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Human papillomavirus genotypes in unvaccinated women in Albania: A public health perspective

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Abstract

Human papillomavirus (HPV) is the most common sexually transmitted infection, affecting approximately four out of five sexually active individuals at some point in their lives. While papillomaviruses generally cause benign tumours, they can sometimes lead to malignant tumours. This study aimed to identify and quantify the different types of HPV present in Albanian women. A cohort study was conducted with 124 women, aged 19 to 58 years, who presented with abnormal squamous epithelial cells. The HPV QUANT-21 Quantitative real-time PCR kit® was employed to identify and quantify both low-risk HPV types (HPV 6, 11, 44) and high or probable high-risk HPV types (HPV 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82). Out of 123 samples analysed, 104 were positive for at least one HPV genotype, resulting in an overall infection frequency of 84.6%. Among these positive cases, the most commonly detected types were HPV 6 (a low-risk type) and HPV 31 and HPV 52 (both high-risk types). The age group with the highest number of positive cases was the 29-38 years old group, with 59 women testing positive (47.9%). Single HPV infections were observed in 48.1% of the cases, while multiple infections were noted as follows: double infections in 39.4% of cases, triple infections in 10.15%, quadruple infections in 5.8%, and fivefold infection in 1.9% of cases. There has been a noticeable increase in the incidence of HPV infection among Albanian women over the years. This rise is likely due to increased awareness and routine check-ups leading to more frequent testing and identification of infections. Although our method identifies only 21 types of HPV—fewer than some other methods—it is both quick and accurate, providing valuable insights into HPV prevalence and types.

Keywords: HPV (Human papillomavirus), low risk HPV types (LR HPV), high risk types (HR HPV), single HPV infection, multiple HPV infection.

1. Introduction

In Albania approximately 1.2 million women aged 15 years and older are at risk for cervical cancer). Each year, around 133 new cases of cervical cancer are diagnosedresulting in 77 deaths. Cervical cancer is the second most common cancer among women and the sixth leading cause of cancer-related deaths for women aged 15 to 44 years in Albania (Bruni *et al.*, 2023).

Persistent infection with high-risk human papillomavirus (HPV) especially types 16 and 18, causes about 99.7% of cervical cancer cases (Okunade 2020). Despite the availability of effective vaccines, HPV infection remains a significant public health challenge, especially among unvaccinated women. HPV types are classified based on their risk association with cervical cancer. (Muñoz *et al.*, 2003).High-risk types: 15 HPV types (directly linked to cervical cancer):16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82, Probable high-risk types: 3 HPV types:26, 53, and 66; Low-risk types (associated with genital warts): 12 HPV types (6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, CP6108)

Globally HPV-16 and HPV-18 cause 70% of l cervical cancers, with slightly higher prevalence in developed regions (72-77%) compared to less developed areas (65-72%). The next six most common HPV types: 31, 33, 35, 45, 52, and 58, account for an additional 20% of cases (Clifford *et al.*, 2006).

The European Union has authorized three HPV vaccines: by: 1.Gardasil, against HPV types 16 and 18 (leading causes of cervical cancer), and types 6 and 11 (causing genital warts and recurrent respiratory papillomatosis,RRP); 2.Cervarix, targets HPV types 16 and 18; 3.Gardasil 9 provides broader coverage against HPV types 6, 11, 16, and 18, and five additional types (31, 33, 45, 52, and 58) (Public Health European Commission. Vaccination).

Gardasil and Cervarix vaccines are up to 90% effective in preventing HPV16/18 infections or related diseases in women over the age of 25. Cervarix, in particular, also shows 70% efficacy against HPV- 31 and HPV-45 in older women.

However, despite their effectiveness, global HPV vaccination uptake remains alarmingly low, with less than 2% of females aged 9-45 years receiving the vaccine. This rate is even more concerning in countries where the incidence of cervical cancer is highest, as vaccination programs are often non-existent (Harper & DeMars 2017). This disparity is even more pronounced in countries like Albania, where cervical cancer incidence is high, but vaccination programs are still developing. In 2023, Albania launched a implemented a national HPV vaccination program targeting girls aged 13 years (Institute of Public Health, Albania). While this initiative represents a significant step forward many women over the target age remain unvaccinated, leaving them vulnerable to HPV infection and related diseases.

