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# Awareness of oral and genital HPV infection in young adolescents prior to gender-neutral vaccination

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Abstract:	Introduction: Oral HPV and oropharyngeal cancer prevalence are increasing, particularly in men. Raising greater awareness of male HP disease is perceived as an important intervention strategy. This study investigated the effectiveness of HPV education on adolescents' perception of HPV disease and the impact of HPV vaccination on their sexual health.  Methods: A HPV questionnaire was completed by 357 UK-based adolescents, aged 12-13 years.  Results: Most adolescents knew HPV causes cervical cancer and HPV vaccination prevents this. A minority acknowledged HPV causes other genital cancers, with under a fifth knowing HPV causes genital warts. Adolescents awareness of HPV transmission activities were limited. There was very poor awareness of oral HPV infection or HPV-induced oropharyngeal cancer. Half of the participants stated HPV vaccination reduced their concerns about STI contraction. Over half of males said they may take more sexual risks following vaccination, whilst a simila proportion of females did not expect their partner to take more risks. Conclusions: Adolescents had little awareness of male HPV infection at the role HPV vaccination can play in preventing these diseases. With variable rates of HPV vaccination uptake in males reported worldwide, this study indicates that in the UK greater emphasis on male HPV dise within educational information is required, to raise better awareness of how HPV affects both genders. As both genders preferred to receive education via healthcare professionals, educating a wider-range of healthcare professionals on oral HPV could help facilitate awareness of HPV's role in head and neck cancer.				

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**Title** – Awareness of oral and genital HPV infection in young adolescents prior to genderneutral vaccination

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#### **ABSTRACT**

Introduction: Oral HPV and oropharyngeal cancer prevalence are increasing, particularly in men. Raising greater awareness of male HPV disease is perceived as an important intervention strategy. This study investigated the effectiveness of HPV education on adolescents' perception of HPV disease and the impact of HPV vaccination on their sexual health.

**Methods:** A HPV questionnaire was completed by 357 UK-based adolescents, aged 12-13 years.

Results: Most adolescents knew HPV causes cervical cancer and HPV vaccination prevents this. A minority acknowledged HPV causes other genital cancers, with under a fifth knowing HPV causes genital warts. Adolescents awareness of HPV transmission activities were limited. There was very poor awareness of oral HPV infection or HPV-induced oropharyngeal cancer. Half of the participants stated HPV vaccination reduced their concerns about STI contraction. Over half of males said they may take more sexual risks following vaccination, whilst a similar proportion of females did not expect their partner to take more risks.

Conclusions: Adolescents had little awareness of male HPV infection and the role HPV vaccination can play in preventing these diseases. With variable rates of HPV vaccination uptake in males reported worldwide, this study indicates that in the UK greater emphasis on male HPV disease within educational information is required, to raise better awareness of how HPV affects both genders. As both genders preferred to receive education via healthcare professionals, educating a wider-range of healthcare professionals on oral HPV could help facilitate awareness of HPV's role in head and neck cancer.

#### **KEY MESSAGES**

- UK adolescents showed good awareness of HPV's association with cervical cancer, but poor knowledge of other HPV-related diseases and the different transmission routes.
- With more countries introducing HPV gender-neutral vaccination, HPV education should have an increased focus on HPV infection within male sexual health.
- Effective communication on oral HPV infection, including transmission routes and preventative measures, needs to be a key focus of healthcare polices.
- Enhanced education of healthcare professionals on oral HPV could help facilitate people's awareness of HPV's role in head and neck cancer.

# **BACKGROUND/RATIONALE**

Human papillomavirus (HPV) is one of the most common sexually transmitted infections (STI)<sup>1</sup>, WHO estimates 291 million women worldwide harbour HPV, with sub-Sahara Africa, Latin America and Eastern Europe having the highest rates of infection<sup>2</sup>. HPV infection differs between ethnicities, with black people having the highest prevalence and is more common in men, with penile HPV prevalence double vaginal, with more men harbouring a high-risk HPV strain<sup>3</sup>. Although HPV is recognised as a genital infection, oral HPV infections are increasing with an average oral prevalence of 11.5% in men and 3.2% in females<sup>4</sup>. Oral HPV infections are linked with oral-genital and oral-anal sexual transmission, although oral-oral transmission, such as open-mouthed kissing/saliva transfer, has been indicated<sup>4,5</sup>.

