



HEALTH PROMOTION

Factors associated with HPV vaccination coverage before pregnancy: a cross-sectional study in a cohort of Pregnant Women

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Keywords

HPV vaccination • Pregnant women • Vaccine hesitancy • Risk perception • Socio-demographic factors

Summary

Background. Human papillomavirus (HPV) infection is a major cause of cervical and other anogenital cancers. Despite the availability of effective vaccines, HPV vaccination coverage remains suboptimal in Italy, particularly among women of childbearing age. Pregnant women represent a key population for investigating vaccine hesitancy and its determinants. This study aimed to explore socio-demographic, behavioural, and perceptual factors associated with HPV vaccination coverage prior to pregnancy, using data from the NEHO cohort in Southern Italy.

Methods. A cross-sectional analysis was conducted on 567 pregnant women enrolled between 2018 and 2020 in the Priolo National Priority Site. HPV vaccination status was obtained from local immunization databases. Risk perception indices (HPI, EHPI, HRPI, RPI), and information sources were assessed via structured questionnaires. Logistic regression and Bayesian Weighted Quantile Sum (bWQS) models were used to identify

associations between vaccination status and independent variables.

Results. Only 7.4% of participants had HPV vaccination coverage prior to pregnancy. Vaccinated women were significantly younger, unmarried, and more likely to have lower educational levels. Higher scores on environmental and exposure hazard perception indices (HPI and EHPI) were positively associated with vaccination uptake. Vaccinated individuals were more likely to attribute health protection responsibility to national institutions and industry leadership. bWQS regression confirmed the relevance of risk perception in shaping vaccination behaviour, with EHPI contributing most to the overall effect.

Conclusion. The results of this study suggest that tailored public health strategies that address risk perception, institutional trust, and population-specific dynamics are essential to increase HPV vaccination coverage and reduce health inequalities.

Introduction

Human papillomavirus (HPV) refers to a group of viruses that cause the most prevalent sexually transmitted infection [1] and represents the second leading cause of cancer linked to an infectious agent [2], being strongly associated with anogenital and oropharyngeal malignancies [3, 4].

HPV-related cancers represent 5% of new global cancer cases [5]. Annually in Europe, there are an estimated 58,169 new cases of cervical cancer and 17,486 cervical cancer deaths [6]. In 2018, the Italian Health System incurred direct costs of €542.7 million for HPV-related diseases, which may increase by €16.2–€37.5 million with innovative cancer therapies [7].

HPV vaccination is a highly effective primary prevention strategy for reducing infections and HPV-related cancer [8]. Herd protection has been significantly observed when vaccination coverage exceeds 50% [9, 10].

Since their introduction in 2006, HPV vaccines have been endorsed by the World Health Organisation (WHO) as a critical public health measure, with official

recommendations beginning in 2009 [11]. In line with these efforts, the WHO has launched the global strategy for the elimination of cervical cancer as a public health problem, based on the so-called “90-70-90” targets: 90% of girls fully vaccinated with the HPV vaccine by age 15, 70% of women screened with a high-performance test by ages 35 and 45, and 90% of women identified with cervical disease receiving appropriate treatment. Achieving these targets is expected to drastically reduce the global burden of HPV-related cancers and underscores the central role of vaccination in comprehensive cancer prevention strategies [12].

Currently, three HPV vaccines are approved for use in the European Union: the bivalent vaccine Cervarix (GlaxoSmithKline Biologicals), the quadrivalent vaccine Gardasil (MSD Vaccins), and the nonavalent vaccine Gardasil 9 (MSD Vaccins), with the latter currently representing the main HPV vaccine in use [13].

In Italy, HPV vaccination has been actively provided free of charge to 11-year-old girls since 2007/2008. Recognizing the advantages of gender-neutral immunization campaigns, the programme was expanded to include 11-year-old boys and was implemented

nationwide by 2018. Additionally, catch-up vaccination is recommended for women up to the age of 26, especially during their initial cervical cancer screening [14]. Beyond this, HPV vaccination in Italy is also recommended for specific high-risk groups, including women treated for high-grade cervical intraepithelial neoplasia (CIN II or III), people living with HIV regardless of age, and men who have sex with men (MSM), who are at increased risk of HPV infection and related diseases [15].

