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Factors influencing HPV knowledge and vaccine acceptability in parents of adolescent children: results from a survey-based study (KAPPAS study)

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ABSTRACT

Human Papillomavirus (HPV) is one of the most common sexually transmitted infections associated with a wide range of diseases and cancers that may affect both genders. Since 2007, the Spanish National Immunization Program includes HPV vaccination, and currently it only targets 12-year-old girls. The objective of our study is to assess differences in the knowledge of HPV and HPV vaccine acceptability according to different factors, and to identify the role of different sources of information. A cross-sectional, multicenter survey research was carried out in twenty-four pediatric offices in Spain, and included parents of children aged 9 to 14 years old. 1,405 valid survey-responses were considered for the analysis. Parental awareness of HPV and HPV vaccine, as well as vaccine acceptability, are still strongly associated with child gender (girls) and age (12–14 years old). HPV knowledge and HPV vaccine acceptability are related to parental gender, HPV vaccination status and having at least one daughter. Parents who consulted a healthcare source to obtain further information about HPV had greater HPV and HPV vaccine knowledge and acceptability. HPV and HPV vaccine awareness and acceptability are strongly associated with child gender and age, which correlates with the current immunization program.

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HPV; HPV vaccine; vaccination; knowledge; acceptability; HPV-related diseases; adolescent; parents; information source; factors

Introduction

Human Papillomavirus (HPV) is one of the most common sexually transmitted infections: it is estimated that between 75% and 80% of sexually active individuals will come into contact with the virus.[1] Although most infections are cleared by the immune system within a few months, about 5%-10% of them may persist.[2] The persistence of HPV infection can cause diseases such as genital warts, precancerous lesions, and certain cancers such as cervical, vulvar, vaginal, anal, penile and head and neck cancers.[3] The prevention of HPV infections through vaccination is the most promising and efficacious strategy against such a common sexually transmitted infection.[2] Currently, there are three vaccines available in Spain: the tetravalent and the bivalent vaccine that are available since 2007, and the non-avalent vaccine that is available since 2017.[4]

In Spain, the National Immunization Program (NIP) commenced in 2007 and currently targets only 12-year-old girls. According to the latest data available, the average vaccination coverage rate in girls in 2019 was 79.0% for the 2-dose schedule.[5] However, since 2018, the Spanish Association of Pediatricians (AEP) recommends HPV vaccination for boys and girls at the age of 12 years, although vaccination for boys is not funded yet.[6]

Over these years, the Spanish studies that evaluated knowledge of HPV, vaccine acceptability and drivers of HPV vaccination had focused exclusively on female or adult populations and were performed in specific regions across Spain, not being representative of the entire country.[7–9] Therefore, in 2019–2020, we conducted the KAPPAS study: **K**nowledge and **A**cceptability of **P**apillomavirus Vaccines in **P**arents of **A**dolescents in **S**pain. It is the first national, cross-sectional, multicenter survey research to assess HPV knowledge and vaccine acceptability among the parents of adolescents in Spain.[10] Recruitment and analysis performed in this study, offer an innovative approach to obtain relevant insights about current HPV vaccination knowledge and acceptability that will be also useful for a future implementation for a gender-neutral vaccination program in the country.

Recommendations on HPV vaccination are widespread across the WHO (World Health Organization) European Region, and the number of countries that have introduced gender-neutral vaccination (GNV) programs, targeting girls and boys, has increased in recent years.[11] A recent targeted literature review highlights that 28% of WHO European countries were providing fully- or partially funded HPV vaccination programs for both genders, girls and boys, by 2018–2019.[9] In those countries where HPV GNV programs have been implemented, vaccine coverage rates reach similar percentages among boys and girls.[12]

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The factors associated with HPV knowledge and vaccine acceptability in adolescents and their parents in countries where HPV vaccine is licensed had been studied in the literature.[13–15] According to a previous systematic literature review that examined seventy non-interventional studies conducted in 16 European countries, the main factors associated with HPV knowledge were female gender, higher education and higher-income group.[13] The factors associated with HPV vaccine acceptability were female gender and younger age of the responding parents, female gender of the child, having received previous vaccinations during the childhood and previous confidence in vaccine efficacy.[13] In addition, other publications found significant correlations between an increased acceptability of HPV vaccine and the improvement of awareness and knowledge of HPV infection and vaccination.[16] Despite all the previous studies, vaccination coverage rates are still suboptimal, and a deeper understanding of factors influencing parental HPV vaccination knowledge and acceptability is critical to ensure the successful implementation of HPV vaccination programs.[17–20]

Moreover, vaccine misinformation and infodemia are increasing threats during the SARS-CoV2 (Severe acute respiratory syndrome coronavirus 2) pandemic.[21,22] The WHO recently published a guide on misinformation management which also underscores the importance of promoting informed health decisions based on accurate and scientific information.[23] Information sources are a critical factor to overcome these threats and few studies have assessing their impact among parents of adolescents for HPV vaccination.[24,25]

The results of the primary objective of the KAPPAS, assessing HPV knowledge and vaccine acceptability in general, are subject of a separate publication and have been already presented elsewhere.[8] Here, we address the results of the secondary objectives of the KAPPAS study, focused on assessing the factors influencing HPV knowledge and vaccine acceptability in parents of adolescent children.

Materials and methods

Study design and setting

This study is an analysis of secondary outcomes of the KAPPAS study: a cross-sectional, multicenter survey research study. Twenty-four (24) sites (public and private) across Spain participated in the study. Recruitment was performed through pediatricians and targeted the fathers, mothers or legal tutors of children (girls and/or boys) aged 9 to 14 years who had been living in Spain for the last 12 months at least.

The study secured the approval of the reference Investigational Ethical Committee (IEC) on January 8, 2019. Other local IEC also approved the protocol when necessary.

