

# **Knowledge of the human papillomavirus by social stratification factors**

Running head: Knowledge of human papillomavirus

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**Conflicts of Interest and Source of Funding:**

None declared. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## **Institutional review board**

The study was approved after institutional review at the Primary Health Care Agency of the Cantabria Government (Spain).

## **Authorship**

All authors have agreed on the final version and meet at least one of the following criteria [recommended by the ICMJE ([http://www.icmje.org/ethical\\_1author.html](http://www.icmje.org/ethical_1author.html))].

## **Abstract**

**Background:** Social determinants of health explain most health inequities. Intermediate determinants dictate differences in the exposure and vulnerability of people based on social stratification. Vulnerable women (lower education level, older age, uninsured, etc.) have lower adherence to recommended Pap smear screening guidelines; however, a gap remains concerning the impact of social determinants on human papillomavirus (HPV) infection.

**Objectives:** To analyze the association between the level of knowledge about HPV-infection and HPV-vaccines with education level and residential setting among a sample of Spanish women.

**Methods:** A cross-sectional study at six primary care centers (Cantabria, Spain). All women >21 years consecutively attended by midwives for routine follow-up were invited to participate during the study period (2015-2016) until a convenience sample was recruited (n=1,288). Participants completed an anonymous questionnaire addressing sociodemographic variables (age, education level and residential setting) and the level of knowledge regarding HPV, including general knowledge about infection and knowledge about the HPV-vaccine. Associations between education level (primary, secondary and university) and residential setting (urban, semi-urban and rural) with the level of knowledge of HPV-infection and HPV-vaccine were calculated using adjusted logistic regressions. Dose-response associations were estimated based on p-trend.

**Results:** Compared to university women, a lower education level was associated with limited or no knowledge of either HPV-infection (odds ratio, OR: 2.13; 95% confidence interval, CI: 1.41-3.21) or the HPV-vaccine (OR: 3.59; 95% CI: 2.16-5.97). Women living in rural areas poorly identified “promiscuity” as a risk factor of HPV ( $p<0.001$ ) and “the use of condoms” as a protective factor ( $p<0.001$ ). Moreover, living in rural areas was associated with limited or no knowledge of HPV-infection (OR: 2.03; 95% CI: 1.46-2.80) and HPV-vaccine (OR: 1.66; 95% CI: 1.13-2.46). There were significant dose-response trends: those who were more educated and living in more urban areas had more knowledge about either HPV-infection or the vaccine ( $p<0.01$  in all cases).

**Discussion:** In our sample, the level of knowledge of HPV-infection and HPV-vaccine was high. However, vulnerable women, defined by a lower education level and living in rural areas, presented a greater lack of knowledge regarding HPV-infection and the HPV-vaccine.

*Keywords:* social determinants of health; papillomavirus infections; papillomavirus vaccines; educational status

According to the World Health Organization (WHO), social determinants of health (SDH) are conditions in which people are born, grow, live, work and age, which are the main factors “*responsible for health inequities - the unfair and avoidable differences in health status seen within and between countries*”. (Davis, & Chapa, 2015; World Health Organization, 2010). The core axis of the WHO’s SDH model is the social and political context, the structural determinants -which define the socioeconomic position- and the intermediate determinants; all of which determine the differences in the exposure and vulnerability of people based on social stratification (Davis, & Chapa, 2015; World Health Organization, 2010). The risk of morbidity is associated with lower levels of education and income (Merino-Ventosa, & Urbanos-Garrido, 2018). Furthermore, inequalities in the diagnosis and survival rates of chronic diseases in relation to SDH have been also well documented (Merino-Ventosa, & Urbanos-Garrido, 2018; Palència et al., 2010).

Infection by human papillomavirus (HPV) is the main cause of cervical cancer (CC) (Chelimo, Woulides, Cameron, & Elwood, 2013; Crosbie, Einstein, Franceschi, & Kitchener, 2013; Goodman, 2015), which is the fourth most common cancer worldwide in women, with an estimated incidence above 500.000 cases per year (Ferlay et al., 2019). Currently, the main preventive strategies for HPV in developed countries are early diagnosis via Pap smear screening tests and vaccination.

In Spain, most screening programs for CC are indicated for women between 21-65 years who have maintained sexual relations (Torné Bladéa et al., 2014). Pap smear tests within this program are usually performed by midwives in primary care settings. According to data from the National Health Survey, around 70% of Spanish women regularly participate in CC screening programs (Barrera-Castillo et al., 2019). Participation depends on program outreach and whether a woman proactively seeks to participate, both

of which are negatively associated with various SDH. For instance, it is well documented that women in a socially vulnerable situation (lower education level, living in rural areas, without health insurance, etc.) undergo Pap smears less frequently (Barrera-Castillo et al., 2019; Damiani et al., 2015; Limmer, LoBiondo-Wood, & Dains, 2014).

Given that there is robust scientific evidence on immunogenicity, safety and efficacy of HPV vaccines (Castellsagué et al., 2012, Joura et al, 2015), most developed countries have also implemented immunization programs for young women before they become sexually active (Bonanni et al., 2011; Cortés et al., 2010). In Spain, the current recommendations include the systematic vaccination of all girls between 9 and 14 years old. Nevertheless, the efficiency of population-level immunization programs is closely related to high coverage rates. Findings from a systematic review including 23 European studies reported that low HPV vaccination was associated with high ethnic minority populations, low socio-economic status, the non-adherence of mothers to CC screening, and the lack of previous vaccinations (Fernández de Casadevante, Gil Cuesta, & Cantarero-Arévalo, 2015).

