Received: 11 December 2024 | Revised: 1 April 2025 | Accepted: 7 April 2025 | Published online: 2 May 2025

DOI: 10.1002/ijgo.70170

CLINICAL ARTICLE

Gynecology

HPV vaccination coverage rate in women undergoing conization for cervical intraepithelial neoplasia in Spain: The COVAR study

Aureli Torné Blade[1] | María del Mar Ramírez Mena[2] | Jesús de la Fuente Valero[3] | Raquel Oliva Sánchez[4] | José Quílez Conde[5] | Manuela Sala Ferichola[6] | Jesús Osuna Pérez[7] | Antonio Rivera[7] | Bruno Herrera Bruch[7] | Gonzalo Fernández[7] | Noelia López[7] | María Villarejo[7] | Marta del Pino Saladrigues[1]

[1]Hospital Clinic de Barcelona, Barcelona, Spain

[2]Hospital Clínico San Carlos, Madrid, Spain

[3]Hospital Universitario Infanta Leonor, Madrid, Spain

[4]Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain

[5]Hospital Universitario de Basurto, Bilbao, Spain

[6]Hospital General Universitario Dr. Balmis, Alicante, Spain

[7]Value & Implementation Global Medical Affairs, MSD Spain, Madrid, Spain

Correspondence
María Villarejo Botija, MSD Spain, C/D. Josefa Valcárcel, 38 – 28027 Madrid, Spain.
Email: maria.villarejo@merck.com

Funding information
Merck Sharp and Dohme Spain

Abstract

Objective: Females subjected to cervical excisional therapy (conization) due to high-grade squamous intraepithelial lesions/cervical intraepithelial neoplasia HSIL/CIN have a higher risk of developing cervical lesions compared to the general population. Research suggests that HPV vaccination may reduce post-treatment HSIL/CIN risk. Since 2014, HPV vaccination is recommended and funded in Spain at regional level for women who had undergone treatment for cervical precancerous lesions (HSIL/CIN2-3 or any other potentially tumoral cytohistological alteration). In 2018, the Ministry of Health standardized the recommendations but the vaccination coverage rate (VCR) for this population has not been published. The COVAR Study aimed to estimate the annual HPV VCR among women undergoing conization for SIL/CIN in Spain and assess sociodemographic and COVID-19 pandemic influence.

Methods: This was a multicentric, cross-sectional retrospective study conducted in six Spanish public hospitals from January 1, 2019, to December 31, 2021.

Results: Annual HPV VCR was 87.3% (1135/1300), increasing to 89.8% (983/1095) in women with a conization for high-grade SIL (HSIL)/CIN. Among vaccinated women, 30.2% (343/1135) were vaccinated after SIL/CIN diagnosis but before conization and 58.3% (662/1135) were vaccinated after conization; the remaining 11.5% (130/1135) received at least one dose before SIL/CIN diagnosis. Of the conizations, 32.4% (517/1594) were performed during the pre-pandemic period, decreasing to 19.6% (312/1594) during the first COVID-19 restriction period; the annual HPV VCR also

Aureli Torné Blade and María del Mar Ramírez Mena have contributed equally to this work.

decreased (30% [259/865] to 20.7% [179/865], $P < 0.001$), for women vaccinated after conization.

Conclusion: The annual HPV VCR in our population was 87.3%, reflecting effective vaccination strategies. The COVID-19 pandemic substantially impacted the annual percentage of conizations and HPV vaccination.

KEYWORDS
cervical cancer, conization, coverage rate, COVID-19, HPV, vaccination

1 | INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted infection worldwide and associated with significant disease burden.[1,2] It is a necessary cause for cervical cancer and high-grade squamous intraepithelial lesions/cervical intraepithelial neoplasia (HSIL/CIN).[3–5] To prevent progression, cervical excisional therapy, or conization, is preferred for HSIL/CIN. However, even after treatment, women are at high-risk, having a five- to ten-fold increased risk of developing cervical cancer and non-cervical HPV-related pre- and tumoral lesions due to persistent HPV infections compared with the general population.[6] Research suggests that this high-risk group would benefit from HPV vaccination, lowering the risk of subsequent HPV-related diseases.[7,8] Although literature reviews emphasize that randomized clinical trials are needed and trials to generate definite evidence are ongoing, vaccination of women undergoing conization for squamous intraepithelial lesions (SIL)/CIN is considered in clinical practice.[9,10]

