease has decreased over the past two decades, there has been a marked increase in HPV-positive OPC. It is estimated that between 55-95% of OPC in Europe is HPV-positive in younger patients\(^7\)\(^8\). Twenty years ago this figure stood at just 20%. In this period, the incidence of HPV-associated OPC in the US has increased by 225%\(^9\) and similar trends are observed in the UK. In Scotland the rates of oropharyngeal cancer have increased more than those of any other cancer\(^10\).

HPV-positive OPC occurs at a younger age and more often in males compared to non-HPV-associated OPC\(^11\). HPV-positive OPC represents a distinct molecular, epidemiologic and clinical entity\(^12\)\(^13\).

Patients presenting with HPV-positive OPC typically lack traditional risk factors such as smoking and alcohol use. As they present at younger age the diagnosis may be more easily overlooked by healthcare practitioners unaware of the changing epidemiology. Risk factors for HPV-positive OPC include age at first intercourse, number of sexual partners and number of oral sex partners\(^6\).
Awareness of the changing epidemiological and risk factor profile of OPC amongst primary care professionals is likely to lead to earlier diagnosis, resulting in improved outcomes. Nevertheless, the learning resources recommended by the RCGP Curriculum to GPs and GP Trainees such as RCGP Learning, e-LfH and BMJ Learning related to HPV infection focus on cervical cancer and cervical screening. Our review of the literature suggested no learning modules available to UK GPs that focus on HPV-associated OPC.

We conducted a survey of General Practitioners to determine the level of awareness of HPV-associated OPC, and identify areas where further educational resources might lead to improved patient outcomes.

**Methods:**

The questionnaire was administered to a convenience sample of General Practitioners attending courses and training meetings, in either a pen and paper or electronic format over a period of 9 months (May 2015 to February 2016) in various regions of the UK (to avoid a selection bias). A 12 item anonymous questionnaire (Table 1) covering demographics, characteristics of HPV-related OPC, developed from literature on the awareness of risk factors for OPC amongst the general public, and the validated Cancer Awareness Measure. Self-rated level of knowledge of OPC was assessed using a Likert scale. Questions on risk factors, presentation, epidemiological trends and the association with HPV were included (Table 1; a copy of the questionnaire has been made available as a supplemental file). These questions were developed with the help from members of the public, but patients were not involved. The relevant checklist, i.e. STROBE checklist was completed (supplemental file).

Statistical analysis was conducted using standard measures of central tendency and spread. The study was exempted from the requirement for Research Ethics Committee (REC) review on the basis that data collection was anonymised and no vulnerable participants were involved (advice from Harrow NHS REC and UCL REC).
**Results:**

96 surveys were distributed in printed form and 411 requests were sent by email to course attendees. 384 questionnaires were completed giving an overall response rate of 72.9%. The response rate for paper questionnaires was higher (85.4%) compared to online distribution (70.1%) (see Supplemental Table 1). 59.1% participants were female. The largest number of participants were from England, but all parts of the UK were included (Table 2). 50.3% of participants were in practice for over 10 years. Table 3 shows the distribution of participants according to years since graduation.

35.2% (135) of participants were in training, 32.8% (126) were salaried GPs and 23.9% (92) were GP Partners; 5.9% (23) reported being in a locum post.

Participants were asked about 13 exposures, and whether they were risk factors of OPC (Figure 1). 271 out of 349 (77.6%) participants who responded to the risk factor question correctly identified HPV as a risk factor for OPC. A similar proportion (71.2%) of participants correctly stated that the rates of HPV-associated OPC have increased.

Smoking, chewing tobacco, current alcohol consumption and past alcohol consumption were the most frequently recognised risk factors (99.4%, 96.6%, 94.3%, 86.5%, respectively). Chewing of catchu and areca nuts, marijuana use and aflatoxin exposure were less frequently recognised (32.9%, 50.4%, 26.4%, respectively). Less than half (41.5%) of participants correctly identified HPV-associated OPC as being more common in males, while 58.8% correctly reported the association with younger age. There were no statistically significant differences between years since graduation or post type and awareness of HPV and OPC.

**Discussion:**

This study is the first to assess the awareness of HPV-associated OPC in a sample of UK General Practitioners. Our results show that more than three-quarters of UK participants who responded to the risk factor question correctly identified HPV as a
risk factor for OPC. However, there is limited awareness of the differences in the demographic profiles of patients presenting with HPV-associated and non-HPV-associated OPC as well as a lack of awareness of other risk factors of OPC.

Cancer of the oropharynx is now thought to be associated with HPV in 70-95% of younger patients and disease outcome is related to the stage of disease at diagnosis. It is therefore important that General Practitioners, who are likely to be the first point of contact for patients, and need to be aware and recognise the characteristics of patients with HPV-associated OPC in order to refer them on to secondary and tertiary care in a timely fashion. These patients may be younger and may not have any history of smoking and drinking, compared with the risk factor profiles of traditional head and neck cancer patients.

Our study demonstrates that further education on the epidemiological trends and patient demographics of HPV-associated OPC is needed to ensure early detection of disease. We provide a learning module which can be accessed online (supplemental file - HPV Oropharyngeal Cancer Module). GP awareness of the role of HPV in OPC may lead to more support for the continued high uptake of national HPV vaccination programmes, thereby maximising opportunity to ensure both individual and herd protection.

Strengths and limitations
Our study is the first to assess the awareness of HPV-associated OPC in a sample of UK General Practitioners. The response rate was high. We instructed all participants to answer the questions consecutively when distributing the paper forms, but participants may have looked at subsequent questions, which could influence their responses. The online questionnaire only allowed questions to be answered in order.

Comparison with existing literature
A recent systematic review by Dodd et al. evaluated the psychosocial impact of HPV-related HNC and investigated the awareness of the link between HPV and HNC among different populations. 41 studies were identified which measured knowledge of the link between HPV and HNC, demonstrating the lowest level of knowledge in
the general population and highest in medical and dental professionals\textsuperscript{16}. However, Signorelli et al. showed that only 38\% of Italian GPs (n=938) recognised the role of HPV in oral disease and oral cancer and concluded that there is a lack of knowledge on HPV infection and vaccination in Italian GPs\textsuperscript{17}. Odone et al. explored reasons for non-vaccination against human papillomavirus in Italy\textsuperscript{18}, providing a useful basis to plan, implement and evaluate targeted educational programmes and training. The link between HPV and OPC was recognised by 43.3\% of primary care physicians in Jordan\textsuperscript{19} and by 54\% of a sample of German physicians\textsuperscript{20}.

A study of 2126 adults in the United States demonstrated that knowledge of HNC among the general public is low. Whilst 54\% of participants identified smoking as a risk factor for HNC, 4.8\% identified alcohol use, and just 0.8\% recognised HPV infection as a risk factor \textsuperscript{(3)}. Family physicians could play a key role in educating the public, and encouraging HPV vaccine uptake.

We report findings of the first study investigating the awareness of HPV-associated OPC risk factors in a sample of UK general practitioners. Awareness in the UK is high but there are gaps in knowledge that could be addressed.

\textbf{Implications for practice}
The failure of 41.2\% of participants to associate HPV-related OPC with younger age should be addressed as only awareness of the fact that there has been a significant rise in younger patients presenting with OPC, often lacking a history of smoking and high alcohol intake, will ensure that HPV-associated OPC will be recognised early.

Following the results of this survey, we have also created a learning module which can be freely accessed at \textit{(LINK VIA BMJ Open homepage)}.

This includes reference to other risk factors that may be underrecognised, such as chewing betel nuts (also referred to as catchu or areca nuts) which are traditional among some communities in Indian, Pakistan and Bangladesh.

In conclusion, this work demonstrates a clear need for further education on a disease which shows a rising incidence, and a changing epidemiology.
Author’s contribution

ML, CV, CK, OJ, RG wrote the first draft of the manuscript with contributions from JH, TF, LM, JW and WY. CV, CK, JH collected the data and analysed these under the guidance of WY, RG and ML. OJ and ML created the online module with advice from LM and TF.

Additional information

Ethical approval: The study was exempted from the requirement for Research Ethics Committee (REC) review on the basis that data collection was anonymised and no vulnerable participants were involved (advice from Harrow NHS REC and UCL REC).