Infection with high-risk HPV strains are associated with genital and oropharynx cancers<sup>6,7</sup>. Globally, cervical is the most common HPV cancer<sup>6</sup>. However, worldwide increases in HPV oropharyngeal cancer (OPC), particularly in young men, means HPV-OPC is now the most

common HPV-related male cancer<sup>7</sup>. Predictions indicate by 2025, HPV-OPC will be more common than cervical cancer due to cervical screening, female-biased HPV vaccination, increasing rates of oral HPV and no early screening for HPV-OPC<sup>3,8</sup>.

Preventing HPV is difficult, transmission occurs by close contact, including touch, meaning an asymptomatic person can unwittingly spread infection<sup>7</sup>. The most effective prevention method is HPV vaccination, which is predominantly administered to women<sup>6</sup> and, since introduction, has reduced female genital and oral HPV disease<sup>9-11</sup>. Increasing rates of male HPV-OPC and a reduction in oral and genital HPV infection in vaccinated men<sup>3,11</sup> has led to currently 22 countries, including Australia, USA and 9 countries in Europe, extending the HPV vaccination to men<sup>11</sup>. In August 2018, after recommendation by the Joint Committee on Vaccination & Immunisation, the UK also agreed to offer gender-neutral HPV vaccination to help prevent more cases of HPV-related cancers, including HPV-OPC; with 12-13 year old male vaccination starting from September 2019<sup>12</sup>.

Female vaccination uptake varies globally and is unlikely to reach the global target of 80% coverage<sup>2</sup>: due to limited awareness of HPV risks, sexual activity values, concerns around vaccination safety, and cost<sup>8-11</sup>. HPV vaccination administration also influences uptake, with a school-based delivery resulting, internationally, in higher vaccination uptake<sup>11,13</sup>. Male HPV vaccination rates differ greatly, with 80% in Australia<sup>11</sup> compared to 56% in the US<sup>14</sup>, with an estimated 25 million US men eligible for HPV vaccination remaining unvaccinated<sup>3</sup>. Globally, adolescent male HPV vaccination is lower when compared to female vaccination at the same stage; which has been related to lack of male awareness of HPV<sup>15,16</sup>. Teenage boys show very limited knowledge regarding HPV in males<sup>16</sup>, with most parents unaware boys could receive

HPV vaccination<sup>17</sup>. Furthermore, this lack of knowledge around oral HPV is an issue regardless of age; a recent review indicated 1% of US adults knew HPV was a risk factor for OPC<sup>18</sup>.

As a limited number of countries are offering gender-neutral HPV vaccination, better education on male HPV disease is seen as an important intervention strategy to increase people's awareness of HPV-OPC and to positively influence male vaccination<sup>19</sup>. As such, it is imperative to understand males' and females' awareness of HPV to determine the effectiveness of current HPV educational material in informing both genders about HPV. Therefore, this study assessed the knowledge and perceptions of 12-13 year old adolescents regarding HPV, transmission routes and sourcing HPV educational information, to determine how to improve adolescents' knowledge of the risks of genital and oral HPV infection.

#### **METHODS**

#### Design

This was an exploratory quantitative study, examining responses of school students to a series of HPV multiple-choice questions. To enable gender comparison the study adopted a between-participants design, comparing males and females on a series of dependent variables relating to knowledge of HPV diseases and vaccination, sources of HPV education used and would prefer to use, and attitudes to what vaccination meant to their sexual health choices.

# **Participants**

Given the exploratory nature ideal sample size power calculations were not performed, the general aim was to obtain a representative sample of at least 300 participants from at least three schools, as has been obtained in similar studies<sup>22</sup>.