Spain was one of the first European countries to recommend and fund HPV vaccines in high-risk populations in addition to adolescents. In 2014, HPV vaccination for high-risk populations was recommended and funded at regional level. However, the groups covered were heterogeneous across the Spanish regions. In 2018, the Spanish Ministry of Health standardized the recommendations for HPV vaccination in high-risk groups and established the categories eligible for funded vaccination, including women who had undergone conization because of SIL/CIN,[11–14] for whom three doses of any vaccine available (Cervarix® [GlaxoSmithKline Biologicals S.A.], Gardasil®, Gardasil9® [MSD B.V.]) is recommended regardless of age. No studies or registries have reported the HPV vaccination coverage rate (VCR) in these women. The COVAR Study aims to estimate for the first time the annual HPV VCR in women undergoing conization for SIL/CIN and identify sociodemographic influences on vaccination.

2 | MATERIALS AND METHODS

2.1 | Study design and population

This was a cross-sectional retrospective study conducted by gynecologists from six Cervical Pathology Units in Spanish public hospitals, representing diverse regions and healthcare environments.

Women who underwent conization from January 1, 2019, to December, 31, 2021 were eligible. Following the recommendations of the American Society for Colposcopy and Cervical Pathology[11] and the Spanish Society of Cervical Pathology and Colposcopy,[12] the criteria for conization were: (1) HSIL/CIN2+ (HSIL/CIN 2–3, adenocarcinoma in situ, atypical glandular cells favor neoplastia, squamous carcinoma) diagnosis in a colposcopy-directed biopsy and/or an endocervical curettage, (2) repeated cytologic result of HSIL in at least two cervical screening tests separated by 12 months in patients with a histologic diagnosis of low-grade SIL (LSIL)/CIN or no lesion, after excluding vaginal HSIL, (3) persistent LSIL/CIN1, and (4) other causes not specified.

All women had an HPV-positive test before conization. Patients were identified using secondary data from their medical charts. Women who underwent conization for conditions unrelated to SIL/CIN were excluded. Women should have a minimum follow-up period of 12 months after conization.

The study protocol was approved by the Central Ethics Committee of the *Hospital Clínico San Carlos* (Madrid) on February 23, 2022 (Internal Code: 22/146-O_M_No SP) and validated by the local Ethics Committees of all participating centers. In accordance with Spanish legislation on observational studies (RD 957/2020), informed consent was waived by the Central Ethics Committee, given the retrospective nature of the study and the use of anonymized data.

2.2 | Variables

Sociodemographic characteristics included age, ethnicity, and parity. Cervical treatment information included indication and date of the conization. HPV vaccination data included the number of doses, time of vaccine administration in relation to SIL/CIN diagnosis and excisional therapy (before/after SIL/CIN diagnosis or conization or between them), and place of vaccination (hospital, outpatient consultation, primary care, private clinic).

The study period included the COVID-19 pandemic lockdown, which could disrupt routine health care for the preventive measures adopted. To assess the impact, patients were stratified according to four periods: pre-pandemic, January 1, 2019, to March 13, 2020; quarantine, March 14, 2020, to May 31, 2020; restriction period I, June 1, 2020, to December 31, 2020; and restriction period II, January 1, 2021 to December 31, 2021. To obtain comparable

periods, the number of patients with cervical excisional therapy was adjusted by period size (annual rate), dividing the number of patients treated in each period by the number of days considered within the period and multiplying by 365. The same approach was used for vaccinations after conization.

2.3 | Study outcomes

The primary objective was to estimate the annual HPV VCR of at least one dose in women who had undergone cervical excisional therapy for SIL/CIN, determined as the percentage of women who had received at least one dose of HPV vaccine among all women who underwent conization during the study period.

Secondary objectives of the study were, first, to estimate the annual HPV VCR for the complete schedule, calculated as the percentage of women who received the complete number of doses according to the intervals and women's age at the time of vaccination. A complete schedule was considered in patients who were receiving the first dose before 14/15 years of age and the second dose at least 6 months later (this population was considered completely vaccinated, new doses not applied) and those who were receiving the first dose after 14/15 years of age and the second and third doses according to the minimum intervals specified in the Summary of Product Characteristics. Second, it aimed to identify sociodemographic characteristics associated with HPV vaccination in our population, and third, to evaluate the impact of the COVID-19 pandemic on the number of conizations and the HPV VCR in the study population vaccinated after conization within the study period.