Survey development

A structured survey was developed to collect epidemiological variables as well as knowledge- and acceptance-related measurements. The questionnaire was developed on the basis of a previous systematic literature review[13] carried out by our group to identify published studies and items used to evaluate parental and/or adolescent HPV knowledge and/or HPV vaccination acceptability. The draft questionnaire was then validated by an Expert Committee comprised of 4 expert pediatricians in HPV and adolescents. It was subsequently tested by means of a cognitive debriefing methodology on a representative sample of 12 parents following the adjustment of wording and comprehensiveness according to the participants' suggestions. The final version of the questionnaire was validated by the Expert Committee.

The survey (included in the Supplementary material) included five sections: 1) *sociodemographic characteristics* (15 items); 2) *knowledge of HPV* (9 items); 3) *knowledge of vaccines and their acceptability in general* (5 items); 4) *HPV vaccination knowledge* (8 items); 5) *HPV vaccine acceptability* (7 items). The points were summated to create a total score. The *Degree of HPV knowledge total* score ranged from 0 to 40, the *Degree of HPV vaccine acceptability* ranged from 0 to 5, the *Degree of HPV vaccination knowledge* ranged from 0 to 21 and the *Degree of knowledge of vaccines and their acceptability in general* ranged from −10 to 10. All questions were either open- or closed using the appropriate response scale depending on the specific question (yes/no, yes/no/not sure, ordinal scale of level of agreement or specific response options, when needed).

Data collection

The parents were invited to complete the study survey (either online or in a paper-and-pen format) by the investigator following the order generated by a randomization tool and according to stratification quotas defined to ensure population representativeness.

An active recall recruitment process was designed to avoid any selection bias, since chronically ill patients may attend pediatrician offices more frequently than healthy children. All children between 9 and 14 years old were identified through investigator databases or medical records and were divided into stratification quotas based on gender (male/female), age (9–11 y.o./12-14 y.o.) and HPV vaccine coverage rate (VCR) in the region (high/low). Parents had to complete the study survey exclusively for the selected son or daughter. All the participants gave their consent before filling in the survey.

Statistical analysis

The potential factors assessed that might influence HPV knowledge and HPV vaccine acceptability were: HPV vaccination status (yes/no); gender (boys/girls), age (9–11 y.o./ 12–14 y.o.); HPV VCR in the region (since the mean national VCR was 77.8% in 2016, latest data available when the protocol was approved, regions with a VCR of ≤77.8% and >77.8% were regarded as low- and high-VCR regions, respectively); the gender of the respondent parent (male/female); region; province; location (urban, semi-urban, rural); type of center (private vs. public); parent's age; educational level; work status; nationality; marital status; parent's vaccination status; number of children; gender of the children in the family (proportion of daughters ≥50% or <50%) and having at least one daughter over the age of 9.

The t-test for independent samples was considered when mean differences associated with dichotomous variables were analyzed. The one-way ANOVA for independent measures was

chosen for polytomous questions. Tukey HSD (Honest Significant Difference) pairwise comparisons were considered. Chi-square tests were computed to measure the association between qualitative variables.

Two regression analyses were performed to evaluate the effect of the different variables on knowledge of HPV and the acceptability of the HPV vaccine. For this purpose, ordinary least squares regression analyses were carried out with best subsets regression as an exploratory model for building regression analyses. A random forest algorithm was considered due to problems with collinearity and link function with the linear regression model when explaining the degree of acceptability of the HPV vaccine.

Results

A total of 3,110 participants were selected and contacted, 1,071 of whom did not answer and 55 declined to participate. After the invalid survey responses had been excluded (n = 79) 1,405 surveys were considered valid for the analysis (1,116 online and 289 paper-based) (see reasons for invalid surveys in Figure S1). The parents' sociodemographic profile is provided in the Supplementary Material (Table S1), most of them were mothers (86.19%) aged between 40 and 49 years (69.11%). 52.38% of the children on whom the survey was completed were girls. The mean age of these children was 11.49 years, and 27.83% of them were vaccinated against HPV. Among the vaccinated ones, 87.98% were girls and 12.02% were boys.

Factors determining HPV knowledge and HPV vaccine knowledge and acceptability

Factors related to the child for whom the survey was completed

Child gender. Parental knowledge and acceptability of HPV vaccine was significantly higher when the parents´ answers refers to a girl compared to a boy ($p < .001$) (Figure 1). Mean estimations are obtained based on the responses to the items of the questionnaire, as described in the Supplementary material.

Total scores for the sections "HPV knowledge" and "knowledge and acceptance of vaccines in general" do not differ significantly by the child gender. (Figure 1).

Child age. The parents who responded the survey about a child aged 12–14 years old obtained slightly but significantly higher mean scores regarding knowledge and acceptability of HPV vaccine compared to parents with a child aged 9–11 years (knowledge of HPV vaccine: $p = .009$; acceptability of HPV vaccine: $p = .001$) (Figure 1). There were no significant

Figure 1. Child-related factors influencing HPV knowledge and HPV vaccine acceptability. (a) Child gender. (b) Child age. (c) Child vaccination status. Boxplot representations of scores for, from left to right, HPV knowledge (score range: 0 to 40), knowledge and acceptance of vaccines in general (score range: −10 to 10), HPV vaccine knowledge (score range: 0 to 21) and HPV vaccine acceptability (score range: 0 to 5). The line inside the box represents the median. The lower and upper boundaries of each box indicate Q1 and Q3, respectively.

differences when comparing both child age groups regarding HPV knowledge and knowledge and acceptance of vaccines in general (Figure 1).

Child's HPV vaccination status. Parents of vaccinated children obtained significantly higher mean scores in all 4 knowledge and acceptability variables compared to those who did not know their child's vaccination status or whose child was not vaccinated (knowledge of HPV: p = .005; knowledge and acceptance of vaccines in general: p = .006; knowledge of HPV vaccine: p < .0001; acceptability of HPV vaccine: p < .001) (Figure 1).