This study focuses on unvaccinated women in Albanai, aiming to assess the prevalence of high – risk HPV types, identify barriers to vaccination, and evaluate awareness levels regarding HPV and cervical cancer prevention. The novelty of this research lies in its focus on unvaccinated adult women – a demographic often overlooked in national vaccination strategies. Given the increasing number of HPV genotypes identified, PCR sequencing techniques could be particularly valuable in research settings. These advanced methods are crucial, as they ensure a broad spectrum of HPV types are detected and identified, reducing the risk of underestimating the involvement of certain HPV types in various lesions (Fontaine *et al.*, 2007).

By highlighting the prevalence of HPV in this population, the study provides crucial insights that could inform catch-up vaccination programs and shape public health policies aimed at reducing cervical cancer rates among older, at-risk women.

2. Materials and Methods

A cohort study enrolled 124 unvaccinated women, aged 19-58, between October 2022 and August 2023. These women presented to "GeniusLab" in Tirana with abnormal squamous epithelial cells, as identified by their gynaecologists. Cervical samples were collected from each participant based on the medical recommendations. Swab samples were stored at temperatures between 2 and 4°C and were analyzed in the laboratory within 24 hours to ensure sample integrity.

HPV DNA extraction was conducted using a commercial Genomic Column DNA Express kit (Sacace Biotechnologies, Italy) following the manufacturer's guidelines. For the specific identification and quantification of HPV types, the HPV QUANT-21 Quantitative Real-Time PCR kit® (Sacace Biotechnologies, Italy) was used. This kit employs real-time amplification of HPV DNA through polymerase chain reaction (PCR) and nucleic acid hybridization techniques. The analysis differentiated between low-risk types (HPV 6, 11, 44) and high- or probable high-risk types (HPV 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82). For the detection and quantification of nucleic acid sequences, the ABI 7500 Real-Time PCR system (Applied Biosystems) was employed.

Statistical analysis was carried out using IBM® SPSS® Statistics (Statistical Package for Social Sciences) version 20 for Windows. To assess significant differences between groups, both the chi-square test and Pearson correlation test were applied. A p-value of less than 0.05 was considered statistically significant, ensuring the rigor of the findings.

"Genius lab" is accredited to perform laboratory analyzes in accordance with S SH ISO/IEC 15189:2012 "Medical Laboratories - Requirements for this and Competence". Since the laboratory performs routine tests for HPV genotyping, there is no need to obtain informed consent from participants. Prior to any data collection, the laboratory requested a written confirmation report confirming that all personal data will be anonymized, and participants will be assigned unique identification codes to protect their privacy. Only de-identified data will be used in analyses and publications. The research protocol, including all data collection tools and participant materials, has undergone rigorous review to ensure compliance with national and international ethical standards.

Detecting human papillomavirus (HPV) is crucial for preventing and managing cervical cancer and other HPV-related diseases. The choice of detection method depends on sensitivity, specificity, cost, and the clinical context. Here's a comparison of the most used HPV detection methods:

PCR (Polymerase Chain Reaction), with Highly Sensitive and Specific. PCR can detect low levels of HPV DNA, even in asymptomatic patients or early infections.

Cytology (Pap Smear) has lower sensitivity compared to HPV DNA tests, especially for detecting precancerous lesions. More operator-dependent, with higher chances of false negatives

Next-Generation Sequencing (NGS) – High-Resolution Analysis. It's more expensive and time-consuming than PCR. Not routinely used for clinical diagnosis due to cost but valuable for research purposes.

3. Results

The study included 123 unvaccinated women, aged between 19 and 58 years, with abnormal squamous epithelial cells. The mean age of the participants was 33.93 years, with a standard deviation of 9.04 years. Out of the total samples collected, 104 women tested positive for at least one HPV genotype, resulting in an overall HPV frequency of 84.6%.

Table 1 illustrates the distribution of HPV-positive cases according to the different age groups of the women, which were divided into four categories with 10-year intervals (19-28 years, 29-38 years, 39-48 years, and 49-58 years). Among these, women in the 29-38 years age group exhibited the highest overall HPV positivity, with a rate of 91.5%.