After approval by the University of Derby's Life Sciences Ethics Committee (16Sw0079) eight Secondary Education schools (11-16 year olds) within the Midlands, UK, were randomly approached to participate. Five, mixed gender state-controlled schools took part, from 2014-2016. All children aged 12-13 years, were provided with information for their main caregiver, explaining study aims and a consent form. Only children with a consent form signed by their caregiver participated, with an average participation rate of 52%. Caregivers supplied an identification number, which linked data collection to consent, ensuring anonymity. Data collection was performed up to 8 weeks after females had received their HPV vaccination.

# **Materials**

Data was collected using a questionnaire focused on HPV diseases and vaccination. Although there are validated HPV questionnaires<sup>18,20</sup>, we developed a new questionnaire, guided by other questionnaires<sup>20-21</sup>, due to the lack of pre-existing questionnaire for male and female 12-13 year-olds that included oral HPV questions. The questionnaire was not designed as a psychometric scale to measure scores on particular constructs; it functioned as a series of individual questions, so factor analysis and measures of reliability such as Cronbach's alpha are not applicable. The questionnaire employed closed questions with dichotomous or multiple-choice answers that young adolescents were able to understand without assistance and simple to answer during a fifty-minute lesson.

# **Procedure**

Data was collected in Personal, Health and Social Education (PHSE) lessons, which are used to educate UK children around sexual health. Students attended a designated HPV mixed gender lesson, in a class-room or school-hall, with the teacher in attendance. After an explanation of

the study's aims, all participants completed the questionnaire individually. The research team monitored completion, addressing questions around clarity, but not providing answers.

After completion of the questionnaire, the research team gave an interactive session, as an incentive for school's participation, around HPV diseases, vaccination and importance of cervical screening.

# Statistical methods

Participants' response to each option in the multiple-choice questions were obtained. Responses containing missing data (<2%) were excluded. Analyses were conducted using chi-squared tests for independence to examine differences in responses between genders (where expected frequencies were low Fisher's exact tests were used). Due to the large number of separate analyses, the alpha level was Bonferroni-adjusted to .001. Power analysis using G\*Power still demonstrated high power (1 –  $\beta$  = .99) for a medium effect size (w = .3) following this adjustment.

#### **Patient and Public Involvement**

PHSE teachers and school nurses helped ensured questionnaire suitability for young adolescents and were involved with recruitment. We would like to thank HPVaction.org and The Swallows Head & Neck charity for their contribution to this manuscript.

#### RESULTS

Data was recorded from 357 participants (129 males, 228 females, gender response rate 35% and 65% respectively) ). The overall percentage of participant response rate (number of actual participants compared to number of children in the year) for each school was:

School 1= 41% (75/183)

School 2= 72% (81/113)

School 3 = 32% (45/148)

School 4 = 63% (68/108)

School 5= 63% (88/138).

The majority of participants (84.2%) were white, with 6.8% mixed/multiple ethnic, 4.8% Asian/Asian British and 3.7% Black/Africa/Caribbean/Black British. Most participants stated no religion (56.3%) or were Christian (34.7%), with 3.6% identifying as Muslim, 1.7% Sikh, 0.6% Hindu and the remaining 3.1% stated their religion as 'other'.

Responses about HPV infection, diseases and vaccination, are in Table 1. Most participants were aware females could be infected with HPV, fewer participants were aware males could be infected, with a significantly higher proportion of females unaware of this (p<.001).

**Table 1**Adolescents' knowledge about HPV.

	% (numb	Gender		
	Total	Male	Female	comparison
	(N = 357)	(N = 129)	(N = 228)	<i>p</i> -value
Who can be infected with HPV?				
Females	95.5 (341)	91.5 (118)	97.8 (223)	.005
Males	53.8 (192)	66.7 (86)	46.5 (106)	< .001*
What diseases can the HPV infection				
cause?				
Cervical cancer	73.1 (261)	58.1 (75)	81.6 (186)	< .001*
Penis cancer	31.7 (113)	42.6 (55)	25.4 (58)	.001*
Anal cancer	24.9 (89)	30.2 (39)	21.9 (50)	.082
Skin cancer	21.6 (77)	27.1 (35)	18.4 (42)	.055
Genital warts	17.1 (61)	17.1 (22)	17.1 (39)	.990
Mouth cancer	14.0 (50)	18.6 (24)	11.4 (26)	.060
Skin warts	5.9 (21)	7.0 (9)	5.3 (12)	.509
Mouth warts	5.6 (20)	7.8 (10)	4.4 (10)	.184
None of the above	2.0 (7)	1.6 (2)	2.2 (5)	>.999 a