Factors related to family/parental characteristics

Parent gender

Mothers obtained significantly higher mean scores than fathers in knowledge of HPV (p < .001), knowledge of HPV vaccine (p < .001) and acceptability of the HPV vaccine (p = .001) (Figure 2). There were no differences in parent gender with regard to knowledge and acceptability of vaccines in general (Figure 2).

Parental HPV vaccination status

Parents who reported to be vaccinated against HPV evinced greater knowledge of HPV vaccine (p = .007) and greater acceptability of HPV vaccine (p < .001) (Figure 2). However, no differences were found for HPV knowledge or acceptability of vaccines in general (Figure 2).

Parental age

The acceptability of the HPV vaccine was not statistically different among groups of parents according to age. However, mean HPV vaccine knowledge was lower in parents aged 30–39 years compared to parents over 40 years (p < .001). Regarding HPV knowledge, parents aged 40–49 years obtained significantly higher mean total scores than those aged 30–39 years (p = .002). Finally, parents aged 50 or older obtained higher means in knowledge and acceptability of vaccines in general (p = .028).

Parental educational level

The average level of knowledge of HPV, HPV vaccine and knowledge and acceptance of vaccines in general increased significantly as the educational level of the parents increased (p < .001 all variables), although no differences were found in their level of acceptability of HPV vaccine.

Having at least one daughter

Having at least one daughter was associated with significantly greater knowledge (p = .004); and acceptability of HPV vaccine (p < .001). No differences were observed for HPV knowledge (Figure 2).

Number of daughters in the family

The mean HPV vaccine knowledge score was significantly higher among families in whom less than 50% of the children were daughters vs. ≥50% being daughters; p < .001. In contrast, the acceptability of HPV vaccine was significantly higher among parents with a lower proportion of daughters in the family (<50% daughters vs. ≥50% daughters; p < .001). No significant differences between the proportion of daughters in the family and the knowledge of HPV and knowledge and acceptance of vaccines in general were found (Figure 2).

Having at least 1 daughter of vaccination age (≥9 years old)

The results showed that having at least one ≥9-year-old daughter was associated with significantly higher scores in HPV vaccine knowledge (p < .001) and acceptability (p < .001). However, no differences were found for HPV knowledge or knowledge and acceptability of vaccines in general (Figure 2).

Other parental or family factors

No significant differences were observed with regard to knowledge of HPV, knowledge of HPV vaccine and acceptability of HPV vaccine when the groups were compared according to: parent's employment status (unemployed vs. part-time vs. full-time), nationality (Spanish vs. other), marital status (married vs. not married) and number of children (1 vs. 2 vs. 3 vs. 4 or more) [data not shown].

Other sociodemographic factors

Region vaccine coverage rate

Statistically significant differences were found when parental knowledge scores in regions with different VCR were compared, although no differences were observed regarding HPV vaccine acceptability (knowledge of HPV (range 0–40): high VCR: 29.35 vs. low VCR: 28.59; p < .001; knowledge and acceptance of vaccines in general (range −10 to 10): high VCR: 6.41 vs. low VCR: 6.77; p = .038; knowledge of HPV vaccine (range 0–21): high VCR: 15.72 vs. low VCR: 15.31; p = .009).

Province, place of residence and type of center

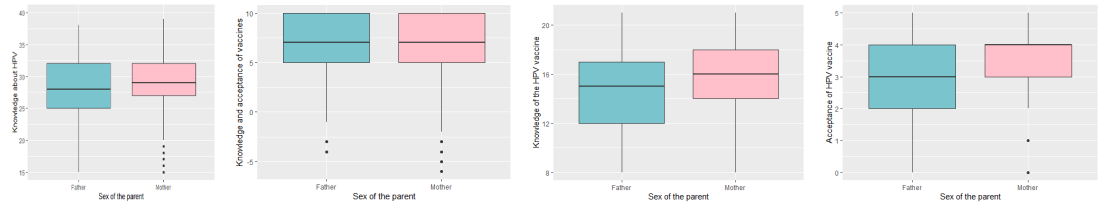
Mean scores in HPV knowledge were not statistically different according to the place of residence. Results considering whether the type of center was public or private did not show significant differences, except for the knowledge and acceptance of vaccines in general (range −10 to 10), which was higher among parents recruited from private centers (public, 6.19 vs. private, 7.50; p < .001).

Multivariate analysis

Knowledge of HPV

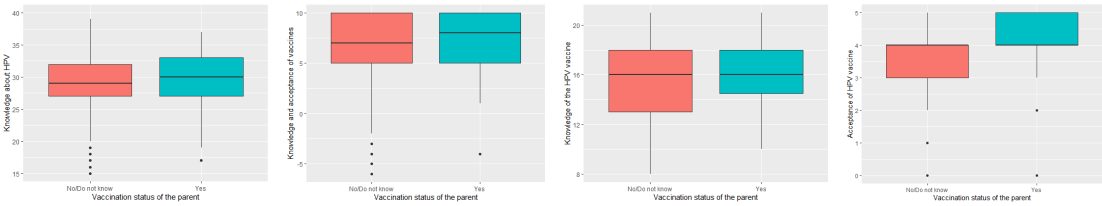
After 11 independent variables that were significantly associated with the degree of knowledge about HPV according to a bivariate t-test analysis had been identified, the multivariate regression model revealed that the most relevant variables for explaining the degree of knowledge of HPV were 1) knowledge of HPV vaccine, 2) consulting a healthcare source about HPV infection. This model accounts for 51.1% of the variance of the knowledge of HPV (Table 1).

a.



