

HEAD AND NECK

# Human papillomavirus-associated cancers: a survey on otorhinolaryngologists' knowledge and attitudes on prevention

## *Carcinomi associati al papillomavirus umano: conoscenze, ruolo e attitudini dei medici otorinolaringoiatri in tema di prevenzione*

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### SUMMARY

Human papillomavirus (HPV) infection is a recognised causal factor associated with oropharyngeal cancers. The global burden of HPV-related oropharyngeal cancers is on the increase and is predicted to surpass the burden of cervical cancer in the near future. As evidence is accumulating on the potential effectiveness of an HPV vaccine in controlling the oropharyngeal cancer epidemic; otorhinolaryngologists assume a key role – not only in the diagnosis and treatment of HPV-related cancers – but also in educating and advocating on HPV prevention. We conducted a survey to assess Italian otorhinolaryngologists' knowledge and attitudes regarding HPV infection, HPV-related oropharyngeal diseases and cancers and available prevention measures, including vaccines. This is the first study conducted in Italy and Europe on this topic. A total of 262 Italian otorhinolaryngologists were recruited during the National Conference of the Italian Association of Otorhinolaryngologists. Our results show that Italian otorhinolaryngologists are knowledgeable regarding HPV infection and have a positive attitude towards HPV vaccine. Our findings provide a useful basis to plan, implement and evaluate targeted educational programmes and training. As we show herein, educational programmes and training specifically focusing on HPV are effective in increasing physicians' knowledge and positive attitudes towards prevention; this ultimately contributes to enhance vaccine uptake among patients and the general population. With the overall aim of controlling the burden of HPV-related cancers, resources and efforts should be devoted to promote continuing education among otorhinolaryngologists and the general medical community and to increase awareness on the role of vaccines in prevention of HPV-related cancers. In this context, there is tremendous opportunity for healthcare providers across fields to cooperate and for public health and otorhinolaryngologist communities to join forces and engage in fruitful collaboration.

KEY WORDS: Human papillomavirus • Head and Neck Neoplasms • Papillomavirus Vaccines • Knowledge • Primary prevention

### RIASSUNTO

*L'infezione da papillomavirus umano (HPV), in particolare HPV 16, è un riconosciuto fattore causale delle neoplasie orofaringee. L'incidenza delle neoplasie orofaringee è in aumento in diversi paesi europei, inclusa l'Italia, e negli Stati Uniti dove accurati modelli matematici hanno stimato che supererà quella del cancro alla cervice nella prossima decade. Recenti evidenze scientifiche supportano la potenziale efficacia del vaccino anti-HPV nel controllare quella che è stata definita "l'epidemia di neoplasie HPV-correlate". In questo contesto, i medici otorinolaringoiatri assumono un ruolo cruciale, non solo nella diagnosi e trattamento di questa patologia, ma anche – come è stato sottolineato dall'American Head and Neck Society – nella prevenzione. Abbiamo condotto un'indagine sulle conoscenze e le attitudini dei medici otorinolaringoiatri italiani in tema di infezione HPV, patologie correlate e prevenzione vaccinale. Si tratta della prima indagine conoscitiva in Italia e in Europa sull'argomento. 262 medici otorinolaringoiatri italiani sono stati reclutati durante il 101° Congresso Nazionale della Società Italiana di Otorinolaringoiatria e Chirurgia Cervico-Facciale, tenutosi in maggio 2014. È stato utilizzato un questionario semi-strutturato sviluppato sulla base delle evidenze disponibili in letteratura e del parere di esperti. Le conoscenze e le attitudini sono state descritte e valutate con tecniche di analisi univariata. È stato inoltre costruito uno score composito di conoscenza. I dati dimostrano come i medici otorinolaringoiatri italiani abbiano, in media, un grado di conoscenza buono dell'infezione HPV e un'attitudine positiva nei confronti della prevenzione, in particolare della vaccinazione. I nostri risultati possono essere una utile base per pianificare, implementare e valutare programmi di educazione continua specifici sul tema della prevenzione dell'infezione da HPV. Come dimostriamo nel nostro studio, programmi di educazione continua specifici sono efficaci nell'aumentare il grado di conoscenza dei medici e l'attitudine positiva nei confronti dei programmi di prevenzione; il che contribuisce a promuovere l'adesione alla vaccinazione nei pazienti e nella popolazione generale. Con l'obiettivo generale di controllare l'epidemia di neoplasie HPV-correlate, maggiori risorse ed energie devono essere dedicate alla formazione e alla diffusione della cultura della prevenzione tra i medici otorinolaringoiatri e la comunità medica in generale. In questo contesto, identifichiamo grande potenziale nella collaborazione tra le comunità e le società scientifiche dell'otorinolaringoiatria e la sanità pubblica.*