Previous studies focused on women's knowledge about HPV-infection and HPV-vaccine have reported a low level of comprehensive knowledge regarding the viral etiology of CC and the clinical presentation of HPV-infection (Anagnostou, Aletras, & Niakas, 2017; Patel, Jeve, Sherman, & Moss, 2016; Yörük, Açıkgöz, & Ergör, 2016), especially among younger populations (Chan, Chan, Ng, & Wong, 2012; Coles, Patel, Allen, Keeping, & Carroll, 2015; McRae, Martin, O'Leary, & Sharp, 2014). Beyond this age-related effect, the implication of other SDH on knowledge about HPV-infection or HPV-prevention is less known. Thereby, the purpose of our study was to describe the level of knowledge about HPV-infection and HPV-vaccine and to explore its association with education level and residential setting on a sample of Spanish women.



## **METHODS**

### **Study design and population**

A cross-sectional study was performed among women attended by midwives for a routine clinical follow-up at public primary health centers in Spain (Cantabria). First, the study was presented to centers via a Primary Health Care Agency, to request the voluntary participation of midwives. Second, we selected a stratified random sample of six midwives working in six primary care centers, so that each residential setting (urban, semi-urban and rural) was represented by two primary care centers. Midwives received training to standardize the study proceedings, including the recruitment of women and data collection based on an ad-hoc designed questionnaire. Subsequently, all women consecutively attended by these midwives between May of 2015 and June of 2016 were invited to participate until the estimated sample size was reached. The inclusion criteria were being 21 years old or over, and a suitable understanding of Spanish language. Sample size was calculated considering the number of women ascribed to each health center, 95% confidence level, 3% of precision and 50% of expected proportion of women with appropriate knowledge on HPV. Lastly, sample size was adjusted for an estimated 15% attrition due to lack of data, indicating a necessary sample of 1,223 women. All participants provided their informed consent. The study was approved after institutional review at the Primary Health Care Agency of the Cantabria Government (Spain).

### **Study variables**

The study questionnaire collected information regarding women's knowledge about HPV. First, the study questionnaire asked if the participants had previously received information about HPV-infection and HPV-vaccine. If women reported having heard of HPV, we also registered the information sources. Subsequently, to assess the level of knowledge on HPV, women were asked to respond to 12 true/false questions, eight for HPV-infection and four for HPV-vaccine. One point was assigned if respondents provided correct answers to each question and zero if they answered incorrectly. Thus, we obtained two scores, one for knowledge on HPV-infection (ranging 0-8 points) and one for knowledge on HPV-vaccine (ranging 0-4 points). These scores were later translated into two categorical variables, grouping the level of knowledge about HPV-infection in null/low (total score: 0-4 points) and mid-high (>4 points), and the level of knowledge on HPV-vaccine in null/low (total score: 0-2 points) and mid-high (3-4 points).

The questionnaire also included sociodemographic data (date of birth, highest level of studies completed and the name of the city/town of residence). Thereafter, responses regarding the level of academic studies were grouped into an ordinal categorical variable, with the following categories: university, including bachelor, master or doctorate studies; secondary, including high school education or vocational training; and primary, including basic/compulsory education or less. Moreover, the cities/towns of residence were later grouped according to their demographic, economic and geographic characteristics into another ordinal categorical variable, for which the categories were urban, including financial cities with more than 200.000 habitants; semi-urban, including satellite towns of urban areas with 10.000-50.000 habitants; and rural, including towns >50 miles away from urban areas and with less than 10.000 habitants.

## **Data analysis**

Of the 1,459 women initially recruited and surveyed, we excluded 171 subjects who were lacking some questionnaire data; thereby, the analyses were conducted with 1,288 women. Nevertheless, data analyses were subsequently performed using two different subsamples. Thus, the association between the education level and residential setting categories with knowledge on HPV-infection was examined only among women who had previously heard about HPV (n=1,111). In addition, the association between the education level and residential setting categories and knowledge on HPV-vaccine was examined only among women who had received prior information regarding the vaccine (n=800). Crude and adjusted odds ratios (OR) and their 95% confidence intervals (CI) for both associations were obtained by means of logistic regressions. Adjustments included age and education level or residential setting categories, when necessary. To test dose-response relationships we calculated a p-value for linear trend using analogous logistic regression analyses modelling ordinal categories of education level and residential setting as continuous variables.

Subsequently, we ran some ancillary analyses in order to check the robustness of the results. First, we replicated the main analyses with a more sensitive cut-off point to define null/low knowledge (0-3 points for HPV and 0-1 for HPV vaccine). We also performed linear regressions using knowledge on HPV and on HPV vaccine as continuous dependent variables, instead of as categorical variables, as performed in the main analyses.

Additionally, to study the combined effect of education level and residential setting, we built a new variable that included all possible strata, from university-urban to primary-rural, defined by the product of the two original variables. Thereafter, we compared the percentage of null/low knowledge on HPV and its vaccine in each stratum with regards the mean percentage of the whole sample.

Statistical analyses were performed using SPSS v.22.0 statistical program (SPSS Inc., Chicago, Illinois) and STATA v.13 (StataCorp, College Station). Values of  $p < 0.05$  were considered statistically significant.