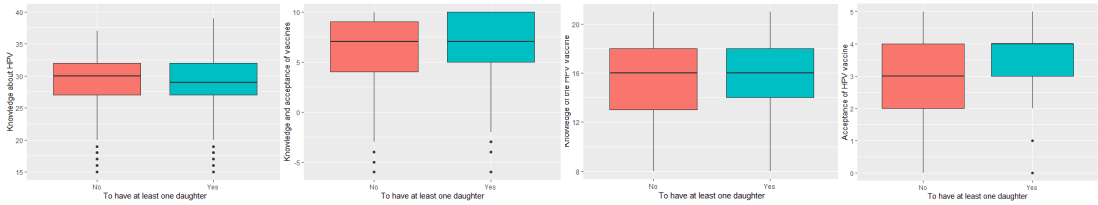
Mean (95%CI); Min. Max				
Father	27.54 (26.80 ; 28.30) 15.00,38.00	6.74 (6.29 ; 7.19) -4.00,10.00	14.41 (13.90 ; 14.90) 8.00,21.00	3.05 (2.83 ; 3.26) 0.00,5.00
Mother	29.15 (28.90 ; 29.40) 15.00,39.00	6.59 (6.41 ; 6.77) -6.00,10.00	15.66 (15.50 ; 15.80) 8.00,21.00	3.42 (3.34 ; 3.49) 0.00,5.00
p	p<0.001	p=n.s.	p<0.001	p=0.001

b.



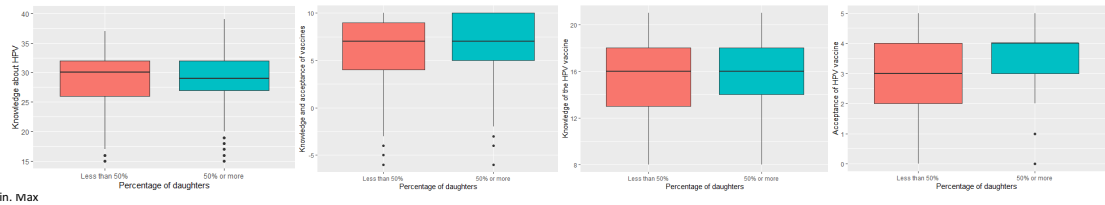
Mean (95%CI); Min. Max				
No/Do not know	28.90 (28.60; 29.10); 15.00,39.00	6.57 (6.40; 6.75); -6.00,10.00	15.40 (15.30; 15.60); 8.00,21.00	3.31 (3.24; 3.39); 0.00,50.00
Yes	29.70 (28.90; 30.50); 17.00,37.00	7.05 (6.50; 7.59); -4.00,10.00	16.10 (15.70; 16.60); 10.00,21.00	4.01 (3.82; 4.20); 0.00,5.00
p	p=n.s.	p=n.s.	p=0.007	p<0.001

c.



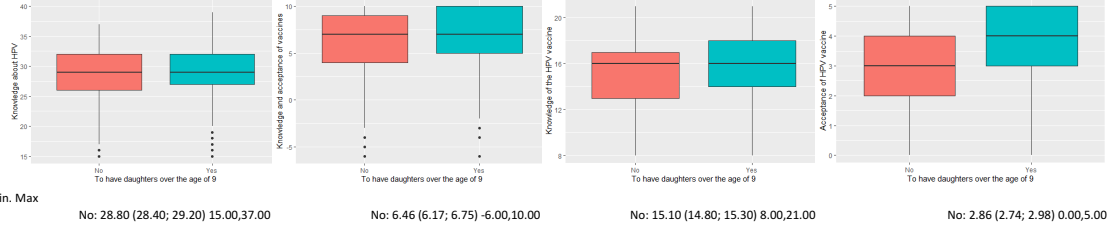
Mean (95%CI); Min. Max				
No	28.90 (28.40; 29.40) 15.00,37.00	6.31 (5.98; 6.64) -6.00,10.00	15.10 (14.80; 15.40) 8.00,21.00	2.89 (2.75; 3.02) 0.00,5.00
Yes	28.90 (28.70; 29.20) 15.00,39.00	6.72 (6.53; 6.91) -6.00,10.00	15.60 (15.50; 15.80) 8.00,21.00	3.55 (3.46; 3.63) 0.00,5.00
p	p=n.s.	p=0.032	p=0.004	p<0.001

d.



Mean (95%CI); Min. Max				
<50%	28.80 (28.40; 29.30) 15.00,37.00	6.42 (6.12; 6.72) -6.00,10.00	15.10 (14.80; 15.40) 8.00,21.00	3.95 (2.82; 3.07) 0.00,5.00
≥ 50%	29.00 (28.70; 29.20) 15.00,39.00	6.70 (6.50; 6.90) -6.00,10.00	15.70 (15.50; 15.90) 8.00,21.00	3.57 (3.48; 3.65) 0.00,5.00
p	p=n.s.	p=n.s.	p<0.001	p<0.001

e.



Mean (95%CI); Min. Max				
No	No: 28.80 (28.40; 29.20) 15.00,37.00	No: 6.46 (6.17; 6.75) -6.00,10.00	No: 15.10 (14.80; 15.30) 8.00,21.00	No: 2.86 (2.74; 2.98) 0.00,5.00
Yes	Yes: 29.00 (28.70; 29.30) 15.00,39.00	Yes: 6.69 (6.48; 6.89) -6.00,10.00	Yes: 15.70 (15.50; 15.90) 8.00,21.00	Yes: 3.64 (3.55; 3.72) 0.00,5.00
p	p=n.s.	p=n.s.	P<0.001	p<0.001

Figure 2. Factors related to family/parental characteristics influencing HPV knowledge and HPV vaccine acceptability. (a) Parent gender. (b) Parental HPV vaccination status. (c) Having at least one daughter. (d) Number of daughters in the family. (e) Having at least one daughter of vaccination age (≥9 y.o.). Boxplot representations of scores for, from left to right, HPV knowledge (score range: 0 to 40), knowledge and acceptance of vaccines in general (score range: −10 to 10), HPV vaccine knowledge (score range: 0 to 21) and HPV vaccine acceptability (score range: 0 to 5). The line inside the box represents the median. The lower and upper boundaries of each box indicate Q1 and Q3, respectively.