PAROLE CHIAVE: Papillomavirus umano • Neoplasie testa-collo • Vaccini anti-papillomavirus • Grado di conoscenza • Prevenzione primaria

## Introduction

Human papillomavirus (HPV) infection is a recognised causal factor associated with head and neck cancers<sup>1</sup>. In particular, the International Agency for Research on Cancer (IARC) of the World Health Organization identified HPV type 16 as a carcinogenic agent responsible for oropharyngeal squamous cell carcinoma (OPSCC) in 2012<sup>2</sup>. Two recent reviews published in *Acta Otorhinolaryngologica Italica* pooled the available evidence on the molecular mechanisms of HPV-induced carcinogenesis, on the diagnostic and clinical features of HPV-induced oropharyngeal carcinomas and their prognosis and management<sup>3,4</sup>. As emerged from the reviews, HPV-related OPSCCs are an independent clinico-pathological entity whose risk factors differ from HPV-unrelated cancers<sup>3,4</sup>. Data from the United States<sup>5</sup>, Australia<sup>6</sup> and selected European countries<sup>7-11</sup> show that HPV-related OPSCC account for up to 90% of all cancers diagnosed. Importantly, the share of total OPSCC related to HPV infection is increasing over time in high-income countries: in the United States, it increased by four fold from 16% to 70% in the last decades<sup>12</sup>; this occurred in parallel with decreasing HPV-unrelated cancer trends<sup>10</sup>. Such tendencies have prompted some authors to suggest that there is an *epidemic* of HPV-induced carcinomas<sup>10,13</sup>. Solid evidence from randomised trials demonstrated that the two available HPV vaccines prevent cervical cancers<sup>14,15</sup> and other non-cervical lesions and cancers<sup>16-18</sup>. The use of HPV vaccine to reduce the increasing burden of oropharyngeal cancers had long been hypothesised<sup>19,20</sup>. Preliminary findings of the first randomised controlled trial to assess HPV vaccine efficacy (VE) in the oral cavity have been recently published<sup>21</sup>. Bivalent HPV vaccine was reported to have a VE of 93% (95% CI = 63% to 100%) in reducing oral HPV infection at four year follow-up; this has potentially vast implications for prevention of HPV associated oropharyngeal cancer<sup>21</sup>. This new evidence combined with the large increase in OPSCC incidence worldwide underlines the crucial role that otorhinolaryngologists have not only in diagnosis and clinical management of HPV-associated OPSCC, but also in prevention of HPV infection. In line with that, the American Head and Neck Society (AHNS) has recently stated that head and neck surgeons share the responsibility of advocating and educating patients, the public and the general medical community on HPV vaccination<sup>22</sup>. Furthermore, there is evidence that healthcare providers' advice and recommendations are the most widely used source of information influencing vaccination uptake and willingness to get vaccinated<sup>23,24</sup>. In this context, it is important to assess otorhinolaryngologists' knowledge and attitudes with regard to HPV as this would inform the design and implementation of targeted medical education programmes with a positive impact on OPSCC prevention<sup>25</sup>.

Limited data is available on this topic. To our knowledge, only one study is available in the literature on a sample of American Head and Neck surgeons' practices, attitudes, and knowledge regarding human papillomavirus-related cancers and vaccines<sup>22</sup>. No similar studies have been carried out in Europe or Italy.

