







RESEARCH PAPER



Perception and knowledge of HPV-related and vaccine-related conditions among a large cohort of university students in Italy

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ABSTRACT

HPV is involved in cervical, anal, penile, vulvar and oropharyngeal cancers, as well as genital warts. It is important to investigate knowledge and attitudes among university students, considering in this age a shift in healthcare decision-making from parents to students themselves. The aim of this study was to estimate knowledge and perception of HPV in terms of potential shame for HPV-related conditions, trust in vaccine efficacy and worry for potential side effects.

The study involved students (18–25 years old) from the Universities of Padua and Verona, Italy. Socio-demographic and behavioural characteristics were collected with a questionnaire (n = 9988). Female gender and older age were positively associated with higher knowledge. The adjusted logistic regression showed an association between the set of perceptions investigated and the vaccination status, while a direct connection with knowledge was not found. However, another adjusted linear regression showed that a good set of perceptions could be partially explained by a high level of knowledge. Perceptions seem to fill an intermediate position between the knowledge and the decision to get vaccinated. The potential shame deriving from asking for HPV-vaccination was not identified as a relevant barrier. Having received information from healthcare workers, family and school showed to be positively associated with the adherence to the vaccination policy.

This study identifies university students as a possible target for HPV vaccination and pinpoints specific areas that might be targeted as first to encourage vaccine uptake. Primary prevention together with screening programmes remains essential in further reducing the burden of HPV-related diseases.

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Introduction

Human Papillomavirus (HPV) infection is the most common sexually transmitted infection, responsible for a large number of pathologies in both women and men. Over 200 HPV types have been identified and classified in high risk (HR) and low risk (LR) types on the basis of their potential to induce cancerous lesions.¹ Globally, the prevalence of HPV infection in women has been estimated around 11.7%, with the highest rates in Sub-Saharan Africa (24.0%).²

About 70–90% of HPV infections are asymptomatic and resolve spontaneously within 1–2 years, but persistent infections with HR types may progress to invasive cancer. HPV-16 and HPV-18 are responsible for more than 70% of all cases of cervical, vaginal and anal cancers worldwide and they account for about 30–40% of cancers of the vulva, penis and oropharynx.³ Nevertheless, non-oncogenic HPV types (mostly types 6 and 11) are extensively involved in the aetiology of genital warts which, however, massively impact on the quality of life.⁴

According with the World Health Organization (WHO), vaccination against HPV is an essential strategy in preventing cervical cancer.⁵ Globally, as of 2017, 71 countries had introduced HPV vaccination for girls, and 11 countries also for boys.⁶ In Italy, since 2007, HPV vaccination has been offered free of charge to all girls in the age of 12 and in 6 out of 21

Italian regions also to older age group and HIV-positive individuals between 2007 and 2010. Since 2015 some regions started to offer HPV vaccine also to boys in the age of 12 and in 2018 a gender-neutral strategy was implemented in all Italian regions.⁷ Moreover, HPV immunization also for unvaccinated females aged more than 12 (in particular to 25-years-old women that undergo cervical screening for the first time) and MSM is recommended.⁸

However, despite the national target for vaccine coverage was set at 95% within 5 years from the start of vaccine implementation in girls,⁹ at the end of 2017 coverage rate stood at around 69% in the first vaccinated cohort (girls born in 1997).¹⁰ As of 2011, coverage rates achieved by the catch-up programmes ranged between 44.3% and 80.0%.¹¹

Suboptimal vaccination coverage can be partly explained by factors associated with Italian parents' hesitancy, including concerns about the vaccine efficacy or possible serious side effects.¹² Furthermore, Roberts et al. found that the proportion of individuals with an incomplete immunisation status was higher in adolescents whose parents acknowledged to be unable to openly discuss their concerns about vaccines with healthcare professionals.¹³

In this context, it is important to investigate knowledge and perception towards HPV and vaccination among

university students, also considering that in this period of their life there may be a shift in health care decision-making from parents and guardians to the students themselves.¹⁴ Knowledge gaps and misrepresented perceptions on HPV and HPV vaccination were detected not only among college students from low-income countries, such as Pakistan,¹⁵ Malaysia¹⁶ and Nigeria,¹⁷ but also from high-income countries, including the US,¹⁸ Canada¹⁹ and Germany.²⁰

The aim of this study was to estimate the students' knowledge and perception about HPV infection in terms of potential shame for HPV-related conditions, trust in vaccine efficacy and worry for potential side effects of the vaccine 8 years after the implementation of the national vaccination programme in Italy.