Despite these efforts, HPV vaccination coverage in Italy remains below the 95% target for 12-year-olds set by the National Vaccination Prevention Plan. According to national data, coverage in the 2021 birth cohort is approximately 51% among girls and 45% among boys, with no Italian region reaching the recommended target established by the National Vaccination Prevention Plan [16].

The prevalence of HPV among pregnant women suggests a higher risk of infection compared to non-pregnant women [17, 18]. HPV infection has been detected in maternal and fetal tissues [19], possibly influenced by physiological and immunological changes occurring during gestation [20, 21].

While the relationship between HPV infection and pregnancy outcomes remains unclear [22], some studies suggest adverse effects such as preterm birth [23], spontaneous abortion [24], premature rupture of membranes [25], intrauterine growth restriction [26], low birth weight [27], hypertensive disorders and fetal death [28]. However, conflicting evidence exists, with some authors finding no significant association [29, 30]. Moreover, a population-level analysis has provided the first evidence that HPV vaccination reduces negative pregnancy outcomes, such as preterm birth and low birth weight, in vaccinated women [31].

Inequalities in HPV vaccination uptake are driven by several factors, including inadequate knowledge about HPV, which is strongly linked to lower vaccination rates. In fact, greater HPV-related knowledge is associated with more positive attitudes toward vaccination and a stronger intention to vaccinate [32]. Although HPV vaccination is ideally administered before sexual debut through school-based programmes, several factors influencing vaccination uptake in adolescents and young adults have been identified, including risk perception, vaccine cost, and healthcare provider recommendations [33], alongside low awareness of HPV infection, particularly among Italian adolescents and young women [34]. Socioeconomic disparities also play a significant role, as lower educational attainment, and socioeconomic status limit access to health information, reduce health-related knowledge, and contribute to unhealthy behaviours [35, 36]. Additional barriers to vaccination include fears of side effects, inconsistent advice from healthcare providers, limited access to reliable information [37, 38], as well as a lack of trust in the medical system [39, 40]. In this perspective, perception of environmental health hazards may reflect a broader cognitive framework related to health risk appraisal and preventive orientation,

potentially influencing attitudes toward preventive behaviours such as vaccination.

This study aims to analyse the factors influencing HPV vaccination coverage prior to pregnancy among women enrolled during pregnancy, with a focus on understanding and addressing disparities in vaccine uptake. Vaccine hesitancy is defined by the World Health Organisation Strategic Advisory Group of Experts (SAGE) as the delay in acceptance or refusal of vaccination despite availability of vaccination services. It is a complex and context-specific phenomenon, varying across time, place, and vaccines, and influenced by factors such as complacency, convenience, and confidence [41]. Pregnant women have recently been identified as a key population for studying vaccine hesitancy, mainly in relation to maternal immunizations such as influenza, Tdap and RSV vaccines, particularly in Western countries where hesitancy has grown significantly [42]. In this context, pregnancy offers a valuable opportunity to explore attitudes toward vaccination more broadly, including previous HPV vaccination behaviours.

By exploring these determinants, this research seeks to bridge gaps in the existing literature and provide actionable insights to inform targeted public health interventions.

Materials and Methods

STUDY DESIGN

This study was conducted using data collected within the NEHO cohort study [43], which employed an previously validated questionnaire and, between January 2018 and January 2020, voluntarily enrolled pregnant women residing in three National Priority Sites for Environmental Remediation (SIN) in Southern Italy, including Crotone, Priolo, and Milazzo, as well as in the corresponding Local Reference Areas (LRAs), characterized by similar geographic and socio-demographic features but were located outside the SIN boundaries. For the present study, 567 participants were selected from the NEHO cohort in the Priolo SIN and its associated LRAs. Vaccination data were retrieved from the provincial immunization database of the local Health Department, which systematically records all administered vaccines, regardless of the setting in which they were delivered (*e.g.*, school-based programmes, vaccination centers, pharmacies, or physicians).