Acknowledgements:

The authors would like to thank the general practitioners who took part in the study for their time and effort in completing the surveys and to the educational bodies who gave us permission to distribute questionnaires at GP training events. Moreover, we would like to thank our public engagement group for their help during the design of the study.

References:


10.1093/jnci/djn011 [published Online First: 2008/02/14]


10.1056/NEJMoa065497 [published Online First: 2007/05/15]


10.1200/JCO.2011.36.4596 [published Online First: 2011/10/05]

10. Association BD. Oral and Oropharyngeal Cancer fact sheet for healthcare professionals. 2017


13. Lechner M, Fenton TR. The Genomics, Epigenomics, and Transcriptomics of HPV-Associated Oropharyngeal Cancer--Understanding the Basis of


Tables

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</tr>
<tr>
<td>2. Stage of GP training</td>
<td>384</td>
</tr>
<tr>
<td>3. Years since graduation</td>
<td>384</td>
</tr>
<tr>
<td>4. Location of current practice</td>
<td>380</td>
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<tr>
<td>5. Likert scale self-rating of knowledge of OPC</td>
<td>350</td>
</tr>
<tr>
<td>6. Warning signs and symptoms of OPC</td>
<td>350</td>
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<tr>
<td>7. Risk factors for OPC</td>
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<tr>
<td>8. Specific risk factors for OPC (asks for yes/no/don’t know response for 13 items)</td>
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<tr>
<td>9. Trends in smoking-related OPC in developed countries</td>
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<tr>
<td>10. Prior knowledge of the link between HPV and OPC before completing the survey.</td>
<td>342</td>
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<tr>
<td>11. Trends in HPV-positive OPC in developed countries</td>
<td>342</td>
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<tr>
<td>12. Comparison of patient profile between HPV-positive and HPV-negative OPC (2 part questions asking about age and gender profile)</td>
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Table 1 – Questionnaire content and number of responses for each question

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<thead>
<tr>
<th>Location of Current Practice</th>
<th>No. of participants</th>
<th>Percentage</th>
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<td>England</td>
<td>169</td>
<td>44.5%</td>
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<tr>
<td>Scotland</td>
<td>103</td>
<td>27.1%</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>76</td>
<td>20.0%</td>
</tr>
<tr>
<td>Wales</td>
<td>32</td>
<td>8.4%</td>
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</table>

Table 2: Location of participants’ current GP practice.

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<th>Years Since Graduation</th>
<th>No. of participants</th>
<th>Percentage</th>
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</thead>
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<td>&lt;2</td>
<td>17</td>
<td>4.4%</td>
</tr>
<tr>
<td>2-5 years</td>
<td>81</td>
<td>21.9%</td>
</tr>
<tr>
<td>5-10 years</td>
<td>93</td>
<td>24.2%</td>
</tr>
<tr>
<td>10-20 years</td>
<td>69</td>
<td>17.9%</td>
</tr>
<tr>
<td>&gt;20 years</td>
<td>124</td>
<td>32.3%</td>
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Table 3: Years since graduation.
**Figure Legends**

**Figure 1:** Participant responses to questions on 10 proven risk factors for OPC, and 3 factors which are not known risk factors.

**Supplemental material**

- Supplemental Table 1
- Copy of the questionnaire handed to UK GPs
- HPV Oropharyngeal Cancer Module
- STROBE checklist
From the editor:

In addition to the reviewers’ comments, we also felt that the quality of study reporting was not at the requisite standard for publication. For example, the methods section was far too brief and did not cover in enough detail the items presented in the STROBE checklist. Likewise, we felt that your discussion section was too brief and did not cover in enough detail the areas recommended in our instructions for authors for research articles (see: http://bmjopen.bmj.com/pages/authors/#research).

Many thanks for pointing this out. We have now extended both the methods section and the discussion section in accordance with the STROBE checklist and in accordance with the instructions for authors.

In addition to this

1- A full questionnaire has been added as a supplemental file.
2- Currently available educational resources to GPs and to the Public in the UK have been reviewed and results have been incorporated in the main body of text.
3- Objectives section at introduction has been expanded
4- Methods
   a. Resources for the survey development clarified with references to prior examples.
   b. Data collection period clarified.
5- Results section has been expanded with further analysis of various data points including differences in awareness between different experience levels and geographical distribution.
6- Discussion:
   a. Implications of practice section expanded and clarified
   b. Comparison with existing literature further detailed as per comments from reviewers.

Response to Reviewer Comments:

Reviewers' Comments to Author:

Reviewer: 1
Reviewer Name: Andrea Salonia
Institution and Country: IRCCS Ospedale San Raffale, Italy
Competing Interests: None declared

I reviewed ms. number bmjopen-2017-018116. In this paper, the Authors report results from a cross-sectional survey aimed at assessing HPV-associated oropharyngeal carcinoma (OPC) awareness among 384 UK general practitioners (GPs). 74% of GPs were aware of HPV-associated OPC, and most of them rated their knowledge as good/very good.

Several general and methodological issues need to be outlined, which unfortunately make the paper not suitable for publication.

In detail:
- The Authors provide data on a very limited and selected set of GPs in a study involving a single European country. How many GSs are there in the UK? How was the study sample selected?

We would like to thank Prof. Salonia for her helpful comments. The objective of this paper was to measure the knowledge of UK GPs on HPV related OPC. We have added a list of other studies in other European countries, in particular Italy, but as the number of similar studies is very limited and methods used are diverse, a direct comparison would not be possible. Yet, overall comparison of the data shows the need for further education of GPs in the UK in line with results from other European countries.
- Samples from all across the UK, including England, Scotland, Wales and Northern Ireland were obtained and were proportional to respective numbers of registered GPs. Nevertheless, we acknowledge the sample selection as one of the limitations of our study.

- How HPV awareness influenced GP clinical practice? Authors should report population-based data on HPV infections and its consequences in the UK.
We have extended the introduction section to make sure these points are all covered.

- HPV vaccination involves young girls and boys, whose health status is usually a concern for pediatricians rather than GPs. Why not including pediatrician in this study?

As opposed to healthcare system in Italy, in the UK, GPs are the primary healthcare providers for both adults and children and children do not have access to paediatricians in the community directly. Furthermore, routine vaccination schedule is overseen and administered by the GPs. GPs in the UK see the vast majority of children and are also the first port of call for patients presenting with symptoms and signs of HPV-related disease, incl HPV OPC

- How is HPV knowledge spread in the UK among GPs and the general population? How does this influence the study result?
Many thanks for this helpful comment. We have looked at the data again and we did not observe any significant variation which we report.

- Please report full questionnaire and not only question subjects
Many thanks for this helpful comment. We have included the full questionnaire in the manuscript.

- Please discuss your results in further detail
Many thanks for this helpful comment. We have extended the results section with additional stats and analyses.

Reviewer 2

COMMENTS TO THE AUTHORS:
Vassie et al conducted a cross-sectional survey on UK General Practitioners' awareness of Human Papillomavirus-associated Oropharyngeal (HPV) Cancers.

The global burden of HPV-related oropharyngeal cancers is on the raise and it is predicted to surpass the burden of cervical cancer in the near future. In this context, general practitioners progressively assume a key role in oropharyngeal cancers' primary prevention and early diagnosis; for this to effectively happen their knowledge and awareness on the topic need to be strengthened.

Assessing GPs' knowledge and awareness on oropharyngeal cancers in a specific setting (the UK) – as done in the paper – can inform the planning and implementation of targeted educational and training interventions. The paper present some basic – still informative - descriptive analysis, its objectives are clearly defined and the paper is overall well written. I believe the paper in its current shape does not provide sufficient data or insight to be presented a full original article, my suggestion would be to re-shape it in a short report or letter to the editor with original data.

Many thanks for the encouraging comments. Having amended and extended the article providing additional analyses we feel that it is suitable for a full paper.

SPECIFIC COMMENTS:
• Author should consider, clarifying or expanding on the following points:
  How was the survey tool developed? by who? was it piloted? was it based on previously published tools? It would be important to include it as supplementary material. If it is already included in the supplementary material, no reference to this is made in the main text.
Many thanks for this helpful comment. We have added all these points. We commented on previously published tools and how it helped us to design the questionnaire. We have also included the questionnaire in the supplemental material in addition to the learning module.