Results

Overall, 9988 students agreed to participate in the study by completing the questionnaire (Figure 1). Socio-demographic and behavioural characteristics are shown in Table 1. Mean age of participants was 20.5 years (SD = 1.81), median age 20.0 years, ranging from 19 to 25. Just over one quarter of students sampled were HPV-vaccinated ($n = 2552/9545^a$; 26.7%); of these, only 81 (3.2%) were men. This included 88% who had received all three doses, 9% who received one or two doses and 3% who booked an appointment to receive the first dose.

As regards knowledge of HPV and HPV-vaccine, 65% of participants correctly answered to 6 or more questions out of 7 and 90% of the sample correctly answered to 5 or more. In Figure 2, mean values of agreement to proposed sentences are shown one at a time, according to the Likert scale adopted.

An adjusted linear regression to assess the effect of socio-demographic and behavioural characteristics on the levels of knowledge and different types perceptions regarding the emotions of shame, trust and fear towards HPV infection and vaccination was conducted. Findings are shown in Table 2. Overall, significant associations of knowledge with female gender (B: 0.14; 95%CI: 0.09 to 0.20), age (B: 0.03; 95%CI: 0.02 to 0.05), lack of a sexual partner (B: -0.13; 95%CI: -0.25 to -0.05), smoking habit (B: -0.05; 95%CI: -0.10 to -0.00), personal or close people's experience of genital warts (B: 0.11; 95%CI: 0.03 to 0.20) and vaccination status (B: 0.19; 95%CI: 0.06 to 0.18) were found.

The aim of the logistic regression analysis was to identify a significant association between knowledge/perceptions and the vaccination status, while controlling for age, gender, age at first intercourse, number of sexual partners smoking habit, sexual orientation, personal or close people's experience of genital warts. The effect of these potential confounders is not shown in the table. Out of the whole study population, 6325 (63.3%) participants were included. Approximately 81% of vaccination statuses were predicted by the model described. The level of shame (OR: 0.77; 95%CI: 0.72 to 0.83), trust (OR:

Knowledge of HPV and HPV vaccine (True/False questions)	
	<ul style="list-style-type: none"> • HPV infection affects only women (F) • HPV infection can occur without symptoms (T) • HPV infection is one of most common sexual transmitted diseases in Italy (T) • Currently, men cannot be vaccinated (F) • HPV vaccine is prescribed only to sexual active people (F) • Among men, HPV vaccine prevents only from genital warts (F) • I cannot receive vaccine because I already had sexual intercourses (F)
Perception (on a 7-point Likert scale)	
Shame of HPV-related conditions	<ol style="list-style-type: none"> 1. I would be embarrassed in case other people knew that I got HPV infection. 2. I would feel ashamed to ask for HPV vaccination because it is a sexual transmittable disease. 3. If others knew I received HPV vaccine, I would be embarrassed. 4. If I were diagnosed an HPV infection, I would be devastated.
Trust in vaccine efficacy	<ol style="list-style-type: none"> 5. Vaccine is efficient in preventing HPV infection. 6. HPV vaccine can prevent genital warts. 7. Vaccine is efficient in preventing cervical cancer in women. 8. Vaccine is efficient in preventing some kinds of penis cancers. 9. Vaccine is efficient in preventing some kinds of oral cancers. 10. Vaccine is efficient in preventing anal cancer. 11. Receiving vaccine is important for my health. 12. Vaccine is efficient in preventing HPV transmission to sexual partner.
Worry about potential side effects of the vaccine	<ol style="list-style-type: none"> 13. In case I were HPV infected, vaccine would be dangerous for my health. 14. Which is according to you the chance of side effects due to HPV vaccine?

Figure 1. Sentences assessing students' knowledge and perception of HPV and vaccine-related conditions. T = true; F = false.