Acceptability of HPV vaccine

The individual bivariate analysis identified 13 independent variables that were significantly associated with the degree of acceptability of the HPV vaccine. The multivariate model for the acceptability of HPV vaccine based on a Random Forest algorithm included the following variables: 1) child's vaccination status, 2) total score in knowledge of HPV vaccine, 3) total score in knowledge and acceptability of vaccines in general, 4)

Table 1. Multivariate models for HPV knowledge and acceptability of HPV vaccine.

	HPV knowledge	HPV vaccine acceptability	
Model	Linear regression (p < .001)	Random forest**/importance of each variable in random forest	
Independent variables*	Knowledge of HPV vaccine	Child's vaccination status	498.180
	Healthcare source consulted about HPV infection (p < .001)	Total score in knowledge of HPV vaccine	245.713
		Total score in knowledge and acceptability of vaccines in general	211.305
		Healthcare source consulted about HPV vaccine	186.464
		Total score in knowledge of HPV	166.057
		Parent's vaccination status	22.316
R^2	0.511	0.533	

*Independent variables are listed in order of importance.
**As the linear regression model has problems with collinearity and link function, a model based on a Random Forest algorithm was developed. The Random Forest model cannot produce regression coefficients, although the order of the variables included is indicative of their relative importance in the model.

healthcare source consulted about HPV vaccine, 5) total score in knowledge of HPV and 6) parent's vaccination status. The model accounts for 53.1% of the variance of the acceptability of the HPV vaccine (Table 1).

Impact of the sources of information consulted and knowledge of HPV, HPV vaccine and its acceptability

Specific analyses were carried out considering the type of source consulted by parents. A distinction was made between healthcare sources, which included pediatricians, general physicians, gynecologists, urologists, nurses, pharmacists and other healthcare professionals; and non-healthcare sources, such as school, family and friends, press, radio/TV, the Internet/social media, amongst others. The results showed that parents who consulted healthcare sources about HPV infection achieved a higher mean knowledge of HPV, knowledge of HPV vaccine and acceptability of HPV vaccine (all of them p < .001), although no differences were observed with regard to knowledge and acceptance of vaccines in general (p = .525) (Figure 3). Similarly, parents who consulted a healthcare source about HPV vaccine had a significantly higher mean score in all 4 main variables: knowledge of HPV (p < .001), knowledge of HPV vaccine (p < .001), acceptability of HPV vaccine (p < .001) and knowledge and acceptance of vaccines in general (p = .003) (Figure 3).

The differences in total scores when the specific healthcare source consulted was considered showed that gynecologists and pediatricians may provide more accurate information to parents. Parents who consulted other healthcare sources tended to obtain lower scores in terms of knowledge of HPV and HPV vaccine and acceptability (Table 2). Knowledge means were also higher when parents consulted the Internet or radio/TV, although their HPV vaccine acceptability was significantly lower. In general, consulting other sources led to lower mean scores in knowledge and acceptability of HPV vaccine (Table 3).

Further information sources

In line with the results of the sources consulted, parents who stated that they would consult a healthcare source to get information about HPV infection or HPV vaccine also obtained significantly higher mean scores in HPV and HPV vaccine knowledge and HPV vaccine acceptability (p < .05 in all three variables, data not shown).

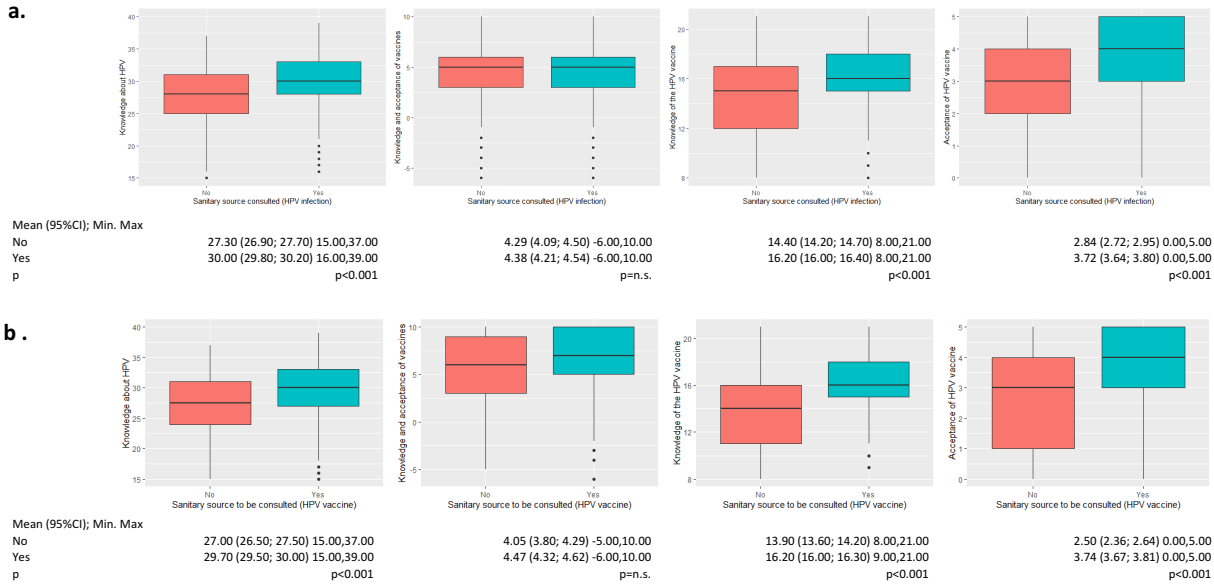


Figure 3. Influence of consulting healthcare sources about HPV infection (a) or HPV vaccine (b) on HPV knowledge and HPV vaccine acceptability. Boxplot representations of scores for, from left to right, HPV knowledge (score range: 0 to 40), knowledge and acceptance of vaccines in general (score range: −10 to 10), HPV vaccine knowledge (score range: 0 to 21) and HPV vaccine acceptability (score range: 0 to 5). The line inside the box represents the median. The lower and upper boundaries of each box indicate Q1 and Q3, respectively.