To further explore the relationship between age and HPV infection, we applied the Pearson correlation test to assess whether there was a linear relationship between the two variables. The test yielded a p-value of 0.01, indicating a statistically significant correlation between age and the presence of HPV infection. This suggests that as age changes, the likelihood of contracting HPV may also shift in a meaningful way, underscoring the importance of targeted screening and prevention strategies in specific age groups.

Table 1. Frequency of HPV-positive cases according to age groups

Age groups	n (%)	HPV positive (%)	p
19 – 28	32 (26)	25 (78.1)	0.01** (χ^2=11.356)
29 – 38	59 (47.9)	54 (91.5)	
39 – 48	21 (17.1)	19 (90.5)	
49 – 58	11 (9)	6 (54.5)	
Total	123 (100)	104 (84.6)	
** p<0.01			

The distribution of HPV types is presented in Figure 1. Of the 21 HPV types targeted in this study, 19 were identified across the sample, with HPV 26 and HPV 33 notably absent from all samples analyzed. The most prevalent high-risk HPV types detected were HPV 31 and HPV 52, both appearing in 19.2% of cases, followed closely by HPV 18, which was found in 13.5% of cases. These high-risk types are particularly significant due to their strong association with cervical cancer and other malignancies.

In contrast, among the low-risk HPV types, HPV 6 was the most frequently identified, appearing in 31.7% of the sample, while HPV 44 was detected in 15.3%. Low-risk types like these are commonly linked to benign conditions, such as genital warts, rather than cancer. The variation in HPV type prevalence emphasizes the importance of comprehensive screening, as different HPV types can lead to a range of health outcomes, from benign lesions to serious cancers.

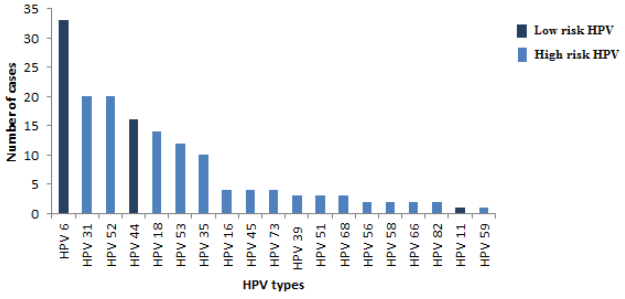

Figure 1. Distribution of identified HPV Types

One of the advantages of this technique is its ability to detect both single infections (with one HPV type) and multiple infections (with two or more HPV types). Among the 104

women who tested positive for HPV, 50 (48.1%) had single infections, while 54 (51.9%) had multiple infections. Of the multiple infections, 41 (39.4%) had double infections, 5 (4.8%) had triple infections, 6 (5.8%) had quadruple infections, and 2 (1.9%) had quintuple infections. Table 2 illustrates the distribution of single and multiple infections by age group.
We applied the Pearson correlation test to assess the linear relationship between age and the presence of single or multiple HPV infections. The test yielded a p-value of 0.209, indicating no statistically significant correlation between age and the presence of single or multiple HPV infections at the 0.05 significance level. Further studies with larger sample sizes may be needed to explore this potential association more thoroughly. Among double infections, the combinations of HPV 52 and HPV 53 (in five cases) and HPV 31 and HPV 6 (in four cases) were the most common. Additionally, the prevalence of multiple infections suggests a complex interaction between different HPV types, which may influence the progression and clinical outcomes of HPV-related diseases.

Table 2. Frequency of single and multiple HPV infections according to age groups.

Age groups	Single infection n (%)	Multiple infections N (%)			
		Double infection n (%)	Triple infection n (%)	Quadruple infection n (%)	Fivefold infection n (%)
19 – 28	13 (52.0)	12 (48.0)			
		8 (32.0)	0 (0.0)	3 (12.0)	1 (4.0)
29 – 38	24 (44.4)	30 (55.6)			
		24 (44.4)	3 (5.6)	2 (3.7)	1 (1.9)
39 – 48	12 (63.2)	7 (36.8)			
		5 (26.2)	1 (5.3)	1 (5.3)	0 (0.0)
49 – 58	1 (16.7)	5 (83.3)			
		4 (66.6)	1 (6.7)	0 (0.0)	0 (0.0)
Total	50 (48.1)	54 (51.9)			
		41 (39.4)	5 (4.8)	6 (5.8)	2 (1.9)

Table 3 illustrates the distribution of HPV types in single versus multiple infections. In single infections, the most common LR HPV type is HPV 6, which accounts for 34% of cases, while the most common HR HPV type is HPV 31, representing 20%. In multiple infections, the most common LR HPV type remains HPV 6, with a prevalence of 29.6%, whereas HPV 52 emerges as the most common HR HPV type, occurring in 27.8% of cases. Notably, HR HPV types HPV 52 ($p < 0.05$) and HPV 53 ($p < 0.001$) are significantly more frequent in multiple HPV infections compared to single HPV infections.