Table 1. Knowledge and perception of HPV-related and vaccine-related conditions by socio-demographic and behavioural characteristics of the study population.

		n	%	Level of knowledge		Level of perceptions					
				Mean	ANOVA	Shame		Trust		Fear	
						Mean	ANOVA	Mean	ANOVA	Mean	ANOVA
Gender	F	6019	60.3	5.86	$p < .001$	3.28	$p < .001$	4.89	$p < .001$	3.34	$p = .035$
	M	3969	39.7	5.67		3.56		4.81		3.40	
Age	18–19 y	3816	38.2	5.77	$p < .001$	3.46	$p < .001$	4.87	$p < .001$	3.40	$p < .001$
	20–21 y	3196	32.0	5.74		3.41		4.83		3.41	
	22–23 y	2211	22.1	5.82		3.31		4.84		3.28	
	24–25 y	765	7.7	5.96		3.21		4.97		3.25	
Degree course attended (grouped by main areas)	1 Health-care professions	2239	23.1	5.84	$p < .001$	3.36	$p < .001$	4.89	$p < .001$	3.29	$p < .001$
	2 Sciences	1899	19.6	5.71		3.46		4.82		3.41	
	3 Humanities	1575	16.2	5.78		3.38		4.80		3.48	
	4 Engineering	1472	15.2	5.62		3.60		4.71		3.55	
	5 Law and Economics	607	6.3	5.69		3.47		4.83		3.46	
	6 Psychology	932	9.6	5.84		3.28		4.81		3.45	
	7 Medicine and Dentistry	978	10.1	6.10		3.07		5.23		2.84	
N. of sexual partners within last 24 months	0	767	9.9	5.74	$p < .001$	3.52	$p < .001$	4.80	$p < .001$	3.38	$p = .004$
	1	4593	59.4	5.84		3.33		4.90		3.34	
	2	1212	15.7	5.84		3.36		4.91		3.30	
	3+	1161	15.0	5.78		3.35		4.86		3.36	
Age at first intercourse	14 y or less	419	5.5	5.82	$p < .001$	3.20	$p < .001$	4.85	$p = .001$	3.41	$p = .033$
	15–16 y	2516	33.0	5.83		3.28		4.86		3.35	
	17–18 y	3498	45.9	5.79		3.38		4.88		3.34	
	19 y or more	1196	15.7	5.84		3.41		4.89		3.31	
Sexual orientation	Heterosexual	9329	94.7	5.79	$p = .007$	3.39	$p = .001$	4.86	$p = .193$	3.36	$p = .342$
	Homosexual	177	1.8	5.83		3.45		4.81		3.28	
	Other	341	3.5	5.87		3.20		4.83		3.37	
Use of birth pill	Yes	1786	31.0	5.93	$p < .001$	3.16	$p < .001$	4.95	$p < .001$	3.29	$p = .008$
	No	3983	69.0	5.85		3.32		4.87		3.36	
Smoking habit	Non-smoker	6927	71.3	5.80	$p = .001$	3.42	$p < .001$	4.88	$p < .001$	3.35	$p = .095$
	Current or ex-smoker	2785	28.7	5.76		3.30		4.81		3.41	
Personal or close people's experience of genital warts	Yes	840	8.5	5.88	$p < .001$	3.25	$p < .001$	4.89	$p = .029$	3.32	$p = .127$
	No	9061	91.5	5.78		3.40		4.86		3.37	
HPV vaccination status	Vaccinated	2552	26.7	5.91	$p < .001$	3.15	$p < .001$	5.01	$p < .001$	3.09	$p < .001$
	Non-vaccinated	6993	73.3	5.77		3.47		4.81		3.46	

Note: numbers may not add up to the total number due to missing data from questionnaire

1.40; 95%CI: 1.29 to 1.52) and fear (OR: 0.77; 95%CI: 0.73 to 0.81) significantly predicted the outcome, while no significant association was found with the level of knowledge (OR: 1.03; 95%CI: 0.96 to 1.19).

Moreover, an adjusted linear regression was performed to predict each perception investigated (shame, trust and fear)

based on the level of knowledge while controlling for age, gender, age at first intercourse, number of sexual partners smoking habit, sexual orientation, personal or close people's experience of genital warts and degree course attended (results are not reported in the table). Out of 9988, 36% of cases were excluded from these analysis because of a missing