The primary aim of this study was to assess Italian otorhinolaryngologists' knowledge regarding HPV infection, HPV-related oropharyngeal diseases and cancers and available prevention measures, including vaccines. The secondary objective was to assess their attitudes, opinions and perceived benefits and barriers against oral HPV infection prevention.

## Materials and methods

We conducted a survey to assess Italian otorhinolaryngologists' knowledge and attitudes regarding HPV infection, HPV-related oropharyngeal diseases and cancers and available prevention measures, including vaccines.

### *The questionnaire*

A semi-structured questionnaire was designed on the basis of the relevant evidence available in the literature, clinical practice guidelines and input from experts in the field. The questionnaire was structured in three parts: the first explored socio-demographic characteristics as well as information about education, training and professional career; the second part investigated their knowledge on HPV infection, HPV-related oral diseases and cancers and available prevention measures, including vaccines; the last section explored opinions and attitudes towards HPV vaccination.

The questionnaire was preliminarily validated through a pilot survey administered to 30 subjects to verify its effectiveness and comprehensibility. On the basis of the feedback obtained through the pilot study, critical points were discussed and revised into the final version of the questionnaire that included 28 items (Appendix 1.A and 1.B report, respectively, the Italian version and the English version of the questionnaire - published online: [www.actaitalica.it](http://www.actaitalica.it)).

The questionnaire was distributed in person to all otorhinolaryngologists during the National Conference of the Italian Association of Otorhinolaryngologists held in Catania, Sicily in May 2014.

### *Analysis*

Data extraction was independently carried out by two co-authors and an electronic database was compiled. Descriptive analyses were performed to describe the study population. A composite HPV knowledge score was built. Seventeen HPV knowledge items were included in the score. In particular, they assessed otorhinolaryngologists' knowledge on: HPV infection transmission route,

HPV-associated diseases, carcinogenic HPV types, available HPV vaccines, recommended vaccination schedules and risk of adverse events, prevention objectives of HPV immunisation programmes and target population, national immunisation coverage targets and role of HPV vaccination in the broader context of primary and secondary prevention of HPV-related cancers.

For each correct answer, a point was added to the composite HPV knowledge score. Blank or wrong answers were given no points. The overall knowledge score was expressed as weighted percentage (%).

Differences in knowledge and attitudes by *a priori* selected relevant variables (including socio-demographic characteristics, area of residence, educational and professional profiles) were explored through univariate regression analysis. P values were derived from chi-square and t-tests. Analyses were carried out using SPSS statistical software (version 21.0).

## Results

### *Socio-demographic characteristics of the study population*

A total of 262 otorhinolaryngologists were included in the study (response rate 22%). Participants' socio-demographic characteristics are summarised in Table I.

The majority of respondents were male (64%,  $n = 168$ ) and 66% had between 35 and 60 years ( $n = 173$ ). With regards to geographical distribution, almost half were from Northern Italy (45.8%,  $n = 120$ ). Overall, almost 50% (46.2%,  $n = 121$ ) had more than 25 years of clinical practice experience; 71% of physicians ( $n = 185$ ) reported to have participated in educational programmes and training specifically focusing on prevention of HPV infection.

### *Level of knowledge on HPV infection and vaccines*

Overall, the average knowledge score was 64.1% (SD = 14.8), ranging from 23.5% to 88.2%. Physicians correctly identified HPV infection transmission routes: sexual (99.2%,  $n = 260$ ) and cutaneous (62.6%,  $n = 164$ ). However, more than half also believed that transplacental (64.5%,  $n = 169$ ), haematic (67.9%,  $n = 178$ ) and air (58%,  $n = 152$ ) were transmission routes of HPV infection.

Moreover, 96% of physicians ( $n = 251$ ) knew that HPV infection is associated with oropharyngeal cancer and 74% ( $n=193$ ) knew it is associated with respiratory papillomatosis. In addition, they were aware of HPV-related diseases: genital warts (80.9%,  $n = 212$ ) and cervical (99.6%,  $n = 261$ ), vulvar and vaginal (79.8%,  $n = 209$ ), anal (80.9%,  $n = 212$ ) and penile (80.2%,  $n = 210$ ) cancer. Less than 20% of respondents (17%,  $n = 45$ ) identified both HPV types 16 and 18 as carcinogenic.