A limit of the study is that no random sampling of the target population was carried out. Do authors have an idea if the sample the limited their analysis to is representative of the UK GPs’ population? 384 (study’s sample size) is which percentage of the UK GPs total population?

Many thanks for this helpful comment. We attended training courses across the country in order to be
sure we get a representative sample. We have also shown that the number of GPs from the different regions in the UK, i.e. England, Wales, Scotland and Northern Ireland are as representative as possible of the overall number of GPs in these regions. We have expanded the relevant section on sample selection to clarify.

- 73% response rate is relatively high - however can author provide data to show there was no selection bias? i.e. can author compare responders and non-responders by selected socio-demographic characteristics?

We attended training courses across the country in order to be sure we get a representative sample. We have also shown that the number of GPs from the different regions in the UK, i.e. England, Wales, Scotland and Northern Ireland are as representative as possible compared with the overall number of GPs located across the country. Unfortunately we do not have any data on the comparison of responders and non-responders, as we did not get any forms back from non-responders or these belong to the group who did not complete the survey, but in view of the fact that we have responses from GPs from all regions of the UK, who attended meetings across the UK, we feel confident that we have a representative sample.

- When was the survey conducted? no reference is made in the text to dates (i.e. months or year)

Many thanks for this helpful comment. We have added this.

- The RESULTS section is very short. Authors might consider expanding on results. In the current shape they do not provide very meaningful insight. What were the risk factors they were more or less aware of (this should be included in the text and not only in the tables)? Did the author consider exploring if level of awareness is associated to selected GPs characteristics (i.e. years since graduation)? Did the author consider adding a section on GPs’ awareness on HPV vaccine?

We are grateful for this helpful comment. We have analysed variables, such as certain demographics (level of training, etc.) vs. awareness and we have expanded the results section. We have also commented on implications with regard to this. Unfortunately we did not obtain any data on the awareness of the HPV vaccine, as we expect that UK GPs would know this, as most routine paediatric care is delivered by UK GPs.

The DISCUSSION session has a too long summary sub-session and a three-line sentence of comparison with existing literature. Authors should refer to and comment more on other published evidence on the topic, for example:

- Signorelli C, et al., [Human Papillomavirus infection and vaccination: knowledge and attitudes of Italian

Many thanks for this helpful comment. We have extended the discussion and section. We have also reviewed and incorporated additional literature, including the two interesting papers suggested by you.
Figure 1: Participant responses to questions on 10 proven risk factors for OPC, and 3 factors which are not known risk factors.
Supplementary data

Paper copy questionnaires

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<th>Number of returned forms</th>
<th>Response rate</th>
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<td>23</td>
<td></td>
</tr>
<tr>
<td>Hillingdon West</td>
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<td>44</td>
<td></td>
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<td>London GP update</td>
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<tr>
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<td></td>
<td></td>
</tr>
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<td>training</td>
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<td></td>
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<tr>
<td>Total</td>
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Online questionnaires

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<tr>
<td>Total</td>
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<td>288</td>
<td>245</td>
<td>8 (2.8%)</td>
<td>85.06%</td>
<td>70.10%</td>
</tr>
</tbody>
</table>

Total response rate: 72.9%

Supplemental Table 1: Response rate for paper copy and online questionnaires
Oropharyngeal Cancer (General Practitioners)

Many thanks for your interest in completing this short questionnaire on oropharyngeal cancers. This questionnaire is part of a study being carried out by UCL Cancer Institute. The study aims to assess current levels of knowledge of oropharyngeal cancers amongst General Practitioners and Clinical Medical Students to gauge if there is a need for greater education and training in this area.

All responses are completely anonymous. If you wish to withdraw from participating you are free to do so at any time whilst completing the questionnaire. As participation is anonymous it will not be possible for us to withdraw your data once you have returned your questionnaire. If you have any concerns or questions, please contact Dr. Claire Vassie (claire.vassie@doctors.org.uk)

1. Stage of GP training/Position
   - ☐ F2
   - ☐ GPST1
   - ☐ GPST2
   - ☐ GPST3
   - ☐ GP (salaried or partner)
   - ☐ Other (please state)

2. Please select your gender:
   - ☐ Female
   - ☐ Male

3. Years since graduation
   - ☐ <2yrs
   - ☐ 2-5yrs
   - ☐ 5-10yrs
   - ☐ 10-20yrs
   - ☐ 20+yrs

4. How would you rate your knowledge of oropharyngeal cancers compared to other General Practitioners?
   - ☐ Very Poor
   - ☐ Poor
   - ☐ Average
   - ☐ Good
   - ☐ Very good

5. There are many warning signs and symptoms of oropharyngeal cancers, please list as many as you can. If you cannot think of any, please write “don’t know” below.

6. Please list risk factors for oropharyngeal cancers. If you cannot think of any, please write “don’t know” below.
7. Which of the following may be risk factors for oropharyngeal cancer?

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Yes</th>
<th>No</th>
<th>Don't know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Alcohol consumption</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past Alcohol consumption</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aflatoxin exposure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietary nitrosamines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chewing of tobacco</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chewing of Betel leaf</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chewing of Catchu and areca nuts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marijuana use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herpes simplex virus infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruit and vegetable consumption</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8. Do you think the rates of smoking-related oropharyngeal cancers in developed countries have changed over the past two decades?

- [ ] Increased
- [x] Decreased
- [ ] Stayed the same
- [ ] Don’t know
Recently, several discoveries have been made about the association between human papillomavirus (HPV) and oropharyngeal cancers.

9. Before today, had you heard about the link between oropharyngeal cancer and HPV?
   
   ☐ Yes  ☐ No  ☐ Not sure

10. Do you think the rates of human papillomavirus (HPV)-associated oropharyngeal cancers in developed countries have changed over the past two decades
    
    ☐ Increased  ☐ Decreased  ☐ Stayed the same
    ☐ Don’t know

11. In comparison to patients with non-HPV associated oropharyngeal cancer, are patients with HPV associated oropharyngeal cancers more likely to be:
    
    a) ☐ Male  ☐ Female  ☐ Same gender composition in both conditions
    ☐ Don’t know
    
    b) ☐ Younger  ☐ Older  ☐ Same age composition in both conditions
    ☐ Don’t know

Thank you for taking the time to complete this questionnaire.
HPV & Oropharyngeal cancer

Know the risks, spot the signs
Aims

- To understand the basic pathology and demographics of HPV infection and oropharyngeal cancer

- To be aware of the risk factors for each and to understand the relationship between HPV and oropharyngeal cancer

- To be able to recognise signs of HPV infection and warning signs of oropharyngeal cancer
What is HPV?

- Human papilloma virus (HPV) is a group of viruses that live and multiply in human skin and mucosal cells.
- HPV is transmitted during skin-to-skin or sexual contact - particularly oral, anal and vaginal sex.
- There are many subtypes, causing: skin warts, verrucas, genital warts and laryngeal papillomas (warts in voice box).
- Some HPV types (particularly HPV-16 and HPV-18) are associated with cervical, anal, genital and oropharyngeal cancers.
- A vaccine is offered to schoolgirls aged 12-13 – no vaccine is currently available for boys (this arrangement is under review by the Joint Committee on Vaccination and Immunisation).
Risk Factors for HPV-associated oropharyngeal cancer

Demographic:
• Male
• Caucasian
• Higher socioeconomic class

Behavioural:
• Many sex and oral sex partners
• History of sex without barrier protection
• Early age first intercourse

Perhaps the most famous case of HPV-associated oropharyngeal cancer is Michael Douglas, who has spoken publically about his diagnosis and treatment many times – although the actor matches the archetypal patient profile and had fairly typical complaint, he stated in an address to the American Head and Neck Society that he was misdiagnosed three times.
Disease timeline

Healthy person  →  Sexual contact  →  HPV acquisition (may experience early lesions depending on subtype, or no symptoms at all)  →  Many years...  →  May develop oropharyngeal cancer
What is oropharyngeal cancer?