Table 3. Distribution of HPV types in single and multiple infections.

HPV Types	Single HPV infection n (%)	Multiple HPV infection n (%)	p-Value
HPV 6	17 (34.0)	16 (29.6)	0.632
HPV 11	0 (0.0)	1 (1.9)	0.334
HPV 44	5 (10.0)	11 (20.4)	0.143
HPV 16	1 (2.0)	3 (5.6)	0.346

HPV Types	Single HPV infection n (%)	Multiple HPV infection n (%)	p-Value
HPV 18	5 (10.0)	9 (16.7)	0.32
HPV 31	10 (20.0)	10 (18.5)	0.848
HPV 35	4 (8.0)	6 (11.1)	0.591
HPV 39	0 (0.0)	3 (5.6)	0.091
HPV 45	1 (2.0)	3 (5.6)	0.346
HPV 51	1 (2.0)	2 (3.7)	0.604
HPV 52	5 (10.0)	15 (27.8)	**0.013***
HPV 53	0 (0.0)	12 (22.2)	**0.0*****
HPV 56	0 (0.0)	2 (3.7)	0.169
HPV 58	0 (0.0)	2 (3.7)	0.169
HPV 59	0 (0.0)	1 (1.9)	0.334
HPV 66	0 (0.0)	2 (3.7)	0.169
HPV 68	1 (2.0)	2 (3.7)	0.604
HPV 82	0 (0.0)	2 (3.7)	0.604
* p<0.05; *** p<0.001			

High-risk (HR) HPV infections, either alone or mixed with low-risk (LR) HPV types, were detected in 81 samples (77.9%). Of these, 28 samples had a single HPV infection, while 53 samples had multiple HPV infections. Low-risk (LR) HPV infections, detected only in the absence of HR HPV types, were found in 23 samples (22.1%), with 22 samples having a single HPV infection and only one sample having multiple HPV infections. Figure 2 illustrates the frequencies of LR and HR HPV infections according to age groups. The age groups of 29-38 years and 39-48 years exhibited the highest percentages of LR HPV and HR HPV infections, respectively.

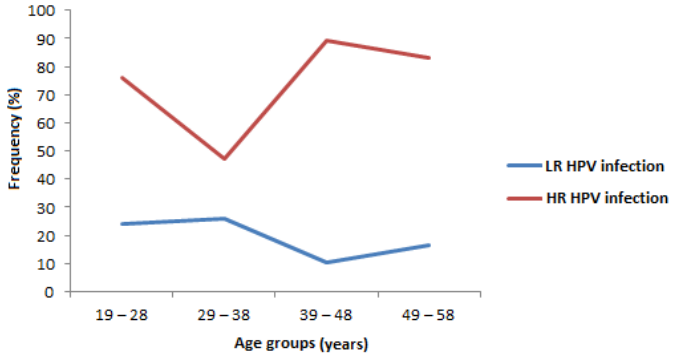

Figure 2. Frequencies of LR HPV and HR HPV infections according to age groups.

4. Discussion

This study aimed to identify HPV infection in a population of unvaccinated women with abnormal squamous epithelial cells. This was achieved using a molecular biology technique that can detect 21 types of HPV, including both single and multiple infections, with high speed and accuracy.

Globally, the prevalence of HPV infection in women is approximately 53.72%. However, this rate is notably higher in patients with abnormal cervical cells compared to those with normal cervical cells, and it varies in smaller sample sizes (fewer than 500 participants) (Zhou *et al.*, 2024). In Albania, various studies have yielded different results due to differences in techniques, sample sizes, and clinical statuses. For instance, the prevalence of HPV infection among women undergoing routine control has been reported as 15.1%, while it is 43.9% in those recommended for Pap tests, and as high as 71.7% in women with abnormal squamous epithelial cells (Filipi *et al.*, 2010; Kone *et al.*, 2017; Bakiri 2014). In contrast, European studies have reported HPV prevalence rates ranging from 70% to 83.3% (Kjær *et al.*, 2014; Dabeski *et al.*, 2019).