2.4 | Statistical analysis

Quantitative variables were expressed as mean ± standard deviation (SD) and categorical variables as absolute numbers and percentages. No inferential analysis was used. Estimates were made using a sample size of 1300 women who underwent conization for SIL/CIN. HPV VCR with a 95% confidence interval and a precision of ±2.8%, considering a population percentage around 50%, was used to generate the most conservative, or largest, sample size. Analysis was performed using R version 4.1.1 and R studio version 1.4.1717.

3 | RESULTS

3.1 | Sociodemographic characteristics associated with HPV vaccination of the study population

A total of 1300 women were included in the study. The mean ± SD age at conization was 40 ± 10 years, 70.2% of women (913/1300) were of white ethnicity. Parity was documented in 61.9% (805/1300); 5.4% (70/1300) were immunosuppressed, and of these, 30% (21/70) were living with HIV and 14.3% (10/70) had undergone solid organ or hematopoietic progenitor transplantation. Conization was the result of HSIL/CIN2+ in 84.2% (1095/1300) of cases, of a cervical screening test showing HSIL but a biopsy showing LSIL/CIN1 or below in 4.7% (61/1300) of patients, of a persistent LSIL/CIN1 in 8% (104/1300) of patients, and of other causes in 3.1% (40/1300) of cases (Table 1; Table S1).

3.2 | Annual HPV VCR

The proportion of women who initiated the HPV vaccination schedule was 87.3% (1135/1300). There were no significant differences across the years of the study period (2019–2021) (Table 1).

Patients with an indication for conization after a biopsy-confirmed diagnosis of HSIL/CIN2+ showed a coverage of 89.8% (983/1095), significantly decreasing to 75.4% (46/61) in patients with a cervical screening test showing HSIL and a biopsy showing LSIL/CIN1 or below ($P = 0.002$) and to 71.2% (74/104) in patients with persistent LSIL/CIN1 ($P < 0.001$) (Table 1).

When stratifying the VCR by the indication for conization and age, the percentage of patients with biopsy-confirmed diagnosis of HSIL/CIN2+ was above 90% in women aged 55 years or less and significantly decreased in older women ($P = 0.001$ for women aged 56–65 years and $P = 0.002$ for woman aged >65 years) (Table 2). For patients with a cervical screening test showing HSIL and biopsy showing LSIL/CIN1 or below, the percentage of patients vaccinated at age 55 years or less decreased to 70.95% (43/61), with the highest ratio in younger women, being 84.2% (16/19) in women aged 28–35 years. For patients diagnosed with persistent LSIL/CIN1, the vaccination ratio in women aged 55 years or less decreased to 61.5% (64/104); younger women being the subgroup with higher ratios (95.5%; 21/22) (Table 2).

Among the vaccinated women ($n = 1135$), 58.3% (662/1135) received the first HPV vaccine dose after the conization while 30.2% (343/1135) received it before the cervical excisional therapy but after SIL/CIN diagnosis. Only 11.5% (130/1135) of women received the first dose before SIL/CIN diagnosis (Table 3), some of them during adolescence. A proportion of 66.9% (759/1135) of women received the vaccination in non-hospital outpatient settings (i.e. primary care or private centers), especially those who were vaccinated before the SIL/CIN diagnosis (86.2%, 112/130) (Table S1).

3.3 | Annual HPV VCR for the complete schedule

Among the women included in the study with detailed data on their HPV vaccination schedule available ($n = 1000$), 0.9% (9/1000) had been vaccinated before or at 15 years of age. All of them had received three doses, following the applicable Summary of Product Characteristics when they were vaccinated. In all, 99.4% (994/1000) received the first dose of the HPV vaccine after 14 years of age and around the conization procedure. Among them, 88.2% (877/994) received three doses (Table S2).