Table 2. Knowledge and acceptability scores according to whether or not respondents had consulted each healthcare source.

Type of source and variable	Gave information about	Not consulted mean (SD)	Consulted mean (SD)	p
Pediatrician				
HPV knowledge	HPV	29.28 (3.89)	29.98 (3.68)	0.001
	HPV vaccine	28.83 (4.22)	29.71 (3.96)	<0.001
Vaccine knowledge and acceptance	HPV	6.64 (3.20)	6.77 (3.07)	0.487
	HPV vaccine	6.53 (3.20)	6.88 (3.02)	0.045
HPV vaccine knowledge	HPV	15.57 (2.81)	16.17 (2.60)	<0.001
	HPV vaccine	15.39 (2.78)	16.16 (2.53)	<0.001
HPV vaccine acceptance	HPV	3.08 (1.33)	3.86 (1.17)	<0.001
	HPV vaccine	2.86 (1.36)	3.83 (1.11)	<0.001
General Physician				
HPV knowledge	HPV	29.60 (3.80)	29.48 (3.88)	0.747
	HPV vaccine	29.26 (4.11)	29.95 (3.87)	0.022
Vaccine knowledge and acceptance	HPV	6.71 (3.17)	6.61 (2.80)	0.755
	HPV vaccine	6.74 (3.11)	6.77 (3.03)	0.916
HPV vaccine knowledge	HPV	15.84 (2.73)	15.79 (2.81)	0.848
	HPV vaccine	15.80 (2.66)	16.20 (2.58)	0.038
HPV vaccine acceptance	HPV	3.40 (1.32)	3.72 (1.20)	0.016
	HPV vaccine	3.38 (1.33)	3.86 (1.07)	<0.001
Gynecologist				
HPV knowledge	HPV	29.21 (3.99)	30.49 (3.19)	<0.001
	HPV vaccine	28.99 (4.25)	30.39 (3.41)	<0.001
Vaccine knowledge and acceptance	HPV	6.63 (3.15)	6.85 (3.13)	0.258
	HPV vaccine	6.60 (3.12)	7.12 (2.98)	0.006
HPV vaccine knowledge	HPV	15.58 (2.85)	16.44 (2.33)	<0.001
	HPV vaccine	15.61 (2.72)	16.54 (2.32)	<0.001
HPV vaccine acceptance	HPV	3.31 (1.37)	3.72 (1.12)	<0.001
	HPV vaccine	3.34 (1.36)	3.78 (1.04)	<0.001
Urologist				
HPV knowledge	HPV	29.58 (3.82)	31.25 (2.19)	0.069
	HPV vaccine	29.35 (4.08)	31.08 (3.46)	0.023
Vaccine knowledge and acceptance	HPV	6.69 (3.15)	8.00 (2.33)	0.240
	HPV vaccine	6.72 (3.10)	8.50 (2.00)	<0.001
HPV vaccine knowledge	HPV	15.83 (2.73)	17.38 (2.20)	0.087
	HPV vaccine	15.85 (2.66)	16.79 (2.19)	0.047
HPV vaccine acceptance	HPV	3.43 (1.32)	3.25 (0.71)	0.492
	HPV vaccine	3.46 (1.31)	3.71 (0.86)	0.176
Nurse				
HPV knowledge	HPV	29.52 (3.82)	30.67 (3.56)	0.008
	HPV vaccine	29.30 (4.11)	30.20 (3.67)	0.021
Vaccine knowledge and acceptance	HPV	6.70 (3.14)	6.73 (3.22)	0.930
	HPV vaccine	6.74 (3.10)	6.86 (3.06)	0.689
HPV vaccine knowledge	HPV	15.79 (2.74)	16.49 (2.48)	0.025
	HPV vaccine	15.82 (2.66)	16.37 (2.51)	0.029
HPV vaccine acceptance	HPV	3.41 (1.32)	3.76 (1.15)	0.020
	HPV vaccine	3.43 (1.32)	3.75 (1.23)	0.011
Pharmacist				
HPV knowledge	HPV	29.56 (3.81)	30.75 (3.66)	0.082
	HPV vaccine	29.37 (4.07)	29.84 (4.49)	0.528
Vaccine knowledge and acceptance	HPV	6.76 (3.16)	7.59 (2.35)	0.103
	HPV vaccine	6.73 (3.11)	7.65 (2.29)	0.036
HPV vaccine knowledge	HPV	15.80 (2.74)	17.35 (2.06)	<0.001
	HPV vaccine	15.84 (2.65)	16.80 (2.58)	0.051
HPV vaccine acceptance	HPV	3.43 (1.32)	3.68 (0.98)	0.171
	HPV vaccine	3.46 (1.31)	3.65 (0.98)	0.432
Other healthcare professionals				
HPV knowledge	HPV	29.49 (3.79)	30.87 (3.88)	<0.001
	HPV vaccine	29.33 (4.07)	30.16 (4.08)	0.074
Vaccine knowledge and acceptance	HPV	6.69 (3.13)	6.78 (3.26)	0.783
	HPV vaccine	6.74 (3.10)	6.92 (2.91)	0.586
HPV vaccine knowledge	HPV	15.76 (2.73)	16.80 (2.66)	<0.001
	HPV vaccine	15.81 (2.65)	16.67 (2.60)	0.004
HPV vaccine acceptance	HPV	3.42 (1.32)	3.59 (1.19)	0.224
	HPV vaccine	3.45 (1.32)	3.63 (0.98)	0.114

Discussion

KAPPAS preliminary findings showed that the degree of knowledge of HPV in Spain is still modest despite high vaccine acceptability.[8] The specific results of the secondary objectives of the study, reported here, suggests that parental awareness of HPV infection and vaccination, as well as HPV vaccine acceptability, are still strongly associated with their children's gender and age, probably influenced by the Spanish NIP, which currently targets only 12-year-old girls. HPV vaccine awareness is greater among parents with children who match the profile currently funded by the NIP. In line with our findings, previous research showed that the acceptability of HPV vaccination among the male population was diminished by a lack of awareness and knowledge and a general perception of lower benefits of HPV vaccination for males.[26]

Table 3. Knowledge and acceptability scores according to whether or not respondents had consulted other non-healthcare sources.