Cervical cancer	73.9 (264)	59.7 (77)	82.0 (187)	< .001*
Penis cancer	33.6 (120)	45.0 (58)	27.2 (62)	.001*
Anal cancer	26.1 (93)	36.4 (47)	20.2 (46)	.001*
Skin cancer	18.5 (66)	19.4 (25)	18.0 (41)	.744
Genital warts	16.5 (59)	20.9 (27)	14.0 (32)	.092
Mouth cancer	15.4 (55)	16.3 (21)	14.9 (34)	.731
Skin warts	6.2 (22)	8.5 (11)	4.8 (11)	.162
Mouth warts	5.3 (19)	7.0 (9)	4.4 (10)	.295
None of the above	2.0 (7)	4.7 (6)	0.4 (1)	.010 a
What activities can spread HPV?				
Sex	90.8 (324)	89.9 (116)	91.2 (208)	.682
Kissing	20.2 (72)	16.3 (21)	22.4 (51)	.168
Saliva	14.3 (51)	19.4 (25)	11.4 (26)	.039
Giving birth	11.2 (40)	17.1 (22)	7.9 (18)	.008
Touch	10.1 (36)	10.1 (13)	10.1 (23)	.998
None of the above	0.6 (2)	0.0 (0)	0.9 (2)	.537 a
How can you prevent becoming				
infected with HPV?				
Use a condom	68.3 (244)	76.0 (98)	64.0 (146)	.020
Have fewer sexual partners	31.4 (112)	31.0 (40)	31.6 (72)	.911
Not touch infected person	19.6 (70)	21.7 (28)	18.4 (42)	.453
Never have sex	15.1 (54)	16.3 (21)	14.5 (33)	.647
Do not take drugs	14.6 (52)	24.0 (31)	9.2 (21)	< .001*
Do not smoke	14.3 (51)	20.2 (26)	11.0 (25)	.017
Do not drink alcohol	10.9 (39)	14.7 (19)	8.8 (20)	.083
Only have sex once married	5.3 (19)	7.0 (9)	4.4 (10)	.295

All comparisons analysed using chi-squared tests unless otherwise indicated.

The majority of participants agreed HPV causes cervical cancer and HPV vaccine prevents cervical cancer, with female agreement significantly higher. Males were more aware HPV causes penis cancer and HPV vaccination can prevent this. Adolescents showed lower awareness of anal cancer although significantly more males agreed HPV vaccination could prevent this disease. Only a sixth of the cohort knew HPV vaccination prevents genital warts.

The cohort did not recognise the association of HPV with oral warts, with only 5.6% and 14.0% knowing HPV causes mouth warts and mouth cancer respectively. There was concomitantly low agreement regarding HPV vaccination preventing these diseases.

<sup>&</sup>lt;sup>a</sup> Fisher's exact test \*  $p \le .001$ 

Nearly all adolescents were aware of HPV's spread by sex but other transmission activities were much less appreciated (Table 1). Both genders were largely unaware of HPV transmission by touch.

Condom usage was seen as the main preventative HPV measure, with the known preventive measure of fewer sexual partners selected by under a third of the cohort. Adolescent males appeared more aware of other HPV transmission activities such as drug taking (p<.001) and smoking.

When asked what HPV vaccination meant for their sexual health there were some clear gender differences. Both genders (73.7%) felt vaccination reminded them of STI risks, with just over half of participants feeling the vaccination reduced their concerns about contracting an STI. A significantly greater proportion of males agreed HPV vaccination may lead to taking more sexual risks that could expose them to STIs, (M=55.1%; F=24.5%, *p*<.001). However, when asked if they felt their partner may take more sexual risks, agreement was similar between genders (M=41.6%; F=39.4%) though significantly more females replied in the negative (M =33.6%; F=55.1%), with a greater proportion of males replying, "don't know" (M=24.8%; F=5.6%, *p*<.001).