TABLE 1 Epidemiologic characteristics and annual HPV vaccination coverage rate in women who underwent a cervical excisional therapy due to a diagnosis of SIL/CIN from January 1, 2019, to December 31, 2021.[a]

Year						
HPV vaccination status	**2019**	**2020**		**2021**		**Total**
Vaccinated	447 (87.3%)	317 (86.8%)		371 (87.7%)		1135 (87.3%)
Not vaccinated	65 (12.7%)	48 (13.2%)		52 (12.3%)		165 (12.7%)
No. valid	512	365		423		1300
P value[b]	–	0.923		0.932		–
Age, years						
HPV vaccination status	≤27	28–35	36–45	46–55	56–65	>65
Vaccinated	82 (93.2%)	375 (90.8%)	418 (88.4%)	182 (84.7%)	66 (71.7%)	12 (63.2%)
Not vaccinated	6 (6.8%)	38 (9.2%)	55 (11.6%)	33 (15.3%)	26 (28.3%)	7 (36.8%)
No. valid	88	413	473	215	92	19
P value[c]	0.61	—	0.29	0.03	<0.001	0.002
Indication of excisional therapy						
HPV vaccination status	HSIL/CIN2+[d]		Pap test HSIL and biopsy ≤ LSIL/CIN1		Persistent LSIL/CIN1	Other
Vaccinated	983 (89.8%)		46 (75.4%)		74 (71.2%)	32 (80.0%)
Not vaccinated	112 (10.2%)		15 (24.6%)		30 (28.8%)	8 (20.0%)
No. valid	1095		61		104	40
P value[e]	—		0.002		<0.001	0.062

Abbreviations: CIN, cervical intraepithelial neoplasia; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; Pap test, Papanicolaou (cervical screening) test; SIL, squamous intraepithelial lesion.

[a]Values are presented as number (percentage) or as number.

[b]*P* value referenced to year 2019.

[c]*P* value referenced to age range 28–35 years.

[d]HSIL/CIN2+ includes biopsy-confirmed diagnosis of HSIL/CIN2-3, adenocarcinoma in situ, atypical glandular cells favor neoplasia, and squamous carcinoma.

[e]*P* value referenced to HSIL/CIN+.

3.4 | Impact of the COVID-19 pandemic on the number of cervical excisional therapies and HPV VCR for at least one dose

The annual conizations significantly decreased during the COVID-19 periods. In our population, 32.4% (517/1595) of the interventions were conducted before the pandemic, adjusted per year, 21.5% (342/1594) ($P < 0.001$) during quarantine, 19.6% (312/1594) and 26.5% (423/1595) during the restriction periods I and II, respectively, ($P < 0.001$) (Table 4).

Among the patients vaccinated after conization, 30% (259/865) received the first dose before the pandemic, adjusted per year, and the impact of COVID-19 was significant during the restriction periods I and II, with 20.7% (179/865) and 22.7% (196/865) of vaccinations, respectively ($P < 0.001$), but not during quarantine (Table 4).

4 | DISCUSSION

To our knowledge, the COVAR Study is the first study estimating the annual HPV VCR in women who underwent conization for SIL/CIN. There are no studies reporting the HPV vaccination coverage in this high-risk population at local or global level.

The annual HPV VCR for at least one dose in women who had undergone conization was 87.3% (1135/1300) in our population. Consequently, approximately 13% (165/1300) of the women in this high-risk category remain unvaccinated, despite the public funding. The results confirm a high compliance with the Spanish national recommendations and highlight the need for targeted efforts to close the vaccination gap and protect vulnerable populations.

Although the HPV vaccination is recommended in Spain regardless of age, annual HPV VCR was higher in younger women (around 90%, 1057/88.9, in women aged ≤55 years), decreasing to 71.7% (66/92) in women aged 56–65 years ($P < 0.001$) and 63.2% (12/19) in the older strata aged 65 years and older ($P = 0.002$), probably as a result of the higher awareness in younger women of the HPV-related risks.[15] In Spain, HPV vaccination was limited to the primary target population without catch-up efforts. Women aged 25–27 years during the study period are distinct from the study's main group (mean age 40 years).