STUDY VARIABLES

Information for this study was collected through questionnaires administered during the third trimester of pregnancy. The data included socio-demographic characteristics (age, marital status, educational level, place of residence, and overcrowding index) and lifestyle habits (alcohol consumption, folate supplementation, physical activity, smoking habits, and breastfeeding duration). HPV vaccination status was recorded as a binary variable (Yes/No).

Environmental and health risk perception was assessed

using four specific indices: Hazard Perception Index (HPI): assessment of perceived environmental hazards in the area of residence; Exposure Hazard Perception Index (EHPI): perception of exposure to these hazards; Health Risk Perception Index (HRPI): perception of health risks related to specific conditions, such as allergies, chronic respiratory diseases, infertility, and cancer; Risk Perception Index (RPI): a composite index integrating various perceptions of environmental and health risks. Participants were also asked about their beliefs regarding responsibility for public health protection. Specifically, they were asked whether they considered national institutions, local institutions, industry leadership, local health authorities (*e.g.*, ASP, general practitioners), and individual citizens to be responsible for safeguarding health. Responses were recorded as binary variables (yes/no) for each actor. In addition, participants were asked to indicate which sources they normally rely on to obtain information about environmental and health risks. These sources included national media, local media, healthcare professionals and organisations, scientists, factory workers, the internet, and personal networks (*e.g.*, family, friends, colleagues). Responses were also collected as binary variables for each information source.

STATISTICAL ANALYSIS

Descriptive statistics were computed for all variables, with categorical variables presented as frequencies and percentages, and continuous variables summarized using medians and interquartile ranges due to non-normal distributions. Associations between HPV vaccination status (Yes/No) and categorical variables (*e.g.*, socio-demographic characteristics, behavioural factors, beliefs about health protection, and information sources) were evaluated using the Chi-square test or Fisher's exact test, as appropriate. A multivariable logistic regression model was performed to explore independent associations with HPV vaccination status. To examine the association between HPV vaccination and all the risk indices, we employed a Bayesian Weighted Quantile Sum (bWQS) regression. The bWQS model estimates both the overall effect of the risk perception indices, EHPI, HPI and HRPI, on HPV vaccination and the individual contribution (weights) of each component to the mixture effect. We modeled HPV vaccination status as the outcome variable (binary), and included age, educational level and marital status as potential confounders. The weights of the indices were constrained to be non-negative and sum to 1, and all model parameters were estimated using Markov Chain Monte Carlo (MCMC) sampling. The model was implemented using the R package bWQS, with default chains and iteration parameters. Results were reported as regression coefficients (β), with corresponding p-values. Statistical significance was defined as $p < 0.05$. All analyses were performed using R software (version 4.3.2).

ETHICS AND REGULATION

All participants provided written informed consent after reading a detailed information sheet. The study was approved by the Ethics Committee "Catania 2" (July

11, 2017, No. 38/2017/CECT2) and was conducted in accordance with the Declaration of Helsinki, the General Data Protection Regulation (EU 2016/679), and Italian regulations on personal data protection.

Results

The analysis of the study population (N=567) revealed several associations between HPV vaccination and socio-demographic and behavioural factors, as shown in Table I. Among the participants, 42 individuals (7.4%) reported being vaccinated for HPV, while 525 (92.6%) were unvaccinated.

Vaccinated individuals were significantly younger than those unvaccinated (22.0 vs. 31.0 years, $p < 0.001$).

Tab. I. Main findings.