## **RESULTS**

### **Sample characteristics**

The mean age was 39.1 years (SD=9.8). The following results refer to the subsamples of women who had previously heard of HPV (n=1,111, 86.3%) and HPV-vaccine (n=800, 62.1%), respectively. Among those who had heard of HPV, 41.7% held university degrees, 45.5% had completed secondary education, and 12.9 had primary level studies. The main residence setting was urban (39.0%), followed by semi-urban (35.8%) and rural (25.2%). Within this group, the main information sources on HPV were television and videos (45.2%), health professionals (35.6%) friends (28.2%), internet (18.9%) relatives (16.7%) and high school/university faculty (12.2%). Regarding the group of women who had prior information of HPV-vaccine, 45.8% held a university degree, 43.6% had performed secondary education, and 10.6% had primary level studies. The residential setting was urban for 36.8% of women, semi-urban in 38.4% and rural in 24.9% of cases.

### **Social stratification factors and knowledge about HPV**

The level of knowledge was medium/high for 69.4% of the women regarding HPV-infection and 66.1% for the HPV-vaccine. As the education level decreased, the level of knowledge regarding HPV-infection was lower. Compared to women with university

degrees, women with primary education had less knowledge regarding the protective effect of male condoms (48.3%;  $p=0.001$ ) and the role of promiscuity as a risk factor (52.5%;  $p<0.01$ ) for acquiring HPV-infection. Moreover, women with primary education also had more difficulty to identify HPV-infection as a cause of CC (41.3%;  $p<0.001$ ) and genital warts (10.5%;  $p<0.001$ ). Regarding knowledge on HPV-vaccine, the findings were similar. Women with a lower education level incorrectly associated the purpose of the vaccine with protection against ovarian cancer (38.38%;  $p<0.001$ ) and demonstrated a poorer identification of the vaccine as being protective against CC (67.1%;  $p<0.001$ ) and genital warts (3.5%;  $p<0.01$ ) (Table 1).

Regarding the residential setting, in rural areas there was significantly less knowledge about HPV-infection. Overall, rural women identified promiscuity less as being a risk factor (49.6%;  $p<0.001$ ) and the male condom as a protective factor of HPV ( $p<0.001$ ). Likewise, HPV-infection was more poorly identified as a cause of CC (55.0%;  $p<0.001$ ) and genital warts (15.0%;  $p<0.01$ ). In addition, the proportion of women knowing that HPV-vaccine also protects for some genital warts was significantly lower among rural women (7.0%;  $p<0.01$ ). Conversely, rural women were more prone to believe that the HPV-vaccine offered prevention against ovarian cancer (29.1%;  $p<0.01$ ). (Table 2)

As the education level decreased, the risk of having null/low knowledge of HPV increased. Compared to university women, the estimated risk of null/low knowledge about HPV-infection was double in women with basic education (adjusted OR=2.13; 95%CI: 1.41-3.21;  $p$ -trend  $<0.001$ ) (Table 3). Regarding knowledge of HPV-vaccine, the effect of education was even more pronounced. The adjusted OR (95%CI;  $p$ -trend) for having null/low knowledge about HPV-vaccine was 1.76 (1.27-2.16;  $p<0.001$ ) for women with

secondary education and 3.59 (2.16-5.97;  $p < 0.001$ ) for women with primary education (Table 3). Table 4 shows that, even adjusting by age and education level, women living in rural areas had a twofold probability of having null/low knowledge on HPV-infection (adjusted OR=2.03; 95%CI: 1.46-2.80;  $p$ -trend  $< 0.001$ ) and HPV-vaccine (OR=1.66 (IC95%: 1.13-2.46;  $p$ -trend=0.01).

According to results presented in Figure 1, the associations between education level and HPV knowledge kept stable across all residential settings. In an equivalent manner, the associations between residential settings and HPV knowledge remained throughout all education levels. Nevertheless, women living in rural areas had systematically less HPV-infection knowledge than women from other residential settings, independently of their education level. Analogously, women with primary education had less knowledge about HPV-vaccine than women with secondary or university studies, with independence of their residential setting.

### **Results from ancillary analyses**

Lastly, when we repeated the analyses using more sensitive cut-off points to define null/low knowledge, the results did not materially change. Moreover, the results were along the same lines and were statistically significant when we modelled knowledge on HPV-infection and on HPV-vaccine as continuous variables (data not shown).

## **DISCUSSION**

In this study population, the level of knowledge on HPV and its vaccine was medium/high. Nonetheless, women with a lower education level and living in rural settings presented misconceptions on the factors and pathologies related with HPV infection and the usefulness of the vaccine.

As expected, most women had heard of HPV. This percentage was higher than findings reported in other studies conducted in the UK, US and Australia (Marlow, Zimet, McCaffery, Ostini, & Waller, 2013) or California (Almeida, Tiro, Rodríguez, & Diamant, 2012). The percentage of women who had heard of the vaccine was also high, albeit lower than other studies (Marlow et al., 2013; Osazuwa-Peters et al., 2017).

In our study, the prevalence of women who identified HPV as being a cause of CC was lower than other studies (Marlow et al., 2013; Mohammed et al., 2018; Osazuwa-Peters et al., 2017). However, if we consider the level of general knowledge on factors involved in the transmission of HPV-infection and on HPV-vaccine, this was high, revealing an appropriate overall understanding of HPV and its health implications. Nonetheless, we should consider that our results refer to women attending a consultation with their midwife, which implies a greater interest in their health. Using this convenience sample to estimate the prevalence of knowledge in the general population could result in overestimation. Clearly, the level of knowledge in women recruited among the general population could be lower. One of the strengths of this study is that we studied the knowledge on HPV in adult women, as few studies are available focusing on the adult population.