The prevalence of HPV infection is particularly high among women aged 29-38 years, at 91.5%. Other studies in Albania have shown that HPV prevalence is highest in the 20-29 years age group (71-86.36%), followed by the 30-39 years age group (69-77.63%) (Bakiri 2014; Filipi *et al.*, 2010). Additionally, a study of Albanian women recommended for Pap tests found that the prevalence was highest in the 25-35 years age group, at 43.6% (Kone *et al.*, 2017). These findings are consistent with studies conducted in Europe, which also report high HPV prevalence in the 30-33 years age group (Pärna *et al.*, 2023) or among women under 41 years of age (Muresu *et al.*, 2022)

The high HPV infection rates observed in the 29-38 years age group, and to a lesser extent in the 39-49 years age group, correspond with the incidence rates of cervical cancer in Europe, where the highest incidence is observed in women aged 40-44 years (Bruni *et al.*, 2023). This alignment underscores the significance of age in HPV infection rates and its potential impact on cervical cancer incidence.

There are several factors related to the high prevalence of HPV infection in this age group in our study, such as younger age at first intercourse, higher number of past and recent sex partners, history of sexually transmitted infections (STIs), and other factors related to sexual activity (de Sanjosé et al., 2018).

Some studies indicate that use of vaccine in older women, can protect against HPV infection and consequently from the related diseases (Suk *et al.*, 2022; Thompson *et al.*, 2021). US Food and Drug Administration (FDA) had expanded in 2018 the approved age range for the use of the 9-valent HPV vaccine to ages 27 to 45 years in women (Merck 2018). All women, especially the age group where the prevalence of HPV infection is higher, have the possibility of vaccination by preventing or reducing related diseases.

The distribution of HPV types and their prevalence depends on the geographical distribution, the characteristics of the sample taken in the study, and heterogeneity of the methods used in the laboratory. HPV 52 (19.2%) and HPV 31 (19.2%) types, which are the most common high risk HPV types identified in our study, are the 7 most widespread in the world and rate from 1.5% (normal cytology) to 14.2% (cervical cancer) and from 1.2% (normal cytology) to 10.4% (high grade lesions), respectively (Bruni *et al.*, 2023). HPV 31 and HPV 52 types, together with others are the five most common in Europe (Muresu *et al.*, 2022; Aleksioska-Papestiev *et al.*, 2018; Nikolic *et al.*, 2024). Other studies done in Albania, revealed that HPV 16 (11.7%; 21.05%; 40.98%) was the most common high risk HPV type (Bakiri 2014; Nallbani *et al.*, 2018; Filipi *et al.*, 2010).

HPV infections were detected in 23 (22.1%) of the 104 HPV-positive individuals as low-risk (LR HPV) and in 81 (77.9%) as high-risk (HR HPV). One reason for the higher rate of HR HPV infections could be that none of the women in the study were vaccinated. The HPV vaccine is known to be highly effective in preventing HR HPV infections (Li *et al.*, 2023).

Single HPV infections were found in 48.1% of cases, with the highest rates of infection (63.2%) in the 39-48 age group. On the other hand, multiple HPV infections occurred in 51.9% of cases, with the highest rates (83.3%) in the 49-58 age group. This increase in multiple infections among older women may be due to decreased immunity and changes in hormone levels (Läsche *et al.*, 2022). However, there was no statistically significant difference between age groups in terms of single versus multiple infections.

Compared to similar studies, the prevalence of single HPV infections in this study was higher than in a study conducted on Albanian women, where it was 39.47%. The prevalence of multiple infections was lower than the 60.53% found in the same Albanian study (Bakiri 2014). Across Europe, varying results for single and multiple HPV infections have been reported. In Italy, for instance, single infections accounted for 77.52% of cases, while multiple infections made up 22.48% (Pisani & Cenci 2024). In Serbia, single and multiple infections were found in 54.4% and 45.6% of cases, respectively (Kovacevic *et al.*, 2021). Similar patterns were observed in Greece, with minor differences in the proportions of single and multiple infections (Kafasi *et al.*, 2024).