Variable	HPV Vaccination Status		p-value
	No (N=525, 92.6%)	Yes (N=42, 7.4%)	
Age	31.0 [28.0;34.0]	22.0 [20.0;28.8]	<0.001
Marital status:			<0.001
Married	330 (62.9%)	13 (31.0%)	
Unmarried	195 (37.1%)	29 (69.0%)	
Educational level:			0.041
High	119 (22.7%)	7 (16.7%)	
Medium	263 (50.1%)	16 (38.1%)	
Low	141 (26.8%)	19 (45.2%)	
Missing	2 (0.4%)	0 (0.0%)	
Crowding index	1.00 [0.75;1.33]	1.20 [0.75;1.50]	0.649
Risk perception:			
HPI	0.54 [0.36;0.71]	0.66 [0.49;0.78]	0.026
HRPI	0.62 [0.36;0.78]	0.75 [0.38;0.80]	0.297
EHPI	0.43 [0.29;0.57]	0.57 [0.43;0.71]	0.023
RPI	0.55 [0.38;0.70]	0.67 [0.46;0.79]	0.052
Habits during pregnancy			
Alcohol consumption:			1.000
No	516 (98.3%)	42 (100%)	
Yes	8 (1.5%)	0 (0.00%)	
Missing	1 (0.2%)	0 (0.0%)	
Folate supplementation:			1.000
No	8 (1.5%)	0 (0.00%)	
Yes	517 (98.5%)	42 (100%)	
Physical activity:			0.396
No	503 (95.8%)	42 (100%)	
Yes	22 (4.2%)	0 (0.00%)	
Smoking:			0.045
No	467 (88.9%)	33 (78.6%)	
Yes	56 (10.7%)	9 (21.4%)	
Missing	2 (0.4%)	0 (0.0%)	
Breastfeeding			0.672
No	263 (50.18%)	21 (50%)	
3 months	74 (14.1%)	6 (14.3%)	
6 months	113 (21.5%)	6 (14.3%)	
Missing	75 (14.3%)	9 (21.4%)	

Unmarried participants were more likely to be vaccinated compared to married ones (69.0% vs. 31.0%, $p<0.001$). Educational level also showed a significant association ($p=0.041$), with a higher proportion of vaccinated individuals having a low educational level (45.2%) compared to unvaccinated ones (26.8%). Conversely, individuals with medium and high educational levels were more prevalent among the unvaccinated group (50.1% and 22.7%, respectively) compared to the vaccinated group (38.1% and 16.7%).

Risk perception indices were assessed, with vaccinated individuals showing significantly higher scores for HPI ($p=0.026$) and EHPI ($p=0.023$), reflecting a greater perception of vulnerability and benefits related to vaccination. Differences in HRPI ($p=0.297$) and RPI ($p=0.052$) were not statistically significant, though trends suggested that vaccinated individuals generally had a higher perception of risk severity and response efficacy. Smoking habits were also significantly associated with vaccination status ($p=0.045$). A higher proportion of smokers was found among vaccinated individuals (21.4%) compared to unvaccinated ones (10.7%), while non-smokers were more prevalent in the unvaccinated group (88.9% vs. 78.6%). Other behavioural variables, including alcohol consumption ($p=1.000$), folate supplementation ($p=1.000$), physical activity ($p=0.396$), and breastfeeding duration ($p=0.672$), did not show statistically significant differences between vaccinated and unvaccinated groups. Tables II and III report participants' beliefs regarding

responsibility for health protection and sources of information on environmental and health risks. These analyses were conducted on the subsample of participants who answered these specific questions, corresponding to 450 out of 525 (85.7%) unvaccinated and 33 out of 42 (78.6%) vaccinated subjects. Participants' beliefs regarding responsibility for health protection showed significant associations with HPV vaccination status (Tab. II). Unvaccinated individuals were more likely to attribute this responsibility to national institutions compared to vaccinated participants (47.8% vs. 24.2%, $p=0.015$). A similar trend was observed with regard to industry leadership, with a higher proportion of unvaccinated individuals identifying this group as responsible, although the result did not reach conventional significance (45.6% vs. 27.3%, $p=0.063$). No significant associations emerged for local institutions (54.0% vs. 42.4%, $p=0.269$), individual citizens (41.6% vs. 48.5%, $p=0.551$), or local health services (50.7% vs. 48.5%, $p=0.951$). Nonetheless, vaccinated individuals tended to assign relatively less responsibility to these latter categories.

Regarding sources of information on environmental and health risks (Tab. III), a significant association was

Tab. II. Responsibility for Health Protection and HPV Vaccination Status.