In addition, 48.9% of physicians ( $n=128$ ) were aware of the existence both bi-valent and quadri-valent vaccines; 3.4% ( $n=9$ ) thought only one vaccine is available and 47%

**Table I.** Socio-demographic characteristics of the study population.

Characteristics	Categories	n (%)
Age (years)	≤ 35	55 (21%)
	36-50	81 (30.9%)
	51-60	92 (35.1%)
	≥ 61	30 (11.5%)
	Missing	4 (1.5%)
Gender	Male	168 (64.1%)
	Female	91 (34.7%)
	Missing	3 (1.2%)
Years of clinical practice	≥40	16 (6.1%)
	39-25	105 (40.1%)
	24-10	86 (32.8%)
	≤9	44 (16.8%)
	Missing	11 (4.2%)
Location of practice in Italy	North	120 (45.8%)
	Centre	43 (16.4%)
	South and islands	88 (33.6%)
	Missing	11 (4.2%)

( $n = 124$ ) ignored that any vaccine against HPV infection existed at all. Among who knew both vaccines exist, 24% ( $n = 31$ ) thought its administration has no risk of side effects and 56% ( $n = 72$ ) were not able to answer the question.

Of interest, 77.5% ( $n = 203$ ) knew that the age target for the administration of the HPV vaccine in young females is 12 years and that 12-year-old girl cohorts are actively offered free of charge the vaccine through the Italian health system. A total of 20% ( $n = 53$ ) of subjects knew that three doses of vaccine were at the time recommended, while 54% ( $n = 141$ ) admitted to not know it. With regard to HPV immunisation coverage rate target, only 12% ( $n = 31$ ) knew the Ministry of Health set it at 95%. Lastly, 35% ( $n = 90$ ) believed that immunisation against HPV did not rule out secondary prevention of HPV-related cancers. The association between general knowledge on HPV and selected relevant variables is reported in Table II. Having participated in education programmes and training on HPV prevention was positively associated with increasing knowledge score ( $p < 0.001$ ). When deconstructing the score and taking into consideration single items, having participated in education programmes and training remained positively associated with better knowledge on HPV transmission routes ( $p < 0.001$ ) and availability of HPV vaccines, (although the latter was not statistically significant,  $p = 0.07$ ). Minor differences in knowledge were reported by geographical origin of respondents. No socio-demographic characteristics were significantly associated with better knowledge on HPV (Table II).

### *Providers' attitudes and opinions on prevention of HPV infection*

The majority of respondents believed that the main objective of HPV vaccination is primary prevention of HPV-related cancers (87%,  $n = 227$ ). When asked about the perceived

**Table II.** Composite HPV Knowledge score and single knowledge items distribution by selected characteristics.

	Overall knowledge score (mean, SD)	<i>p</i> value*	knowledge on HPV infection transmission route (n, %)	<i>p</i> value*	Awareness of existence of both vaccines (N, %)	<i>p</i> value*
<b>Age</b>						
≤35	66.2 (13)	0.1	39 (24.1%)	0.13	33 (25.6%)	0.59
36-50	64 (14.4)		52 (32.1%)		39 (30.2%)	
51-60	60.5 (14.5)		58 (35.8%)		43 (33.3%)	
≥61	61.4 (15.7)		13 (8%)		14 (10.9%)	
<b>Gender</b>						
Male	62.1 (15)	0.26	104 (64.2%)	0.90	74 (57.4%)	0.04
Female	64.3 (13.3)		58 (35.8%)		53 (41.1%)	
missing					2 (1.6%)	
<b>Location</b>						
North	64.7 (13.2)	0.003	73 (45.1%)	0.004	60 (46.5%)	0.88
Centre	66.1 (9.5)		35 (21.6%)		19 (14.7%)	
South and islands	58.8 (16.6)		49 (30.2%)		45 (34.9%)	
missing			5 (3.1%)		5 (3.9%)	
<b>HPV-specific educational programs</b>						
Yes	66.2 (11.3)	<0.001	137 (84.6%)	<0.001	101 (78.3%)	0.07
No	58.6 (16.9)		13 (8%)		18 (14%)	
missing			12 (7.4%)		10 (7.8%)	