Only 20.2% of participants reported researching HPV or the vaccination. The use of health oriented educational sources, talking to parents or reading the educational leaflet schools provide appeared the most common choices (Figure 1). When asked the most preferred source for obtaining information (Figure 2), a lesson with a health care professional was the most popular choice for both genders followed by lessons with school nurse for males and with a teacher for females. Neither gender were interested in sourcing information from

healthcare websites, with the current UK use of providing an educational leaflet poorly received, particularly by males.

#### DISCUSSION

Males' perception of HPV's impact on their health is rarely determined, even though more males harbour HPV infections<sup>3,4</sup>. Furthermore, understanding of HPV and vaccination within the cohort being vaccinated, young adolescents is seldom studied. This study investigated gender difference in 12-13 year olds' understanding around HPV diseases and the effectiveness of HPV education in informing adolescents about sexual health.

The observations that both genders were aware of HPVs association with cervical cancer, with males having lower awareness, and both genders having limited awareness of HPV causing other cancers, confirms other studies<sup>16-24</sup>. Our cohort's poor knowledge that HPV causes warts also ratifies other studies<sup>21-23</sup>.

A concerning finding was the cohort's ignorance of HPV's links with oropharyngeal cancer, with less than one-sixth aware HPV vaccination could help reduce HPV-OPC. As with adolescent girls<sup>10-11</sup>, the boys' knowledge was focused on infection and prevention methods associated with genital STI transmission, with both genders feeling sex was the predominant transmission route. Adolescents' awareness of oral routes of HPV transmission has not been previously described. The incidence of performing oral sex is increasing, with 70% of UK 16-24 year olds undertaking this practice<sup>25</sup>. Young people view oral sex as being risk-free in relation to pregnancy and STI transmission, with teenagers more likely to undertake oral sex than genital and most performing un-protected oral sex<sup>25,26</sup>. As HPV is transmitted by an oral-

genital route, our study shows that oral HPV transmission needs to be better communicated and educational material to have a stronger emphasis towards non-genital HPV disease.

More male focused HPV education is important when you consider our study showed a gender difference in relation to future sexual practices, with more males stating they may take more sexual risks due to HPV vaccination. The influence of HPV vaccination has no impact on sexual behaviour of young adults<sup>10,28,29</sup>. However, with both genders now receiving HPV vaccination our study shows that HPV vaccination limitations of STI protection needs to be better communicated, particularly to young men.

Our study found very few adolescents researched HPV and HPV vaccination. Our female participants had all received the HPV vaccination and so had received a HPV educational leaflet. As very few females had read this leaflet and our participants' low HPV knowledge is comparable to other studies, it would appear the use of educational HPV leaflets had minimal influence on our adolescents' knowledge.

Our participants, regardless of gender, stated they would most like to receive HPV education via a healthcare professional, rather than receiving educational leaflets which the UK health system currently provide to educate 12-13 year old children on HPV disease and vaccination. The use of healthcare professionals is a proven route to increase HPV awareness regardless of age, gender and prior knowledge<sup>18,30</sup> and our study confirms the need to educate the people adolescents feel more comfortable in approaching, rather than expecting young people to undertake independent sexual health education<sup>30</sup>.

With vaccination uptake positively associated with increased HPV knowledge<sup>18</sup>, expanding and enhancing HPV education to a range of healthcare professionals whom the general

population seek advice from, such as dentists<sup>27</sup> and pharmacists, would enable a more comprehensive approach to raising HPV disease awareness. This HPV education could be delivered as Continual Professional Development (CPD) with a gender-neutral approach to HPV disease and an enhanced focus on oral HPV, explaining the impact of gender-neutral vaccination on sexual health.

Our study has some limitations. Participants were from Midlands schools so not geographically diverse; however, the schools had representative ethnicity profiles, so are broadly generalizable to the UK. The participation rate varied between each school, even though each school was proactive in encouraging students to obtain caregiver consent. Furthermore, more females than males took part in the study, due to less males returning signed consent forms. The questionnaire was not validated in the same manner as a psychometric scale, with the use of dichotomous and multiple-choice responses potentially problematic, as participants could select numerous responses to provide apparently correct answers. However, this design allowed for rapid data collection and easier coding than open questions. Despite these limitations, the overall findings of HPV knowledge of our UK participants align with similar worldwide HPV studies and our study is one of the first examining oral HPV knowledge in adolescents and for both genders, and can inform future global studies on less gender-biased HPV education.