In the present study, the highest annual HPV VCR was found in HSIL/CIN2+ patients (89.8%, 983/1095), followed by women

TABLE 2 HPV vaccination coverage rate in women in relation to the SIL/CIN diagnosis and age (in years).[a]

Indication of excisional treatment	HPV vaccination status	Age ≤27[b]	Age 28–35	Age 36–45	Age 46–55	Age 56–65	Age >65	Total
HSIL/CIN2+[c]	Vaccinated	79 (92.9%)	333 (91.5%)	366 (90.1%)	141 (91.6%)	54 (77.1%)	10 (62.5%)	983 (89.8%)
	Not vaccinated	6 (7.1%)	31 (8.5%)	40 (9.9%)	13 (8.4%)	16 (22.9%)	6 (37.5%)	112 (10.2%)
	No. valid	85	364	406	154	70	16	1095
P value[d]		0.827	–	0.536	1	0.001	0.002	0.362
Pap test HSIL and biopsy ≤LSIL/CIN	Vaccinated	3 (100%)	16 (84.2%)	16 (76.2%)	8 (72.7%)	3 (42.9%)	0 (–%)	46 (75.4%)
	Not vaccinated	0	3 (15.8%)	5 (23.8%)	3 (27.3%)	4 (57.1%)	0 (–%)	15 (24.6%)
	No. valid	3	19	21	11	7	0	61
P value[d]		1	–	0.698	0.641	0.057	1	0.539
Persistent LSIL/CIN	Vaccinated	0	21 (95.5%)	22 (75.9%)	21 (56.8%)	8 (61.5%)	2 (66.7%)	74 (71.2%)
	Not vaccinated	0	1 (4.5%)	7 (24.1%)	16 (43.2%)	5 (38.5%)	1 (33.3%)	30 (28.8%)
	No. valid	0	22	29	37	13	3	104
P value[d]		1	–	0.117	0.002	0.019	0.23	0.014
Other	Vaccinated	0	5 (62.5%)	14 (82.4%)	12 (92.3%)	1 (50%)	0 (–%)	32 (80%)
	Not vaccinated	0	3 (37.5%)	3 (17.6%)	1 (7.7%)	1 (50%)	0 (–%)	8 (20%)
	No. valid	0	8	17	13	2	0	40
P value[d]		1	–	0.344	0.253	1	1	0.361

Abbreviations: CIN, cervical intraepithelial neoplasia; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; Pap test, Papanicolaou (cervical screening) test; SIL, squamous intraepithelial lesion.

[a]Values are presented as number (percentage) or as number.

[b]Women ≤27 years are those that could be vaccinated following the recommended calendar, because vaccination started in 2007 in Spain.

[c]HSIL/CIN2+ includes biopsy-confirmed diagnosis of HSIL/CIN2-3, adenocarcinoma in situ, atypical glandular cells favor neoplasia, and squamous carcinoma.

[d]*P* value referenced to age range 28–35 years.

TABLE 3 HPV vaccination time of initiation in relation to the SIL/CIN diagnosis and cervical excision therapy.[a]

HPV vaccination program initiation (receiving first dose)	*N* (%)
Before the diagnosis of SIL/CIN	130 (11.5%)
After the diagnosis of SIL/CIN but before cervical excisional treatment	343 (30.2%)
After the cervical excisional treatment	662 (58.3%)
No. valid	1135

Abbreviations: CIN, cervical intraepithelial neoplasia; SIL, squamous intraepithelial lesion.

[a]Values are presented as number (percentage) or as number.

undergoing treatment for cervical screening result of HSIL but biopsy showing LSIL/CIN1 or less (75.4%, 46/61) and persistent LSIL/CIN1-2 (71.2%, 74/104), significantly lower ($P=0.002$ and $P<0.001$, respectively), suggesting again a high awareness and adherence to the clinical recommendations in women who are informed and sensitive to HPV-linked diseases, although the limited number of patients in the last two groups limits the interpretation of the results. It has been shown that both being well informed about the HPV-diseases risk[15–17] and being within a group in which the vaccine is funded increase the probability of being vaccinated.[18]

Research suggests that HPV vaccination before conization reduces the risk of recurrence after the intervention.[19] Most of the women included in the COVAR Study (88.5%, 1005/1135) were vaccinated during the peri-interventional period, mainly after conization (58.3%, 662/1135) and after SIL/CIN diagnosis but before the cervical excisional treatment (30.2%, 343/1135). Probably, most of these patients were not aware of the recommendations for HPV vaccination until they were included in a high-risk group, such as undergoing a conization, or, alternatively, they were not eligible for funded vaccination before the diagnosis. Additionally, at the time of the intervention, physicians may not know the recommendations for vaccination timing in this population.