\* *p* values obtained through chi-square and one-way ANOVA testing.

usefulness of HPV vaccine, 66% of physicians ( $n = 173$ ) considered HPV vaccine as a public health priority, 28% ( $n = 73$ ) as a very important prevention tool, 3% ( $n = 9$ ) as useful but not essential and 1% ( $n = 3$ ) as absolutely useless. Respondents reported that the ideal target population to receive HPV vaccine is females before the start of sexual activity (74%,  $n = 191$ ). Importantly, 22% ( $n = 56$ ) thought the target population should include both males and females. More than 50% (54.2%,  $n = 142$ ) reported to be asked about HPV vaccination benefits by patients as well as about vaccine side effects (12.6%,  $n = 33$ ) and duration of protection (13.4%,  $n = 35$ ). With regard to perceived barriers to HPV vaccination, respondents identified: inadequate information available to the general public (63.4%,  $n = 166$ ), lack of vaccine benefits perception (66.8%,  $n = 175$ ), parental reluctance (64.9%,  $n = 170$ ) and low healthcare providers' advocacy (59.2%,  $n = 155$ ). Almost all physicians (97%,  $n = 254$ ) expressed their willingness to recommend HPV vaccination to patients.

Participants indicated the following as potential effective strategies to increase HPV vaccine uptake among adolescents: educational campaign through new media (60.7%,  $n = 159$ ), this including websites targeting young people (29%,  $n = 76$ ), school vaccination programmes (38.6%,  $n = 101$ ) and counselling (40.5%,  $n = 106$ ).

## Discussion

The increasing key role of otorhinolaryngologists in pro-

moting prevention of HPV-associated cancers has recently been advocated at the national and international level. Our results show that Italian otorhinolaryngologists are knowledgeable regarding HPV infection and have a positive attitude towards HPV vaccine. These findings are of fundamental importance in light of: 1) the unfolding epidemic of HPV-related head and neck cancers<sup>13</sup> and 2) the mounting evidence on the efficacy of vaccine against HPV oral infection.

Overall knowledge scores exceeded 70% in almost 50% of respondents and, on specific items, it was higher compared to percentages we previously reported among general practitioners<sup>26</sup>. In particular, otorhinolaryngologists scored high on knowledge-based questions on HPV infection transmission and association with oral papillomatosis and oropharyngeal cancers as well as with cervical and other non-cervical cancers. More importantly, a large share of otorhinolaryngologists showed a positive attitude towards prevention of HPV-related cancers considering HPV vaccine as an effective prevention tool and a public health priority.

Some key issues that emerged from the survey merit discussion. First and of crucial significance, the large majority of respondents reported to be asked about the benefits of, side effects and duration of protection HPV vaccine, showing there is high demand for information and advice on it. Second, we report a positive correlation between having participated in educational programs and training and both high knowledge level and positive attitude to-

wards HPV prevention among physicians. This held true for overall knowledge score as well as for single knowledge items underlining the importance of continuous medical education and training to increase the delivery of preventive care<sup>27,28</sup>.

Of note, more than a fifth of physicians thought the target population should include both males and females. This is in line with the new immunisation schedule recommended by Italian scientific societies that include both males and females as HPV vaccine target populations<sup>29</sup>. HPV vaccine is currently recommended to males in the United States<sup>30</sup> and in a few European countries<sup>31</sup>; however, as evidence accumulates on the effectiveness of vaccinating males to prevent HPV-related conditions in the male population as well as to enhance herd immunity in the general population<sup>32,33</sup>, more countries are considering adhering to universal vaccination<sup>18,34</sup>. In particular, experts are increasingly advocating for HPV vaccination in males for the prevention of oropharyngeal cancers<sup>33,35,36</sup>. Lack of knowledge on specific items emerged: less than 20% of respondents correctly identified carcinogenic HPV types and almost half were not aware of the existence both bivalent and quadri-valent vaccines.