In our study, the main sources of information on HPV described by respondents were TV and videos, followed by health professionals. Overall, this coincides with other studies (Almeida et al., 2012). It is important to analyze the role of the media when conveying accurate information on health topics, as mass media constitutes one of the main sources of information. Furthermore, social media is acquiring relevance as a means for obtaining information related to health. Precisely, in the case of HPV, a recent review has proposed to analyze the effect of social media on the knowledge, attitudes and behaviors related to HPV (Ortiz, Smith, & Coyne-Beasley, 2019). However, we must also consider the important role of the health system as being a primary source of information (Almeida et al., 2012). In Spain, midwives are the nursing professionals of reference for reproductive and gynecological aspects within primary health care. Therefore, they have an important role regarding the prevention of HPV infections due to their close contact and follow-up throughout a woman's life. They may also collaborate in promoting participation of women in CC screening programs (Wood et al., 2018). Nonetheless, it is important for health professionals to go beyond the biomedical model, which is based on the reason for consultation, the performance of health exams and symptomatic treatments (Tallon et al., 2017). Rather, other relevant factors must be considered, such as the SDH.

Regarding the education level as SDH, the level of knowledge on HPV-infection and HPV-vaccine was greater among those who had completed higher levels. This was especially noticeable among university graduates; a finding that coincides with other similar studies (Marlow et al., 2013; Montgomery, & Smith-Glasgow, 2012). The importance of the level of education in relation to participation in CC screening has already been revealed by other studies, reporting a greater participation among women with higher education levels (Damiani et al., 2012). It is thus reasonable to believe that this preventive behavior may be associated with a greater



level of knowledge regarding HPV. To conclude, it is important to consider education level as being a decisive factor for correcting inequalities regarding the information known to the population (regarding HPV, sexually transmitted diseases, etc.) and, also, concerning access to early detection programs for cancer. In this sense, some authors have noted that women who have a lower education level participate less in opportunistic programs that are based on the sporadic recruitment of patients, or it is the woman herself who assumes an active role in participation (opportunistic programs) (Damiani et al, 2012; Martín-López et al., 2012).

Regarding the residential setting, women living in rural areas have a poorer level of knowledge about HPV-infection and HPV-vaccine, along the lines of other studies which reported that rural women more poorly identified the relationship between HPV and CC (Blake et al., 2015; Mohammed et al., 2018). This unequal access to information according to the residential setting may be related to different factors. First, in rural areas, a different conception of sexual and reproductive health may exist, and therefore rural women may be more reluctant to share their doubts on gynecological issues. Additionally, they may have more limited access to digital platforms (internet). Thus, it has been documented that people who do not use the Internet are less likely to have information on HPV (Osazuwa-Peters et al., 2017). Lastly, it is important to analyze the model of care of health professionals who work in rural contexts (Mohammed et al., 2018).

If we consider these issues in light of inequality, it is important to consider that women who are most vulnerable (i.e. with a lower education and living in a rural setting) may be more susceptible to suffering an infection by HPV as they more poorly identify both the risk and protective factors. Furthermore, a study performed among female university students found a relationship between

the HPV vaccine status and sexual risk behaviors (Fernández-Feito, Antón Fernández & Paz-Zulueta, 2018). Female university students who were not vaccinated reportedly used fewer barrier methods during sexual relations, which consequently doubled the risk of acquiring sexually transmitted diseases. These findings in the university population could be even more unfavorable in lower strata with a lower education level. Further research is recommended to determine the role of knowledge on HPV and its vaccine on adult women in relation to sexual risk behaviors.

Despite the positive and optimistic trend regarding the awareness of HPV-infection and HPV-vaccine uncovered in our research, many gaps in general knowledge remain. We therefore recommend the need to further examine the knowledge that women have concerning HPV and CC, considering basic SDH, such as education level and residential setting. The informative strategies should not be equal or standard for all women as, not only may their level of knowledge vary, but also their personal circumstances (such as age, sexual life, participation in screening) and social circumstances may differ. The individual analysis of the influence of these SDH is a frequent approach, however a broader approach is necessary in order to establish a more comprehensive national objective which considers both structural and contextual factors. (Penman-Aguilar et al., 2016).

Finally, primary health care and nursing professionals have an important role for detecting and addressing health inequities. Furthermore, it is known that these primary care services are most frequently used by people with a lower socioeconomic level (Morteruel, Rodriguez-Alvarez, Martin, & Bacigalupe, 2018). In Spain, health coverage is free, however, despite this, many people receive inappropriate care, possibly in relation to a lack of information, a lower education level and/or fewer resources. Additionally,

the opportunity that these services represent for facing social inequalities has already been documented, as they are able to identify key dimensions, strategies and goals for improving the orientation of primary care centers towards greater equity. These dimensions specifically include the provision of care that addresses inequity (inequity-responsive care) and which looks beyond the individual, while appreciating their context (contextually-tailored care) (Browne et al., 2012). These informative strategies acquire special relevance in rural settings, where an important gap of knowledge exists compared to urban women (Mohammed et al., 2018).