Type of source and variable	Gave information about	Not consulted mean (SD)	Consulted mean (SD)	p
Internet/social media				
HPV knowledge	HPV	29.07 (3.84)	30.39 (3.62)	<0.001
	HPV vaccine	29.11 (4.07)	30.20 (3.98)	<0.001
Vaccine knowledge and acceptance	HPV	6.72 (3.11)	6.66 (3.20)	0.756
	HPV vaccine	6.76 (3.07)	6.73 (3.14)	0.877
HPV vaccine knowledge	HPV	15.91 (2.69)	16.19 (2.77)	<0.001
	HPV vaccine	15.69 (2.65)	16.38 (2.58)	<0.001
HPV vaccine acceptance	HPV	3.49 (1.31)	3.34 (1.32)	0.040
	HPV vaccine	3.53 (1.29)	3.27 (1.31)	0.002
School				
HPV knowledge	HPV	29.54 (3.83)	30.24 (3.59)	0.070
	HPV vaccine	29.29 (4.14)	30.32 (3.22)	0.002
Vaccine knowledge and acceptance	HPV	6.72 (3.11)	6.50 (3.53)	0.501
	HPV vaccine	6.73 (3.11)	6.95 (2.94)	0.473
HPV vaccine knowledge	HPV	15.76 (2.74)	16.65 (2.57)	0.002
	HPV vaccine	15.78 (2.67)	16.72 (2.29)	<0.001
HPV vaccine acceptance	HPV	3.40 (1.32)	3.73 (1.27)	0.015
	HPV vaccine	3.44 (1.30)	3.75 (1.24)	0.012
Family/Friends				
HPV knowledge	HPV	29.55 (3.89)	29.66 (3.68)	0.587
	HPV vaccine	29.27 (4.15)	29.60 (3.92)	0.161
Vaccine knowledge and acceptance	HPV	6.77 (3.16)	6.60 (3.11)	0.359
	HPV vaccine	6.76 (3.13)	6.70 (3.03)	0.669
HPV vaccine knowledge	HPV	15.89 (2.73)	15.76 (2.74)	0.409
	HPV vaccine	15.79 (2.67)	16.00 (2.61)	0.162
HPV vaccine acceptance	HPV	3.51 (1.32)	3.32 (1.31)	0.016
	HPV vaccine	3.55 (1.29)	3.29 (1.29)	<0.001
Press				
HPV knowledge	HPV	29.34 (3.82)	30.23 (3.71)	<0.001
	HPV vaccine	29.25 (4.09)	29.93 (3.97)	0.019
Vaccine knowledge and acceptance	HPV	6.58 (3.13)	6.90 (3.15)	0.035
	HPV vaccine	6.71 (3.09)	6.91 (3.10)	0.370
HPV vaccine knowledge	HPV	15.65 (2.78)	16.31 (2.55)	<0.001
	HPV vaccine	15.78 (2.68)	16.25 (2.63)	0.012
HPV vaccine acceptance	HPV	3.48 (1.31)	3.31 (1.33)	0.033
	HPV vaccine	3.55 (1.26)	3.09 (1.38)	<0.001
Radio/TV				
HPV knowledge	HPV	29.52 (3.84)	29.78 (3.73)	0.270
	HPV vaccine	29.37 (4.11)	29.43 (3.96)	0.807
Vaccine knowledge and acceptance	HPV	6.59 (3.18)	6.98 (3.03)	0.048
	HPV vaccine	6.71 (3.09)	6.88 (3.08)	0.415
HPV vaccine knowledge	HPV	15.73 (2.78)	16.10 (2.60)	0.029
	HPV vaccine	15.84 (2.66)	15.97 (2.64)	0.470
HPV vaccine acceptance	HPV	3.51 (1.32)	3.24 (1.29)	0.001
	HPV vaccine	3.58 (1.26)	3.05 (1.34)	<0.001
Other				
HPV knowledge	HPV	29.53 (3.76)	30.12 (4.14)	0.079
	HPV vaccine	29.44 (3.96)	28.74 (5.20)	0.185
Vaccine knowledge and acceptance	HPV	6.74 (3.09)	6.39 (3.51)	0.203
	HPV vaccine	6.78 (3.05)	6.37 (3.58)	0.273
HPV vaccine knowledge	HPV	15.81 (2.72)	16.03 (2.83)	0.356
	HPV vaccine	15.92 (2.62)	15.19 (2.97)	0.016
HPV vaccine acceptance	HPV	3.46 (1.30)	3.24 (1.39)	0.071
	HPV vaccine	3.50 (1.28)	3.06 (1.45)	0.004

Furthermore, an association was found between HPV knowledge and HPV vaccine acceptability and parent gender, which was higher among mothers than fathers. These results are in line with the findings of Mortensen et al., 2015, who described that one of the main variables related to HPV knowledge and vaccine acceptability is parent gender.[27] Nevertheless, it is important to mention that the percentage of fathers who answered the KAPPAS survey was 13.81%, which constitutes a small sample size.