The COVID-19 pandemic significantly impacted the number of conizations and the annual HPV VCR in women who underwent a cervical excisional therapy in this study. The number of conizations adjusted per year during the pandemic decreased from 32.4% (517) in the pre-pandemic period to 19.6% (312) in the first COVID-19 restriction period. These findings could reflect the overloading of the Spanish healthcare system during the pandemic, a phenomenon that was also reported in other European countries, indicating that in-hospital treatments of cervical lesions were reduced during the pandemic.[20] Other studies have shown higher reductions due to the pandemic, as of 92% in routine cervical screening, and estimated an increase of cervical cancer diagnoses in the years following the pandemic.[20,21] During the second COVID-19 restriction period and after the restrictions were reduced, the number of conizations increased,

TABLE 4 Potential impact of COVID-19 pandemic in the number of cervical excisional therapies.[a]

	COVID-19 related period				
	Pre-pandemic	Quarantine	Restrictions period (I)	Restrictions period (II)	Total
Period, days	438	79	214	365	
Number of cervical excisional treatments	620 (47.7%)	74 (5.7%)	183 (14.1%)	423 (32.5%)	1300
P value[b]	–	<0.001	<0.001	<0.001	
Adjusted[c] number of women with cervical excisional treatment (per year)	517 (32.4%)	342 (21.5%)	312 (19.6%)	423 (26.5%)	1594[d]
P value[b]	–	<0.001	<0.001	<0.001	
Number of women who started vaccination after cervical excisional treatment	311 (47.0%)	50 (7.6%)	105 (15.9%)	196 (29.6%)	662
P value[b]	–	<0.001	<0.001	<0.001	
Adjusted[c] number of women with vaccinations after cervical excisional treatment (per year)	259 (30.0%)	231 (26.7%)	179 (20.7%)	196 (22.7%)	865[d]
P value[b]	–	0.15	<0.001	<0.001	

[a]Values are presented as number (percentage) or as number.

[b]*P* value referenced to Pre-COVID-19 pandemic period.

[c]Linearly adjusted to 1 year for each period. Annual rate calculated by dividing the number of cervical excisional therapies obtained in each period by the number of days considered within the period and multiplying by 365.

although not to the pre-pandemic levels, suggesting that the health system was starting to normalize.

In our study, most women were of white ethnicity (70.2%, 913/1300). The proportion was particularly high among women who were vaccinated before having a SIL/CIN diagnosis (86.9%, 113/130), compared with those vaccinated at later stages. Similar associations between sociodemographic characteristics and cervical cancer have been established in other studies where mortality rates in women with similar incidences were directly correlated with poverty and having low- or middle-income country origin.[22,23] In Europe, there appears to be a difference between vaccination rates among the different ethnicities, as described in the USA,[24] despite having a public health system with greater capacity and an overall high VCR. However, as the study was not designed to detect differences among ethnic groups, conclusions cannot be drawn.

The study spans different regions across Spain, which aimed to generalize our findings. This study has limitations inherent to its retrospective design. Potential inconsistencies in data registration could affect the selection of the study population. Despite this, risk is expected to be low as cervical excision is a relevant and coded medical procedure, but it could affect date and doses administered within the HPV vaccination program data. Other limitations include the selection of patients with SIL/CIN, which could have been diagnosed using different criteria and methods.

Characterization of the female population receiving cervical excisional therapy provided relevant information of HPV vaccination management in the Spanish National Health System because the HPV vaccine is recommended and funded for high-risk populations. Most women were vaccinated in non-hospital outpatient settings and after the conization. As a result, most preventive measures were deployed in primary care centers. The mean age (40 years) of the population at risk in high-income countries, such as Spain, compares well with previous incidences of cervical cancer, which rises after 25 years of age.[25]

The COVAR Study provides valuable information about HPV VCR in women who underwent conization for a diagnosis of SIL/CIN in Spain; this is a population at higher risk to develop HPV-related diseases in which the HPV vaccine is recommended and funded by the National Health System. However, a considerable percentage of patients remains non-vaccinated and the COVID-19 pandemic impacted cervical excisional therapies, which may increase the incidence of HPV disease in the coming years. Prevention strategies are needed to avoid the consequences of HPV infection.