- The oropharynx is the **space posterior to the oral cavity**, including the tonsils and base of the tongue – food passes through the oropharynx when moving from the mouth the food pipe during swallowing.
- Oropharyngeal cancer arises from the mucosal surface of this space.
- Oropharyngeal cancers are caused by smoking and drinking or by HPV and, hence, can be divided into HPV-positive and HPV-negative cancers. These carry different prognoses.
Risk factors for oropharyngeal cancers

Reversible risk factors:
• HPV exposure
• Heavy alcohol consumption
• **Smoking** (20-a-day for more than 10 years or equivalent amount)
• Some chewing plants and drinks specific to certain countries and cultures
  - betel leaf (a chewing tobacco used in Asia)
  - maté (a stimulant drink from South America)
• **Unconfirmed:** reversible risk factors include: diet, immunosuppression, poor oral hygiene, mouthwash, tooth whiteners, high body weight
Risk factors for oropharyngeal cancers

Non-reversible risk factors:

• Previous cancer:
  - oropharyngeal, oesophageal
  - anal, genital, cervical cancer
  - family history of oropharyngeal cancer

• Genetic conditions
  - *Fanconi anaemia* – patients with short stature with bone changes
  - *Dyskeratosis congentiona* – anaemia, skin rashes, and abnormally shaped fingernails and toenails (particularly elevated risk when young)
Warning signs of oropharyngeal cancer

• Primary swellings and masses in the tongue, tonsils, soft palate, including symptoms like:
  - Ulcerated tonsils that don’t heal
  - White or red patches in the throat
  - Pain or difficulty swallowing and moving the jaw
  - Numbness, pain or discomfort in the throat or tongue
  - Bad breath
  - Earache (especially unilateral)
  - Can be asymptomatic

• (Multiple) secondary swellings or masses in neck which are painless, firm and mobile (neck metastases)

• Unexplained weight loss
Important HPV facts

• HPV is the most common STI in the UK, affecting 75% of sexually active females, often silently

• HPV is also the only STI which affects more men than women

• The risk of many HPV-associated cancers is higher is men who have sex with men
  - 80% of anal cancers and 40% of penile cancers are HPV-associated
Important HPV facts

- In developed countries, rates of oropharyngeal cancers have risen sharply - in some countries, more than 90% of oropharyngeal cancers are HPV-positive amongst younger age groups
  - This is thought to be a result of changing sexual behaviours

- In comparison to patients with HPV-negative oropharyngeal cancer, patients with HPV-positive oropharyngeal cancers are more likely to be:
  - Younger
  - Male

- There are treatment strategies available for HPV-positive oropharyngeal cancer that are not used in HPV-negative oropharyngeal cancer
References

2. Doorbar, “The papillomavirus life cycle.”
4. Gillison, “Human papillomavirus-associated head and neck cancer is a distinct epidemiologic, clinical, and molecular entity.”
8. Weaver, “Epidemiology and natural history of genital human papillomavirus infection.”
10. Gillison et al., “HPV prophylactic vaccines and the potential prevention of noncervical cancers in both men and women.”

Module created by Oliver Jones, UCL Year 6 MBBS, and Dr. Matt Lechner, Hon. Lecturer, UCL Cancer Institute.
<table>
<thead>
<tr>
<th>Section/Topic</th>
<th>Item #</th>
<th>Recommendation</th>
<th>Reported on page #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title and abstract</td>
<td>1</td>
<td>(a) Indicate the study’s design with a commonly used term in the title or the abstract</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</td>
<td>2</td>
</tr>
<tr>
<td>Introduction</td>
<td>2</td>
<td>Explain the scientific background and rationale for the investigation being reported</td>
<td>4</td>
</tr>
<tr>
<td>Objectives</td>
<td>3</td>
<td>State specific objectives, including any prespecified hypotheses</td>
<td>5</td>
</tr>
<tr>
<td>Methods</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study design</td>
<td>4</td>
<td>Present key elements of study design early in the paper</td>
<td>5</td>
</tr>
<tr>
<td>Setting</td>
<td>5</td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</td>
<td>5</td>
</tr>
<tr>
<td>Participants</td>
<td>6</td>
<td>(a) Give the eligibility criteria, and the sources and methods of selection of participants</td>
<td>5</td>
</tr>
<tr>
<td>Variables</td>
<td>7</td>
<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</td>
<td>N/A</td>
</tr>
<tr>
<td>Data sources/</td>
<td>8*</td>
<td>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group</td>
<td>N/A</td>
</tr>
<tr>
<td>measurement</td>
<td></td>
<td></td>
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<tr>
<td>Bias</td>
<td>9</td>
<td>Describe any efforts to address potential sources of bias</td>
<td>7 (strengths and limitations)</td>
</tr>
<tr>
<td>Study size</td>
<td>10</td>
<td>Explain how the study size was arrived at</td>
<td>5</td>
</tr>
<tr>
<td>Quantitative variables</td>
<td>11</td>
<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</td>
<td>N/A</td>
</tr>
<tr>
<td>Statistical methods</td>
<td>12</td>
<td>(a) Describe all statistical methods, including those used to control for confounding</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) Describe any methods used to examine subgroups and interactions</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(c) Explain how missing data were addressed</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
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<td>(d) If applicable, describe analytical methods taking account of sampling strategy</td>
<td>5</td>
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<tr>
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<td>(e) Describe any sensitivity analyses</td>
<td>N/A</td>
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<tr>
<td>Results</td>
<td></td>
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<td>---------------------------------------------</td>
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<td></td>
<td></td>
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<tr>
<td>Participants</td>
<td>13*</td>
<td>(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</td>
<td>6</td>
</tr>
<tr>
<td></td>
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<td>(b) Give reasons for non-participation at each stage</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(c) Consider use of a flow diagram</td>
<td>N/A</td>
</tr>
<tr>
<td>Descriptive data</td>
<td>14*</td>
<td>(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) Indicate number of participants with missing data for each variable of interest</td>
<td>Tables</td>
</tr>
<tr>
<td>Outcome data</td>
<td>15*</td>
<td>Report numbers of outcome events or summary measures</td>
<td>6</td>
</tr>
<tr>
<td>Main results</td>
<td>16</td>
<td>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
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<td>(b) Report category boundaries when continuous variables were categorized</td>
<td>N/A</td>
</tr>
<tr>
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<td>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</td>
<td>N/A</td>
</tr>
<tr>
<td>Other analyses</td>
<td>17</td>
<td>Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses</td>
<td>N/A</td>
</tr>
<tr>
<td>Discussion</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Key results</td>
<td>18</td>
<td>Summarise key results with reference to study objectives</td>
<td>7</td>
</tr>
<tr>
<td>Limitations</td>
<td>19</td>
<td>Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias</td>
<td>7</td>
</tr>
<tr>
<td>Interpretation</td>
<td>20</td>
<td>Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence</td>
<td>7-8</td>
</tr>
<tr>
<td>Generalisability</td>
<td>21</td>
<td>Discuss the generalisability (external validity) of the study results</td>
<td>8</td>
</tr>
<tr>
<td>Other information</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Funding</td>
<td>22</td>
<td>Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based</td>
<td>3</td>
</tr>
</tbody>
</table>

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org
A Cross-Sectional Survey of Awareness of Human Papillomavirus-associated Oropharyngeal Cancers among General Practitioners in the UK

Journal: *BMJ Open*

Manuscript ID: bmjopen-2018-023339.R1

Article Type: Research

Date Submitted by the Author: 11-Jun-2018

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- Gilson, Richard; University College London, Department of Infection and Population Health

Primary Subject Heading: General practice / Family practice

Secondary Subject Heading: Infectious diseases, Medical education and training, Ear, nose and throat/otolaryngology

Keywords: General Practice, Primary Health Care, Human papillomavirus, HPV Vaccines, Oropharyngeal Neoplasms, HPV
A Cross-Sectional Survey of Awareness of Human Papillomavirus-associated Oropharyngeal Cancers among General Practitioners in the UK

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Keywords (5 MeSH headings): General Practice, Primary Health Care, HPV, Human papillomavirus, HPV Vaccines, Oropharyngeal Neoplasms

Word count: 2333

Abstract
Objectives: To examine the level of awareness of the link between human papillomavirus (HPV) and oropharyngeal cancer (OPC) and epidemiological trends in HPV-related OPC among General Practitioners (GPs) in the UK.