The high percentage of multiple infections in this study was expected, as the women included had abnormal squamous vaginal epithelium. Literature suggests that multiple HPV infections are often associated with greater degrees of cervical abnormalities (Su *et al.*, 2024).

The discussion highlights the relationship between vaccination status, age, immune function, and the type of HPV infection (single or multiple), emphasizing the importance of understanding these factors in managing HPV-related diseases.

In 2023, the HPV vaccine was included in the vaccination calendar for Albanian girls aged 13 years (Institute of Public Health, Albania). Data on HPV infection distribution and types prevalent in the population would help in tailoring vaccination strategies. The Gardasil 9 vaccine, which protects against nine types of HPV (HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58), is particularly relevant because these types represent 94.2% of the infections observed in the study. This data suggests that using the Gardasil 9 vaccine would likely be the most effective option for preventing HPV-related conditions in Albanian women.

One limitation of this study is the relatively small sample size, which may limit the generalizability of the findings to larger or more diverse populations. With a smaller sample, the statistical power to detect subtle differences between groups may be reduced, increasing the risk of Type II errors (false negatives). This could mean that associations between HPV types and clinical outcomes might be underestimated. The detection method used in this study may not identify all HPV types, as it primarily targets high-risk genotypes such as HPV 16 and 18. the overall prevalence of HPV infection may be underestimated, and the diversity of HPV types involved in the study population may not be fully captured. This limitation arises from the use of primers specific to high-risk strains, potentially overlooking low-risk or rare HPV types that could still contribute to disease progression.

Future research could incorporate broader-spectrum assays or next-generation sequencing to improve HPV type coverage and provide a more comprehensive understanding of HPV diversity.

By addressing gaps in vaccination coverage and identifying key risk factors among unvaccinated women, this study aims to support expanded vaccination efforts and strengthen cervical cancer prevention strategies in Albania. Since HPV 16 and 18 are predominant, policymakers could prioritize vaccination against these types. This could lead to targeted national vaccination programs for adolescents, reducing the future burden of cervical cancer. The data

could justify public health campaigns aimed at increasing vaccine acceptance, addressing hesitancy, and advocating for free or subsidized vaccines, particularly in rural areas

By integrating HPV findings into public health policy, Albania can enhance cervical cancer prevention, improve screening effectiveness, and reduce health disparities. This evidence-based approach will ultimately decrease HPV-related morbidity and mortality, aligning Albania with global efforts to eliminate cervical cancer as a public health threat.

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Conflict of interests

The authors affirm that they have no competing interests to disclose.

References

Aleksioska-Papestiev, I., Chibisheva, V., Micevska, M., & Dimitrov, G. (2018). Prevalence of Specific Types of Human Papiloma Virus in Cervical Intraepithelial Lesions and Cervical Cancer in Macedonian Women. Medical archives (Sarajevo, Bosnia and Herzegovina), 72(1), 26–30. https://doi.org/10.5455/medarh.2018.72.26-30.

Bakiri F. Analytic study on human papillomavirus (HPV) in the Albanian population. (2014) PhD Thesis, University of Tirana, Albania. https://unitir.edu.al/doktoratura-fjoralda-bakiri-fakulteti-i-shkencave-i-natyrore-departamenti-i-biologjise-2/.

Bruni L, Albero G, Serrano B, Mena M, Collado JJ, Gómez D, Muñoz J, Bosch FX, de Sanjosé S. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in Albania. Summary Report 10 March 2023.

Bruni, L.; Albero, G.; Serrano, B.; Mena, M.; Collado, J.J.; Gómez, D.; Muñoz, J.; Bosch, F.X.; de Sanjosé, S.; ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in the World. Summary Report 10 March 2023. Available online: https://hpvcentre.net/statistics/reports/XWX.pdf?t=1687952491692.

Clifford, G., Franceschi, S., Diaz, M., Muñoz, N., & Villa, L. L. (2006). Chapter 3: HPV type-distribution in women with and without cervical neoplastic diseases. Vaccine, 24 Suppl 3, S3/26–S3/34. https://doi.org/10.1016/j.vaccine.2006.05.026.