### **Limitations**

The methods used in this study present several limitations. First, this study was performed on women who attended the midwife's office in primary care services. Nonetheless, we believe this is an appropriate site for participant recruitment as women with gynecological pathologies or who receive care during pregnancy attend the office, in addition to healthy women undergoing preventive health measures, such as Pap smears. Given that women were surveyed in the context of a clinical consultation, we decided to avoid certain important questions (reason for consultation, whether the woman has children, etc.) that could discourage participation. Additionally, the lack of a validated questionnaire in Spanish on the knowledge of HPV favors the use of different tools designed by each research team. Therefore, it would also be desirable to adapt and validate scales designed in other countries and predominantly in English, such as the instrument designed by Waller et al (Waller, Ostini, Marlow, McCaffery, & Zimet, 2013).

### **Conclusions**

In general, the level of knowledge regarding HPV and its vaccine was high. Nonetheless, it is important to closely consider SDH based on the finding that women with basic education and who live in rural areas more poorly identified the protective and risk factors for HPV and demonstrated greater misconceptions regarding the vaccine, therefore representing a more vulnerable group. Concretely, the education level is the most striking determining factor of having little knowledge of the vaccine and the residential setting is a determining factor towards general HPV knowledge.

## REFERENCES

- Almeida, C. M., Tiro, J. A., Rodríguez, M. A. & Diamant, A. L. (2012). Evaluating associations between sources of information, knowledge of the human papillomavirus, and human papillomavirus vaccine uptake for adult women in California. *Vaccine*, 30, 3003-3008. DOI: 10.1016/j.vaccine.2012.01.079.
- Anagnostou, P. A., Aletras, V. H. & Niakas, D. A. (2017). Human papillomavirus knowledge and vaccine acceptability among adolescents in a Greek region. *Public Health*, 152, 145-152. DOI: 10.1016/j.puhe.2017.07.033.
- Barrera-Castillo, M., Fernández-Peña, R., del Valle-Gómez, M. O., Fernández-Feito, A., & Lana, A. (2019). Social integration and gynecologic cancer screening of immigrant women in Spain. *Gaceta Sanitaria*, in press, DOI: 10.1016/j.gaceta.2019.01.002.
- Blake, K. D., Ottenbacher, A. J., Finney Rutten, L. J., Grady, M. A., Kobrin, S. C., Jacobson, R. M., & Hesse B. W. (2015). Predictors of human papillomavirus awareness and knowledge in 2013: gaps and opportunities for targeted communication strategies. *American Journal of Preventive Medicine*, 48, 402-410. DOI: 10.1016/j.amepre.2014.10.024.
- Bonanni, P., Levi, M., Latham, N. B., Bechini, A., Tiscione, E., Lai, P., & Panatto, D. (2011). An overview on the implementation of HPV vaccination in Europe. *Human Vaccines*, 7, 128-35.

- Browne, A. J., Varcoe, C. M., Wong, S. T., Smye, V. L., Lavoie, J., Littlejohn, D., & Tu, D. (2012). Closing the health equity gap: evidence-based strategies for primary health care organizations. *International Journal for Equity in Health*, 11, 59. DOI: 10.1186/1475-9276-11-59.
- Castellsagué, X., Muñoz, N., Pitisuttithum, P., Ferris, D., Monsonogo, J., Ault, K., ... Saah A. (2011). End-of-study safety, immunogenicity, and efficacy of quadrivalent HPV (types 6, 11, 16, 18) recombinant vaccine in adult women 24-45 years of age. *British Journal of Cancer*, 105, 28-37. DOI: 10.1038/bjc.2011.185.
- Chan, Z. C., Chan, T. S., Ng, K. K., & Wong, M. L. (2012). A systematic review of literature about women's knowledge and attitudes toward human papillomavirus (HPV) vaccination. *Public Health Nursing*, 29, 481-489. DOI: 10.1111/j.1525-1446.2012.01022.x.
- Chelimo, C., Wouldes, T. A., Cameron, L. D., & Elwood, J. M. (2013). Risk factors for and prevention of human papillomaviruses (HPV), genital warts and cervical cancer. *Journal of Infection*, 66, 207-217. DOI: 10.1016/j.jinf.2012.10.024
- Coles, V. A., Patel, A. S., Allen, F. L., Keeping, S. T., & Carroll, S. M. (2015). The association of human papillomavirus vaccination with sexual behaviours and human papillomavirus knowledge: a systematic review. *International Journal of STD & AIDS*, 26, 777-788. DOI: 10.1177/0956462414554629.
- Cortés, J., Martínón-Torres, F., Ramón y Cajal, J. M., Gil, A., Velasco, J., Abizanda, M., ... Garrido, R. (2010). Primary and secondary prevention of cancers of the cervix and vulva: recommendations for clinical practice. *Progresos de Obstetricia y Ginecología*, 53, 1-19.

Crosbie, E. J., Einstein, M. H., Franceschi, S., & Kitchener, H. C. (2013). Human papillomavirus and cervical cancer. *The Lancet*, 382(9895), 889-899. DOI: 10.1016/S0140-6736(13)60022-7.

Damiani, G., Basso, D., Acampora, A., Bianchi, C. B., Silvestrini, G., Frisicale, E. M., & Sassi, F. (2015). The impact of level of education on adherence to breast and cervical cancer screening: Evidence from a systematic review and meta-analysis. *Preventive Medicine*, 81, 281-289. DOI: 10.1016/j.ypmed.2015.09.011.

Damiani, G., Federico, B., Basso, D., Ronconi, A., Bianchi, C. B., Anzellotti, G. M., ... Ricciardi W. (2012). Socioeconomic disparities in the uptake of breast and cervical cancer screening in Italy: a cross sectional study. *BMC Public Health*, 12, 99. DOI: 10.1186/1471-2458-12-99.