Finally, this study could guide strategies to improve the HPV vaccination protocols in Spain. This information can also be useful for other countries that are considering the inclusion of similar high-risk groups in their National Immunization Programs.

AUTHOR CONTRIBUTIONS

ATB, MMRM, JOP, AR, BHR, GF, NL, MV, and MPS designed the study. ATB, MMRM, JFV, ROS, JQC, MSF, and MPS contributed to the acquisition of the data. All authors contributed to the interpretation of the data, critically reviewed the results, and have approved the content of the manuscript.

ACKNOWLEDGMENTS

We thank all patients included in the COVAR Study and all the investigators who have participated: Dr. Isabel Matas (Hospital Clinic de Barcelona), Dr. Pluvio Coronado and Dr. Estefanía Ruiperez (Hospital Clínico San Carlos), Dr. Juan José Hernández Aguado and Dr. Damián Ángel Sánchez Torres (Hospital Universitario Infanta Leonor), Dr. Laura Cánovas López and Dr. Micaela Ana Llamas Sarriá (Hospital Clínico Universitario Virgen de la Arrixaca), Dr. Ana Herranz Lozón, Dr. Isabel Limia Pérez, and Dr. Luis Juez González (Hospital Universitario de Basurto), and Dr. José Antonio López Fernández and Dr. Concepción Donaire González (Hospital General Universitario Dr. Balmis). We also thank IQVIA for the management of the study, analysis of the data, and medical writing assistance with this manuscript. This study was sponsored and financed by MSD Spain.

CONFLICT OF INTEREST STATEMENT

ATB and MSF have no conflicts of interest. MMRM has received consulting and or lecture fees from MSD, GSK, and Roche Diagnostics. JFV has received grants from Uriach and lecture fees from MSD, Italfarmaco and Uriach. ROS has received grants from MSD. JQC has received grants from Exeltis, lecture fees from Gedeon Richter, and consulting fees from Bayer, Organon, and Pfizer. MPS has received consulting fees from MSD and Teladoch, lecture fees from MSD and Roche. JOP, AR, BHB, GF, NL, and MV are full-time employees of MSD Spain. All authors and collaborators that have participated in data acquisition have received a fair market value economic compensation for the study-specific activities.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ORCID