Dabeski, D., Dabeski, A., Antovska, V., Trajanova, M., Todorovska, I., Sima, A. Human papillomavirus infections in women with and without squamous cell abnormalities of the uterine cervix. (2019). Scripta Medica, vol. 50, br. 2, str. 69-76. https://scindeks.ceon.rs/article.aspx?artid=2490-33291902069D.

de Sanjosé, S., Brotons, M., & Pavón, M. A. (2018). The natural history of human papillomavirus infection. Best practice & research. Clinical obstetrics & gynaecology, 47, 2–13. https://doi.org/10.1016/j.bpobgyn.2017.08.015.

Filipi, K., Tedeschini, A., Paolini, F., Celicu, S., Morici, S., Kota, M., Bucaj, E., & De Marco, F. (2010). Genital human papillomavirus infection and genotype prevalence among Albanian women: a cross-sectional study. Journal of medical virology, 82(7), 1192–1196. https://doi.org/10.1002/jmv.21803.

Fontaine, V., Mascaux, C., Weyn, C., Bernis, A., Celio, N., Lefèvre, P., Kaufman, L., & Garbar, C. (2007). Evaluation of combined general primer-mediated PCR sequencing and

type-specific PCR strategies for determination of human papillomavirus genotypes in cervical cell specimens. Journal of clinical microbiology, 45(3), 928–934. https://doi.org/10.1128/JCM.02098-06.

Gardasil 9. Package insert. Merck; 2018. https://www.merckvaccines.com/gardasil9/.

Harper, D. M., & DeMars, L. R. (2017). HPV vaccines - A review of the first decade. Gynecologic oncology, 146(1), 196–204. https://doi.org/10.1016/j.ygyno.2017.04.004.

Institute of Public Health (Albania). National vaccination program. https://www.ishp.gov.al/departamenti-i-kontrollit-te-semundjeve-infektive/programi-kombetar-i-vaksinimit/.

Kafasi, A., Kaparos, G., Pitiriga, V. C., Spanakis, N., Vlachos, N., Thomakos, N., Stournaras, S., & Tsakris, A. (2024). Prevalence of HPV Genotypes among Greek Women in Association with Their Potential to Cause Precancerous Lesions. Microorganisms, 12(7), 1404. https://doi.org/10.3390/microorganisms12071404.

Kjær, S. K., Munk, C., Junge, J., & Iftner, T. (2014). Carcinogenic HPV prevalence and age-specific type distribution in 40,382 women with normal cervical cytology, ASCUS/LSIL, HSIL, or cervical cancer: what is the potential for prevention? Cancer causes & control: CCC, 25(2), 179–189. https://doi.org/10.1007/s10552-013-0320-z.

Kone, E. S., Balili, A. D., Paparisto, P. D., Ceka, X. R., & Petrela, E. D. (2017). Vaginal Infections of Albanian women Infected with HPV and their impact in intraepithelial cervical lesions evidenced by Pap test. Journal of cytology, 34(1), 16–21. https://doi.org/10.4103/0970-9371.197592.

Kovacevic, G., Milosevic, V., Nikolic, N., Patic, A., Dopudj, N., Radovanov, J., Hrnjakovic Cvjetkovic, I., Petrovic, V., & Petrovic, M. (2021). The prevalence of 30 HPV genotypes detected by EUROArray HPV in cervical samples among unvaccinated women from Vojvodina province, Serbia. PloS one, 16(4), e0249134. https://doi.org/10.1371/journal.pone.0249134).

Lässche, M., Gallwas, J., & Gründker, C. (2022). Like Brothers in Arms: How Hormonal Stimuli and Changes in the Metabolism Signaling Cooperate, Leading HPV Infection to Drive the Onset of Cervical Cancer. International journal of molecular sciences, 23(9), 5050. https://doi.org/10.3390/ijms23095050.

Li, C., Hall, T. G., Hall, J. J., & He, W. Q. (2023). Effectiveness of quadrivalent HPV vaccination in reducing vaccine-type and nonvaccine-type high risk HPV infection. Epidemiology and infection, 151, e37. https://doi.org/10.1017/S0950268823000213.

Muñoz, N., Bosch, F. X., de Sanjosé, S., Herrero, R., Castellsagué, X., Shah, K. V., Snijders, P. J., Meijer, C. J., & International Agency for Research on Cancer Multicenter Cervical Cancer Study Group (2003). Epidemiologic classification of human papillomavirus types associated with cervical cancer. The New England journal of medicine, 348(6), 518–527. https://doi.org/10.1056/NEJMoa021641.