Davis, S. L., & Chapa, D. W. (2015). Social determinants of health: Knowledge to effective action for change. *Journal for Nurse Practitioners*, 11, 424-429. DOI: 10.1016/j.nurpra.2015.01.029

Ferlay, J., Colombet, M., Soerjomataram, I., Mathers, C., Parkin, D. M., Piñeros, M., ... Bray, F. (2019). Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *International Journal of Cancer* 144(8), 1941-1953. DOI: 10.1002/ijc.31937

Fernández de Casadevante, V., Gil Cuesta, J., & Cantarero-Arévalo, L. (2015). Determinants in the Uptake of the Human Papillomavirus Vaccine: A Systematic Review Based on European Studies. *Frontiers in Oncology*, 5, 141. DOI: 10.3389/fonc.2015.00141

Fernández-Feito, A., Antón-Fernández, R., & Paz-Zulueta M. (2018). Sexual risk behaviours and PAP testing in university women vaccinated against human papillomavirus. *Atención Primaria*, 50, 291-298. DOI: 10.1016/j.aprim.2017.05.007.

Goodman, A. (2015). HPV testing as a screen for cervical cancer. *British Medical Journal*, 350, h2372. DOI: 10.1136/bmj.h2372.

Joura, E. A., Giuliano, A. R., Iversen, O. E., Bouchard, C., Mao, C., Mehlsen, J., ... Luxembourg A.(2015). A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. *The New England Journal of Medicine*, 372, 711-23. DOI: 10.1056/NEJMoa1405044.13.

Limmer, K., LoBiondo-Wood, G., & Dains, J. (2014). Predictors of cervical cancer screening adherence in the United States: a systematic review. *Journal of the Advanced Practitioner in Oncology*, 5,31-41.

Marlow, L. A., Zimet, G. D., McCaffery, K. J., Ostini, R., & Waller, J. (2013). Knowledge of human papillomavirus (HPV) and HPV vaccination: an international comparison. *Vaccine*, 31, 763-769. DOI: 10.1016/j.vaccine.2012.11.083.

Martín-López, R., Hernández-Barrera, V., de Andres, A. L., Carrasco-Garrido, P., de Miguel, A. G., & Jimenez-Garcia, R. (2012). Trend in cervical cancer screening in Spain (2003-2009) and predictors of adherence. *European Journal of Cancer Prevention*, 21, 82-88. DOI: 10.1097/CEJ.0b013e32834a7e46.

McRae, J., Martin, C., O'Leary, J., & Sharp, L. (2014). "If you can't treat HPV, why test for it?" Women's attitudes to the changing face of cervical cancer prevention: a focus group study. *BMC Women's Health*, 14, 64. DOI: 10.1186/1472-6874-14-64.



- Merino-Ventosa, M., & Urbanos-Garrido, R.M. (2018). Changes in income-related inequalities in cervical cancer screening during the Spanish economic crisis: a decomposition analysis. *International Journal for Equity in Health*, 17, 184. DOI: 10.1186/s12939-018-0894-x.
- Mohammed, K. A., Subramaniam, D. S., Geneus, C. J., Henderson, E. R., Dean, C. A., Subramaniam, D. P., & Burroughs, T. E. (2018). Rural-urban differences in human papillomavirus knowledge and awareness among US adults. *Preventive Medicine*, 109, 39-43. DOI: 10.1016/j.ypmed.2018.01.016.
- Montgomery, K., & Smith-Glasgow, M. E. (2012). Human papillomavirus and cervical cancer knowledge, health beliefs, and preventive practices in 2 age cohorts: a comparison study. *Gender Medicine*, 9, S55-66. DOI: 10.1016/j.genm.2011.11.002.
- Morteruel, M., Rodriguez-Alvarez, E., Martin, U., & Bacigalupe A. (2018). Inequalities in Health Services Usage in a National Health System Scheme: The Case of a Southern Social European Region. *Nursing Research*, 67, 26-34. DOI: 10.1097/NNR.0000000000000256.
- Ortiz, R. R., Smith, A., & Coyne-Beasley, T. (2019). A systematic literature review to examine the potential for social media to impact HPV vaccine uptake and awareness, knowledge, and attitudes about HPV and HPV vaccination. *Human Vaccines & Immunotherapeutics*, in press, DOI: 10.1080/21645515.2019.1581543.

- Osazuwa-Peters, N., Adjei Boakye, E., Mohammed, K. A., Tobo B. B., Geneus, C. J., & Schootman, M. (2017). Not just a woman's business! Understanding men and women's knowledge of HPV, the HPV vaccine, and HPV-associated cancers. *Preventive Medicine*, 99, 299-304. DOI: 10.1016/j.ypmed.2017.03.014
- Palència, L., Espelt, A., Rodríguez-Sanz, M., Puigpinós, R., Pons-Vigués, M., Pasarín, M. I., & Spadea, T. (2010). Socio-economic inequalities in breast and cervical cancer screening practices in Europe: influence of the type of screening program. *International Journal of Epidemiology*, 39, 757–765. DOI: 10.1093/ije/dyq003
- Patel, H., Jeve, Y. B., Sherman, S. M., & Moss E. L. (2016). Knowledge of human papillomavirus and the human papillomavirus vaccine in European adolescents: a systematic review. *Sexually Transmitted Infections*, 92, 474-479. DOI: 10.1136/sextrans-2015-052341.
- Penman-Aguilar, A., Talih, M., Huang, D., Moonesinghe, R., Bouye, K., & Beckles, G. (2016). Measurement of Health Disparities, Health Inequities, and Social Determinants of Health to Support the Advancement of Health Equity. *Journal of Public Health Management and Practice*, 22, S33-42. DOI: 10.1097/PHH.0000000000000373.
- Tallon, M. M., Kendall, G. E., Priddis, L., Newall, F., & Young, J. (2017). Barriers to Addressing Social Determinants of Health in Pediatric Nursing Practice: An Integrative Review. *Journal of Pediatric Nursing*, 37, 51-56. DOI: 10.1016/j.pedn.2017.06.009.
- Torné Bladéa, A., Del Pino Saladrigues, M., Cusidó Gimferrerc, M., Alameda Quitlletd, F., Andia Ortize, D., Castellsagué Piqué, X., & Cortes Bordoy, J. (2014). Guía de cribado del cáncer de cuello de útero en España. *Revista Española de Patología*, 47, 1-43.