Design: Cross-sectional survey

Participants: 384 GPs from England, Scotland, Wales and Northern Ireland.

Setting: The survey was administered at GP training courses and via email to lists of training course attendees.

Primary and secondary outcome measures: Proportion of respondents aware of the link between HPV and OPC; respondents' self-rated knowledge of OPC; proportion of participants aware of the epidemiological trends in HPV-associated OPC.

Results: 384 questionnaires were completed with an overall response rate of 72.9%. 74.0% of participants recognised HPV as a risk factor for OPC, which was lower than knowledge about the role of smoking, chewing tobacco and alcohol consumption (all >90% recognition). Overall, 19.4% rated their knowledge of OPC as very good or good, 62.7% as average, and 17.7% as poor or very poor. The majority (71.9%) were aware that rates of HPV-associated OPC have increased over the last two decades. Fewer than half (41.5%) of the participants correctly identified being male as a risk factor of HPV-associated OPC, while 58.8% were aware that patients with HPV-associated OPC tend to be younger than those with non-HPV-associated disease.

Conclusions: The association of HPV infection with OPC is a relatively recent discovery. Although the level of awareness of HPV and OPC among General Practitioners was high, the characteristics of HPV-associated OPC were less well recognised, indicating the need for further education.
Article Summary

Strengths and limitations of this study

- This study is the first to report on awareness of HPV-associated OPC in a sample of UK General Practitioners.
- This study included GPs from a variety of geographical regions with varying levels of experience.
- This study suggests that further education on the epidemiological trends and patient demographics of HPV-associated OPC may be needed to ensure early detection of disease.
- The main limitation is the unknown representativeness of the sample. Although the response rate was good, we used a convenience sample of GPs and trainees attending training updates, who may have higher or lower levels of knowledge than the wider population of GPs in the UK.

Funding Statement: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors

Competing interests: Nil declared

Introduction
Head and neck cancer (HNC) is a significant cause of morbidity and mortality with over 11,000 new cases diagnosed in the UK each year\(^1\). The most common anatomical sites are the oral cavity, pharynx and larynx, with over 90% of tumours diagnosed being squamous cell carcinomas\(^2\). Survival rates of HNC are related to histological type, primary tumour site, disease stage at time of diagnosis and aetiology. Knowledge of the symptoms, risk factors and epidemiology both in the general population, and among primary care professionals is key to primary prevention and earlier diagnosis\(^3\).

Research in the past decade has revealed the increasing importance of human papillomavirus (HPV) infection as a major risk factor for the development of HNC, in particular oropharyngeal cancer (OPC)\(^4\) \(^5\). Whilst rates of tobacco-related disease have decreased over the past two decades, there has been a marked increase in HPV-positive OPC in many high-income countries. It is estimated that between 55-95% of OPC in Europe is HPV-positive in younger patients\(^5\) \(^6\). Twenty years ago, this figure stood at just 20%. In this period, the incidence of HPV-associated OPC in the US has increased by 225\(^\%\)\(^7\) and similar trends are observed in the UK. In Scotland the rates of oropharyngeal cancer have increased more than those of any other cancer\(^8\).

Diagnosing HPV-positive OPC presents particular challenges for general practitioners (GPs) who may lack detailed knowledge of the disease. HPV-positive OPC represents a distinct molecular, epidemiologic and clinical entity\(^9\) \(^10\). Compared with non-HPV associated HNC, HPV-positive OPC occurs at a younger age and more often in males compared to non-HPV-associated OPC\(^11\). In addition, patients presenting with HPV-positive OPC typically lack traditional risk factors such as smoking and alcohol use. Risk factors for HPV-positive OPC include age at first intercourse, number of sexual partners and number of oral sex partners\(^4\). Early diagnosis is important; HPV-positive OPC is much more responsive to chemotherapy and radiotherapy (82% vs 55%) and has better overall survival rates at 2 years than non-HPV-associated OPC (95% vs 62%)\(^12\). The increasing rates of head and neck cancers and the fact that their outcome depends on early diagnosis, has been recognised in the GP Curriculum of the Royal College of General Practitioners\(^13\).
Awareness of the changing epidemiological and risk factor profile of OPC among primary care professionals is likely to lead to earlier diagnosis, resulting in improved outcomes, but the HPV-related learning resources recommended by the RCGP Curriculum to GPs and GP Trainees (such as RCGP Learning, e-LfH and BMJ Learning) focus on cervical cancer and cervical screening. Our review of the literature did not identify any learning modules available to UK GPs which focus on HPV-associated OPC. In addition, there has been no research to establish current levels of knowledge about HPV-associated OPC among GPs in the UK, which is an essential first step in identifying additional training needs in this area.

This study represents a first step towards understanding awareness of HPV-associated OPC among GPs in the UK, and to identify areas where further educational resources might lead to more targeted knowledge and improved patient outcomes.

**Methods**

We carried out a cross-sectional questionnaire survey with GPs in the UK (Supplementary File 1; STROBE checklist).

**Measures**

We developed a short questionnaire (Supplementary File 2) assessing demographic characteristics of the participants, self-rated knowledge of OPC, awareness of OPC risk factors, awareness of time trends in smoking- and HPV-related OPC, previous awareness of the link between HPV and OPC and perceptions about the characteristics of patients with HPV-associated as opposed to non-HPV OPC. Demographic characteristics included gender, number of years since graduation and current position. Self-rated level of knowledge and assessment of awareness of OPC was assessed using a Likert scale. Knowledge of the symptoms and risk factors for OPC were assessed using items adapted from the Cancer Awareness Measure. Thirteen risk factors (10 true and 3 false) were selected from the epidemiological literature. An open question was used to assess knowledge of the symptoms of OPC, using wording from the Cancer Awareness
Measure. The items developed for the questionnaire were discussed in a multidisciplinary team including general practitioners and a behavioural scientist.

Participants and procedure
As the aims of the study were descriptive, we did not carry out a formal sample size calculation but aimed to recruit around 400 participants from a range of geographical locations, with varying amounts of clinical experience, in line with similar studies of this type. Eligibility criteria were defined as being on the General Medical Council's (GMC) GP register and a local performers list or being currently enrolled in a recognised UK GP training post. The questionnaire was administered to a convenience sample of GPs attending courses and training meetings in paper format and via email lists in online format. Survey Monkey online platform was used to administer the survey via email lists. Paper questionnaires were added as separate collectors to the Survey Monkey database to consolidate responses. The sample included three training events for GPs in London and the North West of England, and five web links sent to working groups, local faculties and event administrators. Each collector was sent and tracked separately (Supplementary Table 1; Supplementary File 3). Data collection continued over a period of nine months between May 2015 and February 2016.

Analysis
Statistical analysis was conducted using standard measures of central tendency and spread. One-way ANOVA test was used for assessing association between years after graduation and awareness of HPV and OPC link. IBM SPSS® v20.0 software was used for statistical analysis. Descriptive data on the main characteristics of the sample has been analysed using Microsoft Excel® version 2013.

Ethical approval
The study was exempt from the requirement for Research Ethics Committee (REC) review on the basis that data collection was anonymised and no vulnerable participants were involved (advice from Harrow NHS REC and UCL REC).

Patient and Public Involvement
No patient and public involvement was sought during the preparation of the questionnaire, as our target group was exclusively medical professionals. However, general practitioners and a behavioural scientist were involved in the development of the survey who are included in the list of authors.

Results

Sample characteristics
A total of 96 surveys were distributed in printed form and 411 requests were sent by email distribution via online lists. Overall, 385 questionnaires were completed giving an overall response rate of 72.9%. 8 of the 385 responses were disqualified. 340 participants completed all the questions and 35 has skipped 1 or more questions. Each question was analysed individually. The response rate for paper questionnaires was higher (85.4%) compared to online distribution (70.1%) (Supplementary Table 1; Supplementary File 3). The demographic characteristics of the sample are shown in Table 1. Overall, 59.1% participants were female. The largest proportion of participants were from England (44.2%), but all parts of the UK were included (Scotland 27.6%, Ireland 19.6%, Wales 8.6%). About half (50.3%) of participants had been in practice for over 10 years (18.4% 10-20y and 31.9% >20 years). Just over a third (35.2%) of participants were in training, 33.5% were salaried GPs and 24.5% were GP Partners. 6.1% reported being in a locum post. When asked about their self-rated knowledge of OPC, 19.4% rated their knowledge of OPC as very good or good, and 62.9% rated their knowledge as average. 17.7% reported poor or very poor knowledge of OPCs.