Some of the explanatory factors observed in this study were also considered as significant variables when the correlation with the degree of acceptability of the HPV vaccine was explained or studied in previous works.[15,28–30] In our study, some of the most relevant variables for explaining the degree of knowledge of HPV and HPV vaccine acceptability proved to be the degree of knowledge of HPV vaccine and consulting a healthcare source about HPV infection.

Previous research has found that the potential predictors of HPV vaccine acceptability are previous knowledge of HPV,[31] and one of the main predictors is advice from healthcare personnel.[6] The role of vaccination status (of parent or child) has been also reported in the literature.[6,32,33] As our group already found, acceptability of the HPV vaccine is a more complex multifaceted construct reflecting the extent to which people delivering or receiving a healthcare intervention consider it to be appropriate, based on anticipated or previous

responses to the intervention.[13] Providing the population with evidence-based scientific data is beneficial and crucial, although it does not necessarily lead individuals to understand or interpret such information correctly.[34] Although poor health literacy is regarded as a cause of vaccine hesitancy, it is rarely considered when this subject is discussed. The association between health literacy skills and vaccine acceptability has been shown to be uneven when general measures are used, and also depends on population characteristics and the type of vaccine in question. Vaccine literacy has been constructed upon the same idea of health literacy, although very few specific measuring tools have been developed hitherto. More of these instruments need to be validated and used extensively with the ultimate aim of assessing vaccine literacy skills and defining interventions geared toward improving them.[35]

With regard to HPV-related information, and in line with the findings reported in the literature,[36] our results showed that the degree of knowledge of HPV and the acceptability of the HPV vaccine tended to increase slightly as the number of sources consulted increased.

Healthcare sources of information (pediatrician, gynecologist, family doctor, etc.) played an important role in providing precise and accurate information about HPV and its vaccine, according to our results. Parents tended to be more aware of HPV- and HPV vaccine-related questions, and their acceptability was higher if they consulted a healthcare source, particularly if it was a pediatrician or a gynecologist. In Spain, pediatricians play a very relevant role in providing advice and recommendations about vaccine in children. On the other hand, gynecologists have traditionally been involved in managing HPV-related diseases, and relevant scientific societies in this field recommend individual-based HPV vaccine recommendation.

Our results underline the need to encourage other groups of healthcare professionals (HCPs) besides pediatricians or gynecologists, such as nurses, urologists and specialists in sexually transmitted diseases, to contribute and to join forces in raising awareness of HPV and the benefits of vaccinating against it, among the population at large. Facilitating HCP-initiated discussions and providing clear information about HPV vaccines is key to increasing vaccine acceptability among boys as well.[26] Johnson et al. reported that providing a recommendation for vaccination was the strongest predictor of vaccination in both genders.[37]

The Internet also plays a very important role in conveying information about HPV and HPV vaccine. It was one of the most common sources of information and was associated with greater knowledge, although this did not translate into higher HPV vaccine acceptability. These findings were similar to those reported by McRee et al.[38] These results highlight the importance of the specific online sources consulted, since Moran et al. emphasized that anti-vaccine websites contain a considerable amount of misinformation.[33] In this regard, targeted, balanced and high-quality information should be provided to the relevant population through the appropriate channels that help to improve the acceptability of HPV vaccination and to achieve the goal of eliminating HPV-related diseases.

Given the changing situation toward HPV GNV programs, coordinated efforts should be made to provide balanced information for evidence-based decision-making about HPV vaccination, as it has also been reinforced through studies in other European countries.[15,38] These efforts should focus on raising awareness about the importance of HPV vaccination, not only in girls but also on scaling up to the male population. Currently, there is solid evidence about the role of HPV in other diseases besides cervical cancer: genital warts, precancerous lesions and anal, penile and oropharyngeal cancers[39] Implementing GNV programs seeks not only to protect the male population from the burden of HPV, but also to contribute to extend herd protection to unvaccinated women and also mitigate the impact of an unexpected potential reduction in coverage.[40] Therefore, HPV vaccination in both genders would contribute to the resilience of the vaccination programs, which is key to reach the elimination of HPV-related diseases.[39,40] In addition, training HCPs and improving the quality of the information available on the Internet or alternative channels are key to increasing HPV vaccine uptake.

Some limitations derived from the nature of this study should be considered. Firstly, parent-reported information is subjective and may be affected by social desirability, inaccuracy or mistakes. In addition, multiple testing can lead to spurious relationships showing statistically significant results. Nevertheless, the high consistency of results among bivariate and multivariate statistical analysis is a proof of its robustness. It also should be remembered that individual healthcare professional attitudes may influence parents' perceptions in terms of knowledge of HPV and acceptability of HPV vaccine. In addition, some predictor factors of HPV vaccine knowledge and acceptability could be missing in the survey. However, this risk is very limited, due to the performance of a previous systematic literature review that was used for the development of the survey. In addition, some factors like income level of families, can be extrapolated by the answers provided to other questions such as employment status and level of studies.

In conclusion, HPV infection and vaccine awareness and acceptability are strongly associated with child gender and age, which correlates with the current NIP in Spain, where only 12-year -old girls are targeted. Our study highlights the role of HCPs as a source of information, meaning that parents who had learnt about the HPV vaccine when consulting a healthcare source had greater HPV and HPV vaccine knowledge and acceptability, thereby helping to achieve and maintain high coverage rates and to reach the elimination of HPV-related diseases.

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List of abbreviations

AEP	Spanish Association of Pediatricians
GNV	Gender-neutral vaccination
HCP	Healthcare professionals
HIC	High-income countries
HPV	Human papillomavirus
HSD	Honest significant difference
IEC	Investigational ethical committee
NIP	National immunization program
SARS-Cov2	Severe acute respiratory syndrome coronavirus 2
VCR	Vaccine coverage rate
WHO	World Health Organization

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