Waller, J., Ostini, R., Marlow, L. A., McCaffery, K., & Zimet, G. (2013). Validation of a measure of knowledge about human papillomavirus (HPV) using item response theory and classical test theory. *Preventive Medicine*, 56, 35-40. DOI: 10.1016/j.ypmed.2012.10.028.

Wood, B., Russell, V. L., El-Khatib, Z., McFaul, S., Taljaard, M., Little, J., & Graham I. D. (2018). "They Should Be Asking Us": A Qualitative Decisional Needs Assessment for Women Considering Cervical Cancer Screening. *Global Qualitative Nursing Research*, 5, 2333393618783632. DOI: 10.1177/2333393618783632.

World Health Organization. (2010). *A conceptual framework for action on the social determinants of health*. Retrieved 30th October 2018 from: [https://www.who.int/sdhconference/resources/ConceptualframeworkforactiononSDH\\_eng.pdf](https://www.who.int/sdhconference/resources/ConceptualframeworkforactiononSDH_eng.pdf)

Yörük, S., Açıkgöz, A. & Ergör, G. (2016). Determination of knowledge levels, attitude and behaviors of female university students concerning cervical cancer, human papilomavirus and its vaccine. *BMC Women's Health*, 16, 51. DOI: 10.1186/s12905-016-0330-6.

Table 1. Percentage of knowledge on HPV-infection and HPV-vaccine according to educational level

	Total n (%)	University % (95% CI)	Secondary % (95% CI)	Primary % (95% CI)	p- trend
Knowledge on HPV-infection <sup>a</sup>					
Sexual promiscuity is a risk factor for HPV	686 (61.7)	68.3 (63.9-72.6)	58.4 (54.0-62.8) **	52.5 (43.9-61.0)**	<0.001
If you regularly use tampons you have a greater risk of acquiring HPV	76 (6.8)	6.0 (3.8-8.3)	7.9 (5.5-10.4)	5.6 (1.5-9.7)	0.741
The performance of Pap-smears provides protection for HPV-infection	594 (53.5)	55.1 (50.4-59.7)	52.9 (48.4-57.3)	50.4 (41.8-58.9)	0.292
The male condom is a protective factor for HPV	609 (54.8)	61.3 (56.8-65.9)	50.7 (46.2-55.2)**	48.3 (39.7-56.8)**	<0.001
If you have no symptoms. you are protected from HPV	53 (4.8)	4.5 (2.5-6.5)	4.9 (3.0-6.9)	4.9 (1.0-8.8)	0.793
HPV can cause cervical cancer	719 (64.7)	75.6 (71.6-79.6)	61.4 (57.0-65.7)***	41.3 (32.8-49.7)***	<0.001
HPV is a risk factor for contracting genital warts	232 (20.9)	27.2 (23.1-31.4)	18.0 (14.6-21.5)**	10.5 (5.1-15.9)***	<0.001
HPV can cause infertility	97 (8.7)	10.2 (7.3-13.0)	8.5 (6.0-11.0)	4.9 (1.0-8.8)	0.060
Knowledge on the HPV-vaccine <sup>b</sup>					
Protects against cervical cancer	647 (80.9)	85.2 (81.5-89.0)	79.7 (75.3-84.0)*	67.1 (56.5-77.6)***	<0.001
Protects against ovarian cancer	193 (24.1)	16.9 (13.0-20.9)	28.1 (23.2-32.9)***	38.8 (27.9-49.8)***	<0.001
Offers protection for some genital warts	110 (13.8)	19.1 (15.0-23.3)	10.6 (7.2-14.0)**	3.5 (0.7-10.0)**	<0.001
Decreases the risk of vaginal infections	65 (8.1)	7.9 (5.0-10.8)	8.0 (5.0-11.0)	9.4 (2.6-16.2)	0.054

HPV: human papilloma virus; CI: confidence interval.