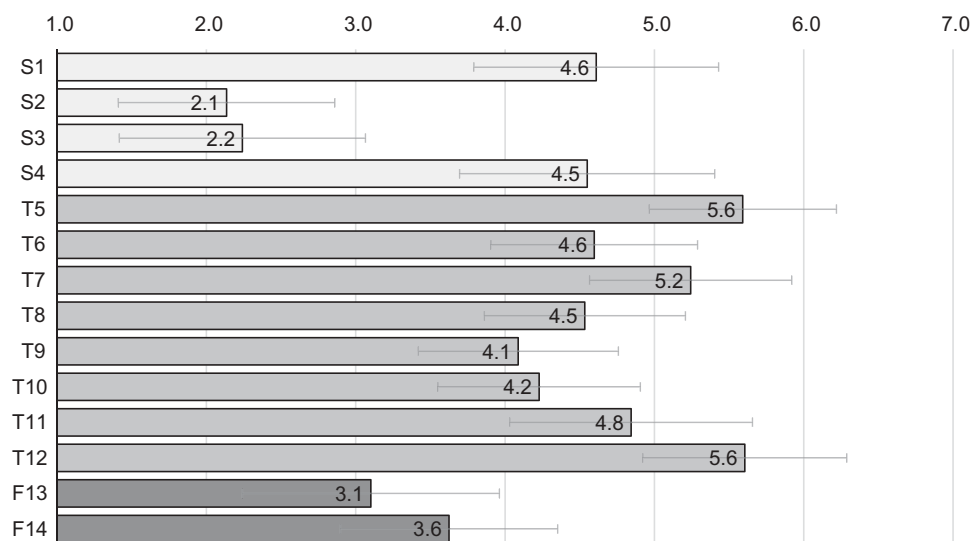


Figure 2. Perception. Level of agreement with each proposed item (see Figure 1 for the description of items). Mean value for each item is reported at the end of the bar. S = shame; T = trust; F = fear.

Table 2. Effect of the socio-demographic and behavioural characteristics on the level of knowledge and perception of HPV-related and vaccine-related conditions.

	reference	Level of knowledge			Level of perceptions									
		Beta-coefficient	95% CI		Shame			Trust			Fear			
			Lower	Upper	Beta-coefficient	Lower	Upper	Beta-coefficient	Lower	Upper	Beta-coefficient	Lower	Upper	
Gender	(male)													
Female		.14	.09	.20	-.16	-.22	-.10	-.03	-.08	.01	.12	.05	.20	
Age		.03	.02	.05	-.06	-.07	-.04	.02	.00	.03	-.06	-.08	-.04	
N. of sexual partners within last 24 months	(1 or 2 partners)													
0		-.13	-.25	-.05	.05	-.08	.18	-.12	-.23	-.02	.02	-.14	.19	
3 or more		-.03	-.10	.03	.02	-.05	.09	-.00	-.06	-.05	.05	-.04	.14	
Age at first intercourse	(15–18 y)													
14 y or less		-.00	-.10	.10	-.11	-.21	.03	-.04	-.13	.05	.05	-.09	.19	
19 y or more		-.00	-.07	.07	.11	.03	.17	.00	-.05	.06	.00	-.08	.10	
Sexual orientation	(heterosexual)													
Other		.05	-.04	.15	-.10	-.21	.05	-.06	-.15	.02	-.02	-.16	.11	
Smoking habit	(non-smoker)													
Current or ex-smoker		-.05	-.10	-.00	-.08	-.14	-.03	-.06	-.10	-.01	.06	-.01	.13	
Personal or close people's experience of genital warts	(no)													
Yes		.11	.03	.20	-.07	-.15	.02	.03	-.04	.10	-.03	-.14	.08	
HPV vaccination status	(non-vaccinated)													
Vaccinated		.19	.06	.18	-.29	-.35	-.22	.22	.17	.28	-.50	-.58	-.42	

Adjusted linear regression.

CI = confidence interval.

value in any variable investigated. There was a significant positive relationship between knowledge and trust (B: 0.12; 95%CI: 0.10 to 0.15), while a negative relationship was detected both for fear (B: -0.13; 95%CI: -0.16 to -0.10) and shame (B: -0.10; 95%CI: -0.12 to -0.07).

Finally, Table 3 shows the association between the type of source of information on HPV and its vaccination used by the students and their mean levels of knowledge and perceptions.

Discussion

Similarly to other recent American researches,^{18,21} this study pointed out that a significant proportion of university students was not vaccinated, particularly among men (only 2.2% of men were vaccinated), highlighting the existing gap of HPV vaccine coverage among university aged individuals.