Awareness of risk factors for OPC
73.9% of the participants reported being aware of the link between HPV and OPC whilst 16.9% reported not having heard of the association and 9.1% reported being unsure. Participants were asked about 13 exposures and whether they were risk factors of OPC or not (Figure 1). Just over three-quarters (77.6% 271 of 349) of the participants who responded to the risk factor question, correctly identified HPV as a risk factor for OPC. Awareness of other well-established risk factors was much higher: smoking (99.4%), chewing tobacco (96.6%), current alcohol consumption (94.3%) and past alcohol consumption (86.5%). Chewing catchu and areca nuts,
marijuana use and aflatoxin exposure were less frequently recognised (32.9%, 50.4%, 26.4%, respectively).

**Knowledge of the epidemiology of HPV-associated OCP**

Most participants (71.9%) correctly stated that the rates of HPV-associated OPC have increased in high income countries over the last two decades (Table 2). However, fewer than half (41.5%) correctly identified HPV-associated OPC as being more common in males. 58.8% correctly reported the association with younger age. There were no statistically significant differences between years since graduation or post type and awareness of HPV and OPC.

**Discussion:**

This study is the first to assess the awareness of HPV-associated OPC in a sample of UK GPs. Our results show that more than three-quarters of UK participants who responded to the risk factor question correctly identified HPV as a risk factor for OPC. However, there is limited awareness of the differences in the demographic profiles of patients presenting with HPV-associated and non-HPV-associated OPC as well as a lack of awareness of other risk factors of OPC.

Cancer of the oropharynx is now thought to be associated with HPV in 70-95% of younger patients\(^5\) and disease outcome is related to the stage of disease at diagnosis\(^3\). It is therefore important that GPs, who are likely to be the first point of contact for patients, are able to recognise the characteristics of patients at risk of HPV-associated OPC in order to refer them on to secondary and tertiary care as early as possible. These patients may be younger and may not have any history of smoking and drinking, in contrast to the risk factor profiles of traditional head and neck cancer patients.

Our study demonstrates that further education on the epidemiological trends and patient demographics of HPV-associated OPC is needed to ensure early detection of disease. We provide a learning module which can be accessed online (Supplementary File 4; HPV-associated Oropharyngeal Cancer Module). GP awareness of the role of HPV in OPC may also lead to more support for the
continued high uptake of national HPV vaccination programmes, thereby maximising opportunity to ensure both individual and herd protection.

**Strengths and limitations**

Our study is the first to assess the awareness of HPV-associated OPC in a sample of UK GPs and benefited from the inclusion of participants from all four UK nations. It is of immediate relevance, taking into account that it assesses awareness of a disease which shows a rapidly rising incidence, and a changing epidemiology.

41,985 GPs (82.16% of the total number of registered GPs in the UK) were registered in England in September 2016, 4,953 GPs, excluding locums, in Scotland in January 2017 (9.7%), 2,887 GPs in Wales, including 634 locums, in March 2016 (5.6%) and 1,274 GPs, excluding locums, in Northern Ireland in October 2015 (2.49%), respectively. Comparing these data with our sample, we need to acknowledge that participants from England (n=165; 44.2%) are under-represented and that participants from Scotland (n=103; 27.6%), Wales (n=32; 8.6%) and Northern Ireland (n=73; 19.6%) are over-represented. We instructed all participants to answer the questions consecutively when distributing the paper questionnaires, but they may have looked at subsequent questions which could have influenced their responses leading to an overestimation of knowledge. The online questionnaire only allowed questions to be answered in order. Although the response rate was high for a survey of GPs, we do not have data on non-responders so we are unable to test for response bias. The main limitation of the study is the use of a convenience sample, recruited at GP educational events, and via email lists of event attendees and regional faculties. By recruiting participants attending training courses and educational events, we may have included GPs who were more up-to-date, leading to an overestimation of knowledge levels. Training events included GP related topics in general and were not related to head and neck pathology or HPV. In addition, we developed some of the questionnaire items specifically for the study and although they were reviewed by the study team and had good face validity, further psychometric validation would be appropriate prior to further use.

**Comparison with existing literature**

A recent systematic review by Dodd et al. evaluated the psychosocial impact of HPV-related HNC and investigated the awareness of the link between HPV and HNC
among different populations. Forty-one studies were identified which measured knowledge of the link between HPV and HNC, demonstrating the lowest level of knowledge in the general population and highest in medical and dental professionals\textsuperscript{21}. However, Signorelli et al. showed that only 38\% of Italian GPs (n=938) recognised the role of HPV in oral disease and oral cancer and concluded that there is a lack of knowledge on HPV infection and vaccination in Italian GPs\textsuperscript{22}. Odone et al. explored reasons for non-vaccination against human papillomavirus in Italy\textsuperscript{23}, providing a useful basis to plan, implement and evaluate targeted educational programmes and training. The link between HPV and OPC was recognised by 43.3\% of primary care physicians in Jordan\textsuperscript{24} and by 54\% of a sample of German physicians\textsuperscript{25}.

A study of 2126 adults in the United States demonstrated that knowledge of HNC among the general public is low. Whilst 54\% of participants identified smoking as a risk factor for HNC, 4.8\% identified alcohol use, and just 0.8\% recognised HPV infection as a risk factor\textsuperscript{14}. Family physicians could play a key role in educating the public and encouraging HPV vaccine uptake.

We report findings of the first study investigating the awareness of HPV-associated OPC risk factors in a sample of UK general practitioners. Awareness in the UK is high but there are gaps in knowledge that should be addressed.

\textit{Implications for practice}

The failure of 41.2\% of participants to recognise younger age as a characteristic of HPV-related OPC patients should be addressed. Good awareness of the fact that there has been a significant rise in younger patients presenting with OPC, often lacking a history of smoking and high alcohol intake, will help ensure that HPV-associated OPC is recognised early. Younger patients with HPV-associated OPC often present with asymmetrical tonsils and without knowledge of this disease and its presentation in the absence of classical risk factors makes it likely that early diagnosis is missed.

Our results clearly demonstrate the need for awareness campaigns to make UK GPs more aware of this rapidly evolving disease. We have created a learning module
which can be freely accessed online (Supplementary File 4; HPV-associated Oropharyngeal Cancer Module). This includes reference to other risk factors that we showed to be frequently underrecognised, such as chewing betel nuts (also referred to as catchu or areca nuts) which are traditional among some communities in Indian, Pakistan and Bangladesh.

In conclusion, this study suggests a clear need for further education for GPs on a disease which shows a rising incidence, and a changing epidemiology.

Author’s contribution

ML, CV, CK, OJ, RG wrote the first draft of the manuscript with contributions from JH, TF, LM, JW and WY. CV, CK, JH collected the data and analysed these under the guidance of WY, RG and ML. OJ and ML created the online module with advice from LM and TF.

Data Sharing Statement

All data from this study are included in the present work.

Additional information

Ethical approval: The study was exempted from the requirement for Research Ethics Committee (REC) review on the basis that data collection was anonymised and no vulnerable participants were involved (advice from Harrow NHS REC and UCL REC).

Acknowledgements:

The authors would like to thank the general practitioners who took part in the study for their time and effort in completing the surveys and to the educational bodies who gave us permission to distribute questionnaires at GP training events.