Muresu, N., Sotgiu, G., Marras, S., Gentili, D., Sechi, I., Cossu, A., Dettori, A., Pietri, R. E., Paoni, L., Ghi, M. E., Bagella, M. P., Marrazzu, A., Cossu, A., Genovesi, A., Piana, A., & Saderi, L. (2022). Cervical Screening in North Sardinia (Italy): Genotype Distribution and Prevalence of HPV among Women with ASC-US Cytology. International journal of environmental research and public health, 19(2), 693. https://doi.org/10.3390/ijerph19020693.

Nallbani, G., Abazaj, E, Filipi, K., Ylli, A., Shehu, T., Shundi, L. (2018). Prevalence of high-risk human papillomavirus and distribution of HPV16/18/45 types in Albanian young women before HPV vaccination. Albanian medical journal 1, 29-33. https://www.ishp.gov.al/table-of-contents-albanian-medical-journal-2018-1/.

Nikolic, N.; Basica, B.; Strbac, M.; Terzic, L.; Patic, A.; Kovacevic, G.; Velicki, R.; Petrovic, D.; Mandic, A.; Petrovic, V. Prevalence of Carcinogenic Genotypes of HPV-Infected

Women in a Ten-Year Period (2014–2023) in Vojvodina, Serbia. Medicina 2024, 60, 922. https://doi.org/10.3390/medicina60060922.

Okunade K. S. (2020). Human papillomavirus and cervical cancer. Journal of obstetrics and gynaecology: the journal of the Institute of Obstetrics and Gynaecology, 40(5), 602–608. https://doi.org/10.1080/01443615.2019.1634030.

Pärna, K., Nygård, M., Tisler, A., Toompere, K., Naaber, P., Ratnik, K., Ķīvīte Urtāne, A., Zodzika, J., Stankūnas, M., Baltzer, N., & Uusküla, A. (2023). Age-specific and genotype-specific carcinogenic human papillomavirus prevalence in a country with a high cervical cancer burden: results of a cross-sectional study in Estonia. BMJ open, 13(6), e069558. https://doi.org/10.1136/bmjopen-2022-069558.

Pisani, T., & Cenci, M. (2024). Prevalence of Multiple High Risk Human Papilloma Virus (HR-HPV) Infections in Cervical Cancer Screening in Lazio Region, Italy. Cancer diagnosis & prognosis, 4(1), 42–45. https://doi.org/10.21873/cdp.10283.

Public Health European Commission. Vaccination. Human papilloma virus (HPV). https://health.ec.europa.eu/vaccination/hpv_en.

Su, Y., Zheng, T., Bi, Z., Jia, X., Li, Y., Kuang, X., Yang, Y., Chen, Q., Lin, H., Huang, Y., Huang, S., Qiao, Y., Wu, T., Zhang, J., & Xia, N. (2024). Pattern of multiple human papillomavirus infection and type competition: An analysis in healthy Chinese women aged 18-45 years. Human vaccines & immunotherapeutics, 20(1), 2334474. https://doi.org/10.1080/21645515.2024.2334474.

Suk, R., Liao, K., Bauer, C. X., Basil, C., & Li, M. (2022). Human Papillomavirus Vaccine Administration Trends Among Commercially Insured US Adults Aged 27-45 Years Before and After Advisory Committee on Immunization Practices Recommendation Change, 2007-2020. JAMA health forum, 3(12), e224716. https://doi.org/10.1001/jamahealthforum.2022.4716.

Thompson, E. L., Garg, A., Galvin, A. M., Moore, J. D., Kasting, M. L., & Wheldon, C. W. (2021). Correlates of HPV Vaccination Intentions Among Adults Ages 27-45 Years Old in the U.S. Journal of community health, 46(5), 893–902. https://doi.org/10.1007/s10900-021-00968-3.

Zhou, D., Xue, J., Sun, Y., Zhu, L., Zhao, M., Cui, M., Zhang, M., Jia, J., Luo, L. (2024). Patterns of Single and Multiple HPV Infections in Female: A Systematic Review and Meta-analysis // Heliyon. p. e35736. https://doi.org/10.1016/j.heliyon.2024.e35736.