Overall, students investigated showed a good level of knowledge on HPV infection and HPV vaccination,

contrary to previous research which found greater gaps knowledge about HPV among college students also in high-income countries.^{18–20} Nevertheless, the comparison between these different studies must be done cautiously, because of the different methods performed to test knowledge levels about HPV. This high level of knowledge detected seems to be promising in the light of robust evidences about a positive association between women's awareness on HPV and HPV vaccination uptake.^{22,23} However, higher knowledge is not always associated with higher vaccine uptake or, at least, its contribution does not necessary play a predominant role. In a recent meta-analysis, the contribution of knowledge has been resized in favour of other factors, such as physician's recommendation or parents' beliefs.²⁴ Another systematic review exploring barriers and facilitators to HPV vaccination of young women in high-income countries shows how parents seem keen to retain a crucial role in decision-making on

Table 3. Knowledge and perception of HPV-related and vaccine-related conditions by source of information.

		n	%	Mean	Perception																			
					Knowledge					Shame					Trust					Fear				
					Difference between means	ANOVA	Mean	Difference between means	ANOVA	Mean	Difference between means	ANOVA	Mean	Difference between means	ANOVA	Mean	Difference between means	ANOVA						
Healthcare workers	No	6582	65.9	5.71	0.23	$p < .001$	3.52	-0.38	$p < .001$	4.79	0.20	$p < .001$	3.46	-0.27	$p < .001$									
	Yes	3406	34.1	5.94			3.14			4.99			3.19											
Friend	No	9061	90.7	5.78	0.07	$p = .029$	3.41	-0.23	$p < .001$	4.85	0.06	$p = .031$	3.37	-0.06	$p = .154$									
	Yes	927	9.3	5.85			3.18			4.91			3.31											
Family	No	7817	78.3	5.76	0.13	$p < .001$	3.45	-0.28	$p < .001$	4.83	0.13	$p < .001$	3.40	-0.17	$p < .001$									
	Yes	2171	21.7	5.89			3.17			4.96			3.23											
TV	No	8354	83.6	5.78	0.05	$p = .024$	3.39	0.01	$p = .733$	4.85	0.05	$p = .015$	3.36	0.02	$p = .649$									
	Yes	1634	16.4	5.83			3.40			4.90			3.38											
Internet	No	8813	88.2	5.76	0.20	$p < .001$	3.40	-0.09	$p = .009$	4.85	0.08	$p = .002$	3.38	-0.14	$p < .001$									
	Yes	1175	11.8	5.96			3.31			4.93			3.24											
Newspaper	No	9479	94.9	5.78	0.18	$p < .001$	3.40	-0.19	$p < .001$	4.85	0.08	$p = .039$	3.37	-0.11	$p = .063$									
	Yes	509	5.1	5.96			3.21			4.93			3.26											
School	No	7106	71.1	5.73	0.20	$p < .001$	3.43	-0.14	$p < .001$	4.82	0.13	$p < .001$	3.41	-0.15	$p < .001$									
	Yes	2882	28.9	5.93			3.29			4.95			3.26											

behalf of their daughters and healthcare professionals appeared to reinforce this position.²⁵

Effect of socio-demographic and behavioural characteristics on knowledge and perception

According with the primary results of the regression analysis, females were significantly more acquainted with HPV infection and they showed a lower level of shame than males. Interestingly, concerns about possible side effects following vaccination were higher in females. This result is in line with findings from other studies^{18,19,26} and it should not be ignored by information campaigns designed to improve HPV awareness among young adults. Interestingly, no effect of the sexual orientation was noted for neither the knowledge nor the perception. The use of birth control pill was also associated to better outcomes both regarding knowledge and perceptions: this finding could be partially explained by a previous contact with healthcare professionals, since in Italy a medical prescription for receiving birth pill is required. Nevertheless, the study identified in the healthcare workers the source of information with the highest positive impact on all outcomes investigated (see below), in line with other and diverse contexts from Italy,²⁷ USA²⁸ and Asia.²⁹ Moreover, the girls using the birth-pill could be represent a sample of selected students who are more informed than others about sexually transmitted diseases.

The age played a key role in the knowledge of HPV and perceptions. Surely, the exposition to health-related information increases with the age, in line with another Italian study on a sample of adolescents and young women aged 14–24 years as the adjusted OR was 1.14 (95%CI: 1.08 to 1.20) for every 1-year increment.³⁰ This finding is of crucial importance, since it has to be taken into account the fact that a preventive intervention such HPV vaccination can provide a better protection if taken in a younger age.