References:


19. BMA. General practice in the UK – background briefing. 2017


Table 1: Demographic characteristics of the sample and self-rated knowledge of OPC (n=376)

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>154</td>
<td>40.9</td>
</tr>
<tr>
<td>Female</td>
<td>222</td>
<td>59.1</td>
</tr>
<tr>
<td><strong>Stage of training/position</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F2</td>
<td>6</td>
<td>1.6</td>
</tr>
<tr>
<td>GPST1</td>
<td>44</td>
<td>11.7</td>
</tr>
<tr>
<td>GPST2</td>
<td>36</td>
<td>9.6</td>
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<tr>
<td>GPST3</td>
<td>49</td>
<td>13.1</td>
</tr>
<tr>
<td>GP (salaried or partnered)</td>
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<tr>
<td>Locum</td>
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<tr>
<td><strong>Years since graduation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 years</td>
<td>17</td>
<td>4.4</td>
</tr>
<tr>
<td>2-5 years</td>
<td>81</td>
<td>21.9</td>
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<tr>
<td>5-10 years</td>
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<tr>
<td>10-20 years</td>
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<td>17.9</td>
</tr>
<tr>
<td>20+ years</td>
<td>124</td>
<td>32.3</td>
</tr>
<tr>
<td><strong>Location of current practice (n=373)</strong></td>
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<td></td>
</tr>
<tr>
<td>England</td>
<td>165</td>
<td>44.2</td>
</tr>
<tr>
<td>Scotland</td>
<td>103</td>
<td>27.6</td>
</tr>
<tr>
<td>Wales</td>
<td>32</td>
<td>8.6</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>73</td>
<td>19.6</td>
</tr>
<tr>
<td><strong>Self-rated knowledge of OPC (n= 350)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very poor</td>
<td>5</td>
<td>1.4</td>
</tr>
<tr>
<td>Poor</td>
<td>57</td>
<td>16.3</td>
</tr>
<tr>
<td>Average</td>
<td>220</td>
<td>62.9</td>
</tr>
<tr>
<td>Good</td>
<td>65</td>
<td>18.6</td>
</tr>
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</table>
Table 2: Knowledge about HPV-associated OPC (n=342)

<table>
<thead>
<tr>
<th>Aware of OCP-HPV link before today?</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>253</td>
<td>73.9</td>
</tr>
<tr>
<td>No</td>
<td>58</td>
<td>16.9</td>
</tr>
<tr>
<td>Not sure</td>
<td>31</td>
<td>9.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Over the last 2 decades, have rates of HPV-OPC:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased</td>
<td>246</td>
<td>71.9</td>
</tr>
<tr>
<td>Decreased</td>
<td>9</td>
<td>2.6</td>
</tr>
<tr>
<td>Stayed the same</td>
<td>29</td>
<td>5.6</td>
</tr>
<tr>
<td>Don’t know</td>
<td>68</td>
<td>19.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compared with non-HPV-OPC, are HPV-OPC patients…</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>142</td>
<td>41.5</td>
</tr>
<tr>
<td>Female</td>
<td>74</td>
<td>21.6</td>
</tr>
<tr>
<td>Same gender</td>
<td>43</td>
<td>5.2</td>
</tr>
<tr>
<td>Don’t know</td>
<td>83</td>
<td>21.9</td>
</tr>
<tr>
<td>Younger</td>
<td>201</td>
<td>58.8</td>
</tr>
<tr>
<td>Older</td>
<td>48</td>
<td>14.1</td>
</tr>
<tr>
<td>Same age</td>
<td>18</td>
<td>5.3</td>
</tr>
<tr>
<td>Don’t know</td>
<td>75</td>
<td>21.9</td>
</tr>
</tbody>
</table>
Figure Legends

Figure 1: Participant responses to questions on 10 proven risk factors for OPC, and 3 factors which are not known risk factors.

Supplementary Files
- Supplementary File 1; STROBE checklist
- Supplementary File 2; Copy of the questionnaire handed to UK GPs
- Supplementary File 3; Supplementary Table 1
- Supplementary File 4; HPV-associated Oropharyngeal Cancer Module
Figure 1: Participant responses to questions on 10 proven risk factors for OPC, and 3 factors which are not known risk factors.

162x81mm (300 x 300 DPI)
<table>
<thead>
<tr>
<th>Section/Topic</th>
<th>Item #</th>
<th>Recommendation</th>
<th>Reported on page #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title and abstract</td>
<td>1</td>
<td>(a) Indicate the study’s design with a commonly used term in the title or the abstract</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</td>
<td>2-3</td>
</tr>
<tr>
<td>Introduction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Background/rationale</td>
<td>2</td>
<td>Explain the scientific background and rationale for the investigation being reported</td>
<td>4</td>
</tr>
<tr>
<td>Objectives</td>
<td>3</td>
<td>State specific objectives, including any prespecified hypotheses</td>
<td>5</td>
</tr>
<tr>
<td>Methods</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study design</td>
<td>4</td>
<td>Present key elements of study design early in the paper</td>
<td>5</td>
</tr>
<tr>
<td>Setting</td>
<td>5</td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</td>
<td>5-6</td>
</tr>
<tr>
<td>Participants</td>
<td>6</td>
<td>(a) Give the eligibility criteria, and the sources and methods of selection of participants</td>
<td>6</td>
</tr>
<tr>
<td>Variables</td>
<td>7</td>
<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</td>
<td>N/A</td>
</tr>
<tr>
<td>Data sources/</td>
<td>8*</td>
<td>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group</td>
<td>N/A</td>
</tr>
<tr>
<td>measurement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bias</td>
<td>9</td>
<td>Describe any efforts to address potential sources of bias</td>
<td>7 (strengths and limitations)</td>
</tr>
<tr>
<td>Study size</td>
<td>10</td>
<td>Explain how the study size was arrived at</td>
<td>6</td>
</tr>
<tr>
<td>Quantitative variables</td>
<td>11</td>
<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</td>
<td>N/A</td>
</tr>
<tr>
<td>Statistical methods</td>
<td>12</td>
<td>(a) Describe all statistical methods, including those used to control for confounding</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) Describe any methods used to examine subgroups and interactions</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(c) Explain how missing data were addressed</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(d) If applicable, describe analytical methods taking account of sampling strategy</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(e) Describe any sensitivity analyses</td>
<td>N/A</td>
</tr>
</tbody>
</table>
### Results

<table>
<thead>
<tr>
<th>Items</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants</strong></td>
<td>13*&lt;br&gt;(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed&lt;br&gt;(b) Give reasons for non-participation at each stage&lt;br&gt;(c) Consider use of a flow diagram</td>
</tr>
<tr>
<td><strong>Descriptive data</strong></td>
<td>14*&lt;br&gt;(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders&lt;br&gt;(b) Indicate number of participants with missing data for each variable of interest</td>
</tr>
<tr>
<td><strong>Outcome data</strong></td>
<td>15*&lt;br&gt;(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included&lt;br&gt;(b) Report category boundaries when continuous variables were categorized&lt;br&gt;(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</td>
</tr>
<tr>
<td><strong>Main results</strong></td>
<td>16&lt;br&gt;(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included</td>
</tr>
<tr>
<td><strong>Other analyses</strong></td>
<td>17&lt;br&gt;(a) Report numbers of outcome events or summary measures&lt;br&gt;(b) Report category boundaries when continuous variables were categorized&lt;br&gt;(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</td>
</tr>
<tr>
<td><strong>Discussion</strong></td>
<td>18&lt;br&gt;(a) Summarise key results with reference to study objectives</td>
</tr>
<tr>
<td><strong>Limitations</strong></td>
<td>19&lt;br&gt;(a) Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias</td>
</tr>
<tr>
<td><strong>Interpretation</strong></td>
<td>20&lt;br&gt;(a) Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence</td>
</tr>
<tr>
<td><strong>Generalisability</strong></td>
<td>21&lt;br&gt;(a) Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence</td>
</tr>
<tr>
<td><strong>Other information</strong></td>
<td>22&lt;br&gt;(a) Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based</td>
</tr>
</tbody>
</table>

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org
Oropharyngeal Cancer (General Practitioners)

Many thanks for your interest in completing this short questionnaire on oropharyngeal cancers. This questionnaire is part of a study being carried out by UCL Cancer Institute. The study aims to assess current levels of knowledge of oropharyngeal cancers amongst General Practitioners and Clinical Medical Students to gauge if there is a need for greater education and training in this area.