<sup>a</sup> Among women who had heard of HPV (n=1,111)

<sup>b</sup> Among women who had heard of HPV vaccine (n=800)

Differences by educational level derived from logistic regression (reference category: university): \*p<0.05; \*\*p<0.01; \*\*\*p<0.001

Table 2. Percentage of knowledge on HPV-infection and HPV-vaccine according to type of residence area

	Total n (%)	Urban % (95% CI)	Semiurban % (95% CI)	Rural % (95% CI)	p-trend
Knowledge on HPV-infection <sup>a</sup>					
Sexual promiscuity is a risk factor for HPV	686 (61.7)	67.2 (62.7-71.7)	64.3 (59.4-69.1)	49.6 (43.6-55.7)***	<0.001
If you regularly use tampons you have a greater risk of acquiring HPV	76 (6.8)	7.6 (5.0-10.2)	6.3 (3.8-8.8)	6.4 (3.4-9.5)	0.495
The performance of Pap-smears provides protection for HPV-infection	594 (53.5)	55.2 (50.4-60.0)	53.0 (48.0-58.0)	51.4 (45.4-57.5)	0.315
The male condom is a protective factor for HPV	609 (54.8)	62.6 (57.8-67.3)	55.5 (50.5-60.5)*	41.8 (35.8-47.7)***	<0.001
If you have no symptoms. you are protected from HPV	53 (4.8)	5.1 (2.9-7.3)	3.5 (1.6-5.5)	6.1 (3.1-9.0)	0.682
HPV can cause cervical cancer	719 (64.7)	69.3 (64.8-73.7)	66.6 (61.8-71.3)	55.0 (49.0-61.0)***	<0.001
HPV is a risk factor for contracting genital warts	232 (20.9)	23.8 (19.7-27.9)	21.9 (17.7-26.0)	15.0 (10.6-19.4)**	0.007
HPV can cause infertility	97 (8.7)	11.5 (8.4-14.7)	5.8 (3.4-8.2)**	8.6 (5.1-12.0)	0.090
Knowledge on the HPV-vaccine <sup>b</sup>					
Protects against cervical cancer	647 (80.9)	82.0 (77.4-86.5)	82.1 (77.6-86.5)	77.4 (71.3-83.4)	0.239
Protects against ovarian cancer	193 (24.1)	19.4 (14.7-24.1)	25.4 (20.4-30.4)	29.1 (22.6-35.7)**	0.011
Offers protection for some genital warts	110 (13.8)	17.3 (12.9-21.8)	14.7 (10.6-18.8)	7.0 (2.3-10.8)**	0.002
Decreases the risk of vaginal infections	65 (8.1)	9.2 (5.7-12.7)	6.8 (3.9-9.9)	8.5 (4.4-12.7)	0.704

HPV: human papilloma virus; CI: confidence interval.

<sup>a</sup>Among women who had heard of HPV (n=1,111)

<sup>b</sup>Among women who had heard of HPV vaccine (n=800)

Differences by type of residence derived from logistic regression (reference category: urban): \*p<0.05; \*\*p<0.01; \*\*\*p<0.001

1 Table 3. Association between knowledge of HPV-infection and HPV-vaccine according to educational level

	University	Secondary	Primary	p-trend
Null/low knowledge on HPV-infection <sup>a</sup> , n (%)	113 (24.4)	168 (33.3)	59 (41.3)	
Crude OR (95% CI)	1.00	1.54 (1.17-2.05)	2.18 (1.47-3.23)	<0.001
Adjusted OR (95% CI) <sup>b</sup>	1.00	1.48 (1.11-1.97)	2.13 (1.41-3.21)	<0.001
Null/low knowledge on the HPV-vaccine <sup>c</sup> , n (%)	92 (25.1)	132 (37.8)	38 (44.7)	
Crude OR (95% CI)	1.00	1.81 (1.32-2.50)	3.68 (2.26-6.00)	<0.001
Adjusted OR (95% CI) <sup>b</sup>	1.00	1.76 (1.27-2.16)	3.59 (2.16-5.97)	<0.001

2 HPV: human papilloma virus; OR: odds ratio; CI: confidence interval.

3 <sup>a</sup>Among women who had heard of HPV (n=1,111)4 <sup>b</sup>Adjusted by age (years) and type of residence area (urban; semiurban; rural)5 <sup>c</sup>Among women who had heard of HPV vaccine (n=800)

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13 Table 4. Association between knowledge of HPV-infection and HPV-vaccine according to type of residence area

	Urban	Semiurban	Rural	p-trend
Null/low knowledge on HPV-infection <sup>a</sup> , n (%)	111 (25.6)	109 (27.4)	120 (42.9)	
Crude OR (95% CI)	1.00	1.09 (0.80-1.49)	2.18 (1.58-3.00)	<0.001
Adjusted OR (95% CI) <sup>b</sup>	1.00	1.10 (0.81-1.51)	2.03 (1.46-2.80)	<0.001
Null/low knowledge on the HPV-vaccine <sup>c</sup> , n (%)	82 (27.9)	104 (33.9)	85 (42.7)	
Crude OR (95% CI)	1.00	1.33 (0.94-1.88)	1.93 (1.32-2.82)	0.002
Adjusted OR (95% CI) <sup>b</sup>	1.00	1.30 (0.91-1.86)	1.66 (1.13-2.46)	0.010

14 HPV: human papilloma virus; OR: odds ratio; CI: confidence interval.

15 <sup>a</sup>Among women who had heard of HPV (n=1,111)16 <sup>b</sup>Adjusted by age (years) and educational level (university; secondary; primary)17 <sup>c</sup>Among women who had heard of HPV vaccine (n=800)

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25 **Figure legend**

26 Figure 1. Percentage of null/low knowledge on human papillomavirus (HPV)-infection (left  
 27 figure, blue color) and HPV-vaccine (right figure, green color) across all the strata. The red line  
 28 represents the percentage of null/low knowledge on HPV-infection (30.6%) and HPV-vaccine  
 29 (33.9%) in the whole sample