To conclude, both genders knowledge of HPV disease was poor and was mainly focused on cervical cancer. Both genders were less aware of male HPV disease, reducing young males' awareness of the consequence of HPV infection on their sexual health. As HPV ignorance reduces vaccination uptake, educational material accentuating HPV in males, and how vaccination will reduce HPV prevalence, could positively influence male HPV vaccination

uptake. Greater awareness around oral HPV and HPV-OPC is also essential. As both genders preferred sourcing HPV education from a healthcare professional, more gender-neutral education on HPV provided to a range of healthcare professionals could help inform the general population on HPV disease in both genders.

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The lead author Dr Gillian Knight, contributed to the content of this manuscript by: designing the HPV questionnaire and consent forms, obtaining ethical approval, recruitment of schools and the data collection within schools. She wrote the original draft of the introduction and discussion sections of the manuscript.

The co-author, Dr Ben Roberts undertook the data analysis of the questionnaire, which included the correct coding of the questionnaire for SPSS analysis, performing statistical analysis and presentation of the data. Dr Roberts also wrote the original draft of the methodology section of the manuscript.

Dr Knight and Dr Roberts worked together to determine the key findings from the data analysis and then to write the original draft of the results section of the manuscript.

They have also worked together to revise the manuscript after review and to respond to the reviewers comments.

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Figure 1: Sources adolescents used to obtain information about HPV and HPV vaccination.

Figures shown are percentages of males and females who reported they had used the source to research HPV or HPV vaccination. Overall, 20.2% of each gender reported using one or more of these sources. Proportions of males and females were compared for each source using chi-squared tests, but there were no significant differences between genders (all p > .001).

Figure 2: Adolescents' preferred sources to obtain information about HPV and HPV vaccination

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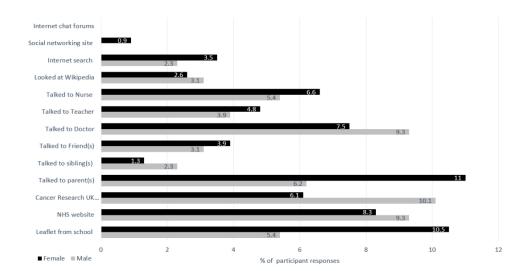


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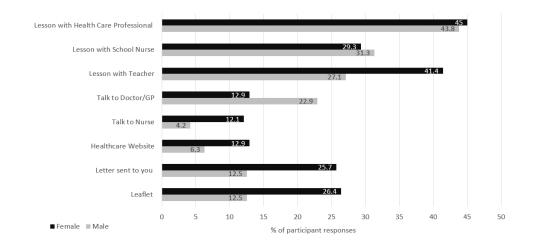


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# Contributorship statement:

The lead author Dr Gillian Knight, contributed to the content of this manuscript by: designing the HPV questionnaire and consent forms, obtaining ethical approval, recruitment of schools and the data collection within schools. She wrote the original draft of the introduction and discussion sections of the manuscript.

The co-author, Dr Ben Roberts undertook the data analysis of the questionnaire, which included the correct coding of the questionnaire for SPSS analysis, performing statistical analysis and presentation of the data. Dr Roberts also wrote the original draft of the methodology section of the manuscript.

Dr Knight and Dr Roberts worked together to determine the key findings from the data analysis and then to write the original draft of the results section of the manuscript.

They have also worked together to revise the manuscript after review and to respond to the reviewers comments.

As part of the review requirements, the authors of this manuscript obtained contribution from HPVaction.org and The Swallows Head & Neck charity, in revising the original manuscript in accordance with reviewer's comments. The Swallows Head & Neck charity required no amendments to the manuscript. HPVaction.org suggested a few minor amendments, which were incorporated in the revised manuscript.