All responses are completely anonymous. If you wish to withdraw from participating you are free to do so at any time whilst completing the questionnaire. As participation is anonymous it will not be possible for us to withdraw your data once you have returned your questionnaire. If you have any concerns or questions, please contact Dr. Claire Vassie (claire.vassie@doctors.org.uk)

1. Stage of GP training/Position
   - ☐ F2
   - ☐ GPST1
   - ☐ GPST2
   - ☐ GPST3
   - ☐ GP (salaried or partner)
   - ☐ Other (please state)

2. Please select your gender:
   - ☐ Female
   - ☐ Male

3. Years since graduation
   - ☐ <2yrs
   - ☐ 2-5yrs
   - ☐ 5-10yrs
   - ☐ 10-20yrs
   - ☐ 20+yrs

4. How would you rate your knowledge of oropharyngeal cancers compared to other General Practitioners?
   - ☐ Very Poor
   - ☐ Poor
   - ☐ Average
   - ☐ Good
   - ☐ Very good

5. There are many warning signs and symptoms of oropharyngeal cancers, please list as many as you can. If you cannot think of any, please write “don’t know” below.

6. Please list risk factors for oropharyngeal cancers. If you cannot think of any, please write “don’t know” below.
7. Which of the following may be risk factors for oropharyngeal cancer?

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Yes</th>
<th>No</th>
<th>Don't know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Alcohol consumption</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past Alcohol consumption</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aflatoxin exposure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietary nitrosamines</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Chewing of tobacco</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chewing of Betel leaf</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chewing of Catchu and areca nuts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marijuana use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herpes simplex virus infection</td>
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<td></td>
<td></td>
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<tr>
<td>Human papillomavirus infection</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Family history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruit and vegetable consumption</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8. Do you think the rates of smoking-related oropharyngeal cancers in developed countries have changed over the past two decades?

- ☐ Increased
- ☐ Decreased
- ☐ Stayed the same
- ☐ Don't know
Recently, several discoveries have been made about the association between human papillomavirus (HPV) and oropharyngeal cancers.

9. Before today, had you heard about the link between oropharyngeal cancer and HPV?
   - ☐ Yes
   - ☐ No
   - ☐ Not sure

10. Do you think the rates of human papillomavirus (HPV)-associated oropharyngeal cancers in developed countries have changed over the past two decades
   - ☐ Increased
   - ☐ Decreased
   - ☐ Stayed the same
   - ☐ Don't know

11. In comparison to patients with non-HPV associated oropharyngeal cancer, are patients with HPV associated oropharyngeal cancers more likely to be:
   a) ☐ Male
      - ☐ Female
      - ☐ Same gender composition in both conditions
      - ☐ Don't know
   b) ☐ Younger
      - ☐ Older
      - ☐ Same age composition in both conditions
      - ☐ Don't know

Thank you for taking the time to complete this questionnaire.
**Supplementary data**

### Paper copy questionnaires

<table>
<thead>
<tr>
<th>Event</th>
<th>number of GP attendees</th>
<th>Number of returned forms</th>
<th>Response rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>North London GP training</td>
<td>23</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Hillingdon West London GP update</td>
<td>55</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>North West England GP training</td>
<td>18</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>96</strong></td>
<td><strong>82</strong></td>
<td><strong>85.4%</strong></td>
</tr>
</tbody>
</table>

### Online questionnaires

<table>
<thead>
<tr>
<th>Web link</th>
<th>Sent Invites</th>
<th>Started</th>
<th>Complete</th>
<th>Not eligible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Web link 1</td>
<td>120</td>
<td>93</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>Web link 2</td>
<td>94</td>
<td>72</td>
<td>68</td>
<td>4</td>
</tr>
<tr>
<td>Web link 3</td>
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<td>11</td>
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<td>0</td>
</tr>
<tr>
<td>Web link 4</td>
<td>92</td>
<td>78</td>
<td>65</td>
<td>3</td>
</tr>
<tr>
<td>Web link 5</td>
<td>80</td>
<td>34</td>
<td>28</td>
<td>1</td>
</tr>
</tbody>
</table>

| Completion rate | 85.06% |
| Response rate   | 70.10% |

**Total response rate:** 72.9%

**Supplementary Table 1:** Response rate for paper copy and online questionnaires
HPV & Oropharyngeal cancer

Know the risks, spot the signs
Aims

• To understand the basic pathology and demographics of HPV infection and oropharyngeal cancer

• To be aware of the risk factors for each and to understand the relationship between HPV and oropharyngeal cancer

• To be able to recognise signs of HPV infection and warning signs of oropharyngeal cancer
What is HPV?

- Human papilloma virus (HPV) is a group of viruses that live and multiply in human skin and mucosal cells
- HPV is transmitted during skin-to-skin or sexual contact - particularly oral, anal and vaginal sex
- There are many subtypes, causing: skin warts, verrucas, genital warts and laryngeal papillomas (warts in voice box)
- Some HPV types (particularly HPV-16 and HPV-18) are associated with cervical, anal, genital and oropharyngeal cancers
- A vaccine is offered to schoolgirls aged 12-13 – no vaccine is currently available for boys (this arrangement is under review by the Joint Committee on Vaccination and Immunisation)
Risk Factors for HPV-associated oropharyngeal cancer

Demographic:
• Male
• Caucasian
• Higher socioeconomic class

Behavioural:
• Many sex and oral sex partners
• History of sex without barrier protection
• Early age first intercourse

Perhaps the most famous case of HPV-associated oropharyngeal cancer is Michael Douglas, who has spoken publically about his diagnosis and treatment many times – although the actor matches the archetypal patient profile and had fairly typical complaint, he stated in an address to the American Head and Neck Society that he was misdiagnosed three times.
Disease timeline

Healthy person → Sexual contact → HPV acquisition (may experience early lesions depending on subtype, or no symptoms at all) → Many years... → May develop oropharyngeal cancer
What is oropharyngeal cancer?

- The oropharynx is the **space posterior to the oral cavity, including the tonsils and base of the tongue** – food passes through the oropharynx when moving from the mouth the food pipe during swallowing
- Oropharyngeal cancer arises from the mucosal surface of this space
- Oropharyngeal cancers are caused by smoking and drinking or by HPV and, hence, can be divided into HPV-positive and HPV-negative cancers. These carry different prognoses.
Risk factors for oropharyngeal cancers

Reversible risk factors:

- **HPV exposure**
- **Heavy alcohol consumption**
- **Smoking** (20-a-day for more than 10 years or equivalent amount)
- Some chewing plants and drinks specific to certain countries and cultures
  - betel leaf (a chewing tobacco used in Asia)
  - maté (a stimulant drink from South America)

- **Unconfirmed**: reversible risk factors include: diet, immunosuppression, poor oral hygiene, mouthwash, tooth whiteners, high body weight
Risk factors for oropharyngeal cancers

Non-reversible risk factors:

• Previous cancer:
  - oropharyngeal, oesophageal
  - anal, genital, cervical cancer
  - family history of oropharyngeal cancer

• Genetic conditions
  - Fanconi anaemia – patients with short stature with bone changes
  - Dyskeratosis congenita - anaemia, skin rashes, and abnormally shaped fingernails and toenails (particularly elevated risk when young)
Warning signs of oropharyngeal cancer

• Primary swellings and masses in the tongue, tonsils, soft palate, including symptoms like:
  - Ulcerated tonsils that don’t heal
  - White or red patches in the throat
  - Pain or difficulty swallowing and moving the jaw
  - Numbness, pain or discomfort in the throat or tongue
  - Bad breath
  - Earache (especially unilateral)
  - Can be asymptomatic

• (Multiple) secondary swellings or masses in neck which are painless, firm and mobile (neck metastases)

• Unexplained weight loss
Important HPV facts

- HPV is the most common STI in the UK, affecting 75% of sexually active females, often silently
- HPV is also the only STI which affects more men than women
- The risk of many HPV-associated cancers is higher is men who have sex with men
  - 80% of anal cancers and 40% of penile cancers are HPV-associated
Important HPV facts

• In developed countries, rates of oropharyngeal cancers have risen sharply - in some countries, more than 90% of oropharyngeal cancers are HPV-positive amongst younger age groups
  - This is thought to be a result of changing sexual behaviours

• In comparison to patients with HPV-negative oropharyngeal cancer, patients with HPV-positive oropharyngeal cancers are more likely to be:
  - Younger
  - Male

• There are treatment strategies available for HPV-positive oropharyngeal cancer that are not used in HPV-negative oropharyngeal cancer
References

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8. Weaver, “Epidemiology and natural history of genital human papillomavirus infection.”
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