The absence of a sexual partner negatively affected knowledge and trust compared with people with a more stable presence of a sexual partner. This finding may raise questions about the communication strategy adopted. In our context, information on the transmissibility of HPV may not have received enough attention. For example, in other countries like Australia and in the Anglosphere in general, only in the recent years the vaccine has started to be referred as the HPV vaccine, rather than the cervical cancer vaccine, in order to extend to male population as well the perception of benefiting from this vaccine.³¹

Students who smoke showed a lower level of knowledge, next to a lower shame. This could be explained by the fact that people following a healthier lifestyle may have a stronger interest in HPV issues as well. Smokers seem to have less concerns about implications from HPV infection, but at the same time a lower trust in a preventive vaccine.

A previous contact with information on HPV, having likely occurred in vaccinated participants and those having a past experience with genital warts, was also significantly associated with higher knowledge, consistently with results from Koshiol et al. showing that women who reported treatment for genital warts, are more likely to have heard of HPV (OR: 2.4; 95%CI:

1.4 to 4.2) and to receive accurate information about HPV, such as HPV causes cancer (OR: 2.7, 95%CI: 1.8 to 4.3).³²

A more detailed comment on single questions may be worth, because of the nuances within each area investigated. Questions regarding *shame* towards HPV-related conditions (sentence 1 to 4) revealed a consistent difference: embarrassment arising from the possibility of being diagnosed with HPV infection and subsequent devastation were only slightly over the cut-off value of 4 but in any case more than two times higher than shame deriving from asking for HPV-vaccination or from disclosing to other their possible HPV vaccinated-status (around 2/7 points). Overall *trust* in vaccine efficacy (sentence 5–12) was high. In all cases, the level of agreement is above 4/7 points. More in detail, vaccine was perceived to be more efficient in preventing HPV infection, cervical cancer rather than all other kinds of HPV-related cancers (some kinds of penis, oral and anal cancers) and genital warts. The awareness of the vaccine as a tool to prevent transmission to the sexual partner was also quite high. Agreement with both sentences concerning *fear* for possible vaccine side effects (sentence 13 and 14) stood below 4/7 points. The vaccine was not perceived as a dangerous for health in case of the administration after an HPV infection would have occurred. In particular, the results did not identify relevant barriers in HPV vaccine uptake in the shame deriving from asking for HPV-vaccination or from disclosing to other their possible HPV vaccinated-status. As opposite, an American study¹⁸ revealed that among college students the strongest concerns about the vaccine were related to family and friends finding out if the students were to get vaccinated.

Relationship between knowledge, perception and vaccination status

In this study, the status of being vaccinated against HPV was associated to a significantly higher average level of knowledge (as well as a substantially better pattern in terms of shame, trust and fear), but the level of knowledge, surprisingly, did not show to be a predictor for the HPV vaccination status, rising an important issue as regards the decision behind the choice whether receiving the vaccine or not. However, the same logistic regression brought to light a strong association between perceptions and the vaccination status. At first sight, the rationale behind this decision seems to lie on an emotional basis, rather than on a well-informed appraisal. However, according to results of the study, this good set of perceptions could be explained at least partially by the high level of knowledge. As confirmed shown in the adjusted linear regression, increases in the level of knowledge successfully reduce the feeling of shame for HPV-related conditions and enhance trust in the protection offered by the vaccine.

In this scenario, perceptions seem to fill an intermediate position between the knowledge and the decision to receive the vaccine. However, the knowledge remains a *primum movens* which is worth to be targeted in health promotion and communicable disease prevention.

The role of different sources of information

Having received information from healthcare workers showed to have a relevant and positive effect on knowledge, shame, trust and fear compared with all other sources of information used to get acquainted and documented on HPV and HPV vaccine. Similar studies already pointed at healthcare providers as a reliable source of information able to improve vaccine uptake³³ and knowledge also in males.³⁴ A recent systematic review³⁵ showed that one of the major facilitators of HPV vaccination among adolescents is the recommendation of a physician or other healthcare workers.

However, the same review also identified parental acceptance and peer encouragement as important facilitators. Rosen et al.³⁶ found that female adolescents who received information on HPV infection from their mothers had not only higher knowledge, but also a better perception on HPV vaccines. This evidence is in line with our study, reporting a determinant role of family members and friends in reducing the perceived shame.