To our knowledge, this is the first study conducted in Italy and in Europe on the topic. Only one study, published on *JAMA Otolaryngology – Head & Neck Surgery*, is available in the literature on a sample of American Head and Neck surgeons' practices, attitudes and knowledge regarding HPV-related cancers and vaccines<sup>22</sup>. The authors reported that the respondents were relatively knowledgeable about HPV and had generally positive attitudes and beliefs about HPV education and vaccination. Although such findings are in line with our results, we argue that such knowledge is likely to be setting-specific and to vary depending on factors such as local healthcare systems, health policy strategies and medical curricula and training.

Although limited data is available on otorhinolaryngologists, several recent studies have explored knowledge of HPV among healthcare providers, including general practitioners (GPs)<sup>37-41</sup> and other specialists<sup>41-43</sup>. We have previously reported on Italian GPs' knowledge and perceived role in HPV prevention identifying some lack of knowledge on specific areas and room for improvement in communication with parents and adolescents on the topic<sup>26</sup>. In line with our findings, studies conducted with other specialists highlighted the importance of educating healthcare providers involved at different levels in HPV prevention<sup>37-45</sup>.

Although those estimates come from heterogeneous studies and are likely to be influenced by the competing effect of different socio-demographic, genetic and environmental risk factors as well as HPV-testing methods and quality<sup>46</sup>, such high percentages underlines how HPV-related OPSCC burden is a relevant clinical and public health

concern and suggests that primary prevention may play a key role in reducing it.

The findings we report must be considered in light of limitations. First, the relatively low response rate limits the generalisability of our findings to the population of Italian otorhinolaryngologists. This has historically been a critical issue when conducting research among medical professionals as reported elsewhere<sup>43</sup>. However, the only other available study on the topic conducted in the United States had a similar sample size and response rate<sup>22</sup>. The small sample size might have prevented our analysis to have enough statistical power to detect specific factors associated with knowledge and attitudes toward HPV prevention. Lastly, we were not able to compare characteristics of respondents and non-respondents. Given the study design, we cannot rule out the risk of selection bias; in fact, assuming that more committed and knowledgeable physicians are more likely to complete the survey, this might have led to an overestimation of the overall knowledge on HPV infection and prevention. On the other hand – different from other similar studies which were self-administered online<sup>22,43</sup> – our survey was administered in person by trained staff, this limiting the risk of information bias. Finally, the questionnaire focused on primary prevention and did not explore otorhinolaryngologists' knowledge on available diagnostic tools for HPV infection, a topic of growing interest<sup>43</sup>. However, to increase the response rate we preferred to keep the questionnaire relatively short and we plan to explore this and other topic in future surveys.

## Conclusions

The global burden of HPV-related oropharyngeal cancers is increasing and is predicted to surpass the burden of cervical cancer in the near future<sup>12</sup>. As evidence is accumulating on the potential effectiveness of HPV vaccine in controlling the oropharyngeal cancer epidemic<sup>13,21</sup>, otorhinolaryngologists assume a key role – not only in the diagnosis and treatment of HPV-related cancers – but also in educating and advocating on HPV prevention<sup>22</sup>.

To our knowledge, this is the first study conducted in the European Union to assess otorhinolaryngologists' knowledge and attitudes on HPV infection and prevention. Our results show that Italian otorhinolaryngologists are knowledgeable regarding HPV infection and have a positive attitude towards HPV vaccine. However, we identified areas of potential improvement. Our findings provide a useful basis to plan, implement and evaluate targeted educational programmes and training. As we showed herein, educational programmes and training specifically focusing on HPV are effective in increasing physician knowledge and positive attitude towards prevention<sup>23</sup>. In a global context of growing vaccine hesitancy, this would contribute to enhance vaccine uptake among patients and the general population<sup>47-51</sup>. With the overall aim of

controlling the burden of HPV-related cancers, resources and efforts should be devoted to promote continuing education among otorhinolaryngologists and the general medical community and to increase awareness on the role of vaccines in prevention of HPV-related cancers. In this context, there is tremendous opportunity for healthcare providers across fields to cooperate and for public health and otorhinolaryngologist communities to join forces and engage in fruitful collaboration.

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