María Villarejo https://orcid.org/0000-0001-8723-6443

REFERENCES

1. Drolet M, Benard E, Perez N, Brisson M, Group HPVVIS. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. *Lancet*. 2019;394(10197):497-509. doi:10.1016/S0140-6736(19)30298-3
2. Lei J, Ploner A, Elfstrom KM, et al. HPV vaccination and the risk of invasive cervical cancer. *N Engl J Med*. 2020;383(14):1340-1348.
3. Kjaer SK, Dehlendorff C, Belmonte F, Baandrup L. Real-world effectiveness of human papillomavirus vaccination against cervical cancer. *J Natl Cancer Inst*. 2021;113(10):1329-1335.
4. Dehlendorff C, Baandrup L, Kjaer SK. Real-world effectiveness of human papillomavirus vaccination against vulvovaginal high-grade precancerous lesions and cancers. *J Natl Cancer Inst*. 2021;113(7):869-874.
5. Denslow SA, Rositch AF, Firnhaber C, Ting J, Smith JS. Incidence and progression of cervical lesions in women with HIV: a systematic global review. *Int J STD AIDS*. 2014;25(3):163-177.
6. Ebisch RMF, Rutten DWE, IntHout J, et al. Long-lasting increased risk of human papillomavirus-related carcinomas and Premalignancies after cervical intraepithelial neoplasia grade 3: a population-based cohort study. *J Clin Oncol*. 2017;35(22):2542-2550.
7. Martinez-Gomez X, Curran A, Campins M, et al. Multidisciplinary, evidence-based consensus guidelines for human papillomavirus (HPV) vaccination in high-risk populations, Spain, 2016. *Euro Surveill*. 2019;24(7): 1700857.
8. Jentschke M, Kampers J, Becker J, Sibbertsen P, Hillemanns P. Prophylactic HPV vaccination after conization: a systematic review and meta-analysis. *Vaccine*. 2020;38(41):6402-6409.
9. Eriksen DO, Jensen PT, Schroll JB, Hammer A. Human papillomavirus vaccination in women undergoing excisional treatment for cervical intraepithelial neoplasia and subsequent risk of recurrence: a systematic review and meta-analysis. *Acta Obstet Gynecol Scand*. 2022;101(6):597-607.
10. Kechagias KS, Kalliala I, Bowden SJ, et al. Role of human papillomavirus (HPV) vaccination on HPV infection and recurrence of HPV related disease after local surgical treatment: systematic review and meta-analysis. *BMJ*. 2022;378:e070135.
11. Perkins RB, Guido RS, Castle PE, et al. 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis*. 2020;24(2):102-131.
12. Asociación Española de Patología Cervical y Colposcopia Guía de prevención secundaria del cáncer de cuello uterino AEPCC. 2022.
13. Limia-Sánchez A, Pérez-Martín JJ, Navarro Alonso JA. Ponencia de Programa y Registro de Vacunaciones en grupos de riesgo de todas las edades y en determinadas situaciones. 2018.
14. Ramirez M, de la Fuente J, Andia D, Jose Hernandez J, Fiol G, Torne A. HPV vaccination coverage in women between 15 and 55 years old in Spain: temporal trend during the period 2007-2020. *Int J Gynaecol Obstet*. 2022;158(3):705-713.
15. Kim J, Dove MS, Dang JHT. Sociodemographic factors associated with HPV awareness/knowledge and cervical cancer screening behaviors among caregivers in the U.S. *BMC Womens Health*. 2022;22:335.
16. Song J, Ni YH, Fang J, et al. The levels of women's awareness, experience, acceptability and preference for vaginal human papillomavirus (HPV) self-sampling in three provinces of China: a cross-sectional study. *BMC Womens Health*. 2024;24:343.
17. Shah PM, Ngamasana E, Shetty V, Ganesh M, Shetty AK. Knowledge, attitudes and HPV vaccine intention among women in India. *J Community Health*. 2022;47:484-494.
18. Del Pino M, Martí C, Torras I, et al. HPV vaccination as adjuvant to Conization in women with cervical intraepithelial neoplasia: a study under real-life conditions. *Vaccines (Basel)*. 2020;8(2):245.
19. European Centre for Disease Prevention and Control. *Efficacy, effectiveness and safety of HPV vaccination in women with conisation: a systematic review and meta-analyses*. ECDC; 2024.
20. Ivanus U, Jerman T, Gasper Oblak U, et al. The impact of the COVID-19 pandemic on organised cervical cancer screening: the first results of the Slovenian cervical screening programme and registry. *Lancet Reg Health Eur*. 2021;5:100101.
21. Castanon A, Rebolj M, Pesola F, Pearmain P, Stubbs R. COVID-19 disruption to cervical cancer screening in England. *J Med Screen*. 2022;29(3):203-208.
22. Singh D, Vignat J, Lorenzoni V, et al. Global estimates of incidence and mortality of cervical cancer in 2020: a baseline analysis of the WHO global cervical cancer elimination initiative. *Lancet Glob Health*. 2023;11(2):e197-e206.
23. Spayne J, Hesketh T. Estimate of global human papillomavirus vaccination coverage: analysis of country-level indicators. *BMJ Open*. 2021;11(9):e052016.
24. Stefanos R, Lewis RM, Querec TD, Gargano JW, Unger ER, Markowitz LE. High impact of quadrivalent human papillomavirus vaccine across racial/ethnic groups: National Health and nutrition

examination survey, 2003–2006 and 2015–2018. *Hum Vaccin Immunother*. 2024;20(1):2308378.
25. Arbyn M, Weiderpass E, Bruni L, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *Lancet Glob Health*. 2020;8(2):e191-e203.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Blade AT, del Mar Ramírez Mena M, de la Fuente Valero J, et al. HPV vaccination coverage rate in women undergoing conization for cervical intraepithelial neoplasia in Spain: The COVAR study. *Int J Gynecol Obstet*. 2025;171:415-422. doi:10.1002/ijgo.70170