Information acquired at school contributed to knowledge similarly to what healthcare workers did, but did not seem to be as much efficient in reducing shame and fear and enhance trust in vaccine. These findings raise a reasonable doubt on the accuracy of information conveyed.

Strength and limitations

This study has several limitations. First, participation in this study was on a completely free and voluntary basis. Because of the study settings, we were not aware of the number of students who decided not to take part in the study in each classroom by not returning the questionnaire, or by verbally refusing in advance to receive the questionnaire. Thus, we were not able to estimate the answering rate. On this basis, we could neither exclude a potential selection bias nor predict the direction of this bias.

This was not a multi-centre study. The study population included university students from several faculties. These results may not be inferred to the same aged Italian population because of undeniable effects of the educational level on HPV awareness and perception and not even to the entire Italian college students due to the convenience sample used.

Not all participants accurately completed questionnaires in every single required fields, leaving a slightly different denominator for each computation due to missing values.

Females in the age group 18–19-year-old were exposed to free-to-charge HPV-vaccination offered within the framework of the national vaccination programme. This may affect HPV awareness and overall knowledge in this group by being over-exposed compared to older students and male students, despite efforts to try to control for this confounder.

It is not possible to exclude the presence of a social desirability bias, by providing answers perceived as ‘correct’ in the social setting, especially as regards the trust in vaccination. However, the anonymous nature of the survey and the self-administration modality should have contribute to reduce this bias, at least partially. Similarity, the effect of a recall bias cannot be excluded as well, in particular with regards to recall of information about

the vaccination status. As reported in other studies,³⁷ this bias could substantially affects the accuracy of this information, however the nature of the sample and the level of knowledge showed may limit the magnitude of the influence of this bias.

In spite of these limitations, the very large sample size – approximately ten thousand participants involved – is a strength worth mentioning of our study.

Conclusions

These data suggest the presence of a good framework for implementing a coordinated and comprehensive strategy to prevent HPV related diseases, as recommended by WHO, identifying in the university students a possible target for HPV vaccination. By digging deeply into perceptions, this study provides further evidence for identifying specific areas that might be targeted as first to encourage primary prevention and vaccine uptake. Alarmingly, increasing trends in HPV-related cancers – in particular anal and head and neck cancers which affect also male population – have been observed in the last decade.³⁸ The role of primary prevention together with screening programmes is essential in controlling this increase.

In agreement with the main findings of our study, a winning strategy to overcome HPV vaccine hesitancy could be based on a correct communication style aimed not only at providing cognitive elements, but also at stimulating positive perceptions, reducing fears and shame and increasing trust on HPV vaccine efficacy. According to a recent systematic review,³⁵ both school-based vaccination programmes and peer encouragement were identified as facilitators for HPV uptake among adolescents. These data encourage the dissemination of accurate information and positive messages to promote HPV vaccination also in the university context, trying to create positive reinforcements among university students.

Our findings may thus be useful in developing effective health education strategies and materials to raise confidence of HPV and HPV vaccines, and in turn to boost public confidence and acceptability.

Materials and methods

Sample

From October 2015 to May 2016, students were recruited from different faculties of the University of Padua and the University of Verona, Italy. Participants were recruited on a completely free and voluntary basis and they were not offered any form of compensation for their time. Participants were eligible if they identified themselves as 18–25 years of age and enrolled in one of the courses offered by the University of Padua or the University of Verona. Degree courses attended by the sample were classified in the following seven main areas: (i) health-care professions, (ii) sciences, (iii) humanities, (iv) engineering, (v) law and economics, (vi) psychology, (vii) medicine and dentistry.

Data collection

Members of the research group visited the classrooms on several given days and all students in attendance were invited to complete the questionnaire. Participants were given oral information about the purpose of the study, and reassurance of confidentiality and anonymity regarding all collected data. The questionnaire was then distributed to all participants, with consent inferred from completion of the questionnaire. Participants were asked about their socio-demographic characteristics (age, gender, nationality, area of residence), number of sexual partners in the previous 24 months, age at first sexual intercourse, sexual orientation, use of contraceptive methods (birth pill), smoking habit, personal or close people's experience with genital warts, HPV vaccination status. The questionnaire was adapted from Schaefer et al.³⁹ In detail, past experience with genital warts was assessed with two questions: 'Have you ever been diagnosed with genital warts (condylomata)?' and 'Do you know anybody who had been diagnosed with genital warts (condylomata)?'. Participants who had answered positively to one or both these questions as regards previous personal or close people's experiences with genital warts were coded as 'experienced'. The HPV vaccination status was assessed by asking participants to tick a box that best described their current situation. Response options were 'I have completed the series of three shots for the HPV vaccine', 'I have started but not completed the series of three shots for the HPV vaccine', 'I have scheduled an appointment with my doctor to receive the HPV vaccine', 'I have not received the HPV vaccine or scheduled an appointment to receive the HPV vaccine'. Participants who had received at least one dose of the HPV vaccine or had declared to have booked an appointment to receive the first dose were coded as 'vaccinated'. Participants' knowledge of HPV was assessed with a set of the following seven True/False questions (Figure 1). A score was calculated then for every participant: one point for each correct answer to the True/False question; zero points for each wrong or missing answer. The score ranged from 0 (no knowledge) to 7 points (maximum knowledge). Data about the sources of information were also collected by asking participants to tick a pre-labelled box: as possible sources of information we investigated a selection of persons (healthcare workers, a friend, a family member), means of communication (TV, internet and social networks, newspapers or magazines) and school education. Multiple answers were possible. As regards the perception, the three main areas of investigation of this study – given by perceived shame of potential HPV-related and vaccine-related conditions, trust in vaccine efficacy and worry for potential vaccine side effects – were assessed with 14 sentences listed in Figure 1. Questions were presented in a random order on the questionnaire. Participants were asked to grade their agreement with each sentence on a 7-point Likert scale, where 1-point means total disagreement (1 = 'I fully disagree') and 7-point means complete agreement (7 = 'I fully agree'). The value of 4-point was chosen as arbitrary cut-off. The questionnaire took approximately 15 minutes to complete. A pilot survey with a small sample (n = 40) from the individuated target population was conducted. Face validity was tested by measuring the importance of items in the proposed questionnaire. Items rated with a mean value ≥ 3 on a 5-point Likert scale were maintained. Pretesting was also used to ensure that items were clearly written and interpreted

correctly. According to results and issues raised by the pilot study, no questions were added or deleted and minor grammatical and lexical changes were made in the final version to improve understandability.

Data were treated with full confidentiality in accordance with Italian legislation. Written informed consent was obtained from all participants. To ensure anonymous nature of the data the informed consents were collected separately from questionnaire. This study complies with the Declaration of Helsinki and the study protocol was approved by the ethical committee of the Padua Provincial Authority (date of approval 7/30/2015).

Statistical analysis

Means and one-way between subjects analysis of variance (ANOVA) were calculated to estimate students' knowledge of HPV and perceived shame for a potential HPV infection, trust and worry regarding HPV and vaccine related issues by socio-demographic, behavioural characteristics and means of communication used.

The effects of socio-demographic and behavioural characteristics on knowledge and perception was assessed with a linear regression analysis, adjusting for age, gender, age at first intercourse, number of sexual partners, smoking habit, sexual orientation, personal or close people's experience of genital warts and HPV vaccination status, which were assumed as potential confounders. All variables were entered in a single step. Another adjusted linear regression was conducted to study the effect of knowledge on perception itself, while controlling for socio-demographic and behavioural characteristics.

A logistic regression model was developed to examine factors associated with vaccination status adjusting for age, gender, age at first intercourse, number of sexual partners, smoking habit, sexual orientation, personal or close people's experience of genital warts and degree course attended.

Statistical significance for all tests was set at $p \leq 0.05$ (two-sided).

Data input was carried out using REDCap software platform⁴⁰ and statistical analysis was performed using IBM® SPSS Statistics® version 23.

Note

[a] 443 participants did not declare their vaccine status.

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Authors' contribution

All authors contributed to the article and approved the final version.

SC: study conception and design, drafting of the manuscript. CB: intellectual content, drafting of the manuscript. TB: study conception, supervision. AB: data interpretation and supervision. MF: statistical analyses, interpretation of data and drafting of the manuscript. DG:

interpretation of data and drafting of the manuscript. SM: study conception and design, data collection. VB: study conception, design, supervision and drafting of the manuscript.

Disclosure of potential conflicts of interest

VB received grants for taking part on advisory boards and at expert meetings, and for acting as speaker and/or organizer of meetings/congresses. The other authors have no potential conflicts of interest to disclose.

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