Who is responsible for health protection?	HPV Vaccination Status		p-value
	No, n (%) N=450/525	Yes, n (%) N=33/42	
Industry leadership			0.063
No	245 (54.4%)	24 (72.7%)	
Yes	205 (45.6%)	9 (27.3%)	
National Institution			0.015
No	235 (52.2%)	25 (75.8%)	
Yes	215 (47.8%)	8 (24.2%)	
Local institutions			0.269
No	207 (46.0%)	19 (57.6%)	
Yes	243 (54.0%)	14 (42.4%)	
Individual citizens			0.551
No	263 (58.4%)	17 (51.5%)	
Yes	187 (41.6%)	16 (48.5%)	
Local health services (e.g., Local Health Authority, GPs)			0.951
No	222 (49.3%)	17 (51.5%)	
Yes	228 (50.7%)	16 (48.5%)	

Proportion refers to 450 unvaccinated (85.7% of the total unvaccinated group) and 33 vaccinated (78.6% of the total vaccinated group) participants without any missing data on these items.

Tab. III. Information Sources on Health Risks and HPV Vaccination Status.

Main sources of information on health risk	HPV Vaccination Status		p-value
	No, n (%) N=450/525	Yes, n (%) N=33/42	
National mass media			0.702
No	209 (46.4%)	17 (51.5%)	
Yes	241 (53.6%)	16 (48.5%)	
Local mass media			0.297
No	279 (62.0%)	24 (72.7%)	
Yes	171 (38.0%)	9 (27.3%)	
Healthcare organisations and professionals			0.642
No	345 (76.7%)	27 (81.8%)	
Yes	105 (23.3%)	6 (18.2%)	
Scientists			1.000
No	411 (91.3%)	31 (93.9%)	
Yes	39 (8.67%)	2 (6.06%)	
Factory workers			0.032
No	419 (93.1%)	27 (81.8%)	
Yes	31 (6.89%)	6 (18.2%)	
Internet			1.000
No	191 (42.4%)	14 (42.4%)	
Yes	259 (57.6%)	19 (57.6%)	
Personal networks			0.622
No	299 (66.4%)	20 (60.6%)	
Yes	151 (33.6%)	13 (39.4%)	

Proportion refers to 450 unvaccinated (85.7% of the total unvaccinated group) and 33 vaccinated (78.6% of the total vaccinated group) participants without any missing data on these items.

found with reliance on factory workers. Vaccinated individuals reported greater reliance on this group compared to unvaccinated participants (18.2% vs. 6.9%, $p=0.032$). While the remaining sources did not show statistically significant associations, some trends were noted. Unvaccinated participants reported slightly higher reliance on local media (38.0% vs. 27.3%, $p=0.297$), health professionals (23.3% vs. 18.2%, $p=0.642$), and personal networks such as family, friends, or acquaintances (33.6% vs. 39.4%, $p=0.622$). Minimal differences were observed for scientists (8.67% vs. 6.06%, $p=1.000$), national media (53.6% vs. 48.5%, $p=0.702$), and internet (57.6% in both groups, $p=1.000$). Logistic regression models (Tab. IV) were used to assess associations between HPV vaccination status and various risk perception indices, adjusted for age, marital status, and educational level.

Higher scores on the HPI were significantly associated with increased odds of HPV vaccination (OR=0.90; 95% CI: 0.827, 0.988; $p=0.026$), as were higher scores on the EHPI (OR=0.86; 95% CI: 0.780, 0.957; $p=0.005$). These results suggest that individuals perceiving more environmental hazards or exposure risks were more likely to be vaccinated. The HRPI did not reach

Tab. IV. Regression models.

	OR	CI - lower	CI - higher	p-value
HPI	0.90	0.827	0.988	0.026
Unmarried	0.97	0.920	1.017	0.193
Educational Level (High)	0.96	0.910	1.017	0.171
Educational Level (Low)	0.97	0.909	1.031	0.314
Age	1.01	1.006	1.017	<0.001
HRPI	0.27	0.048	1.313	0.113
Unmarried	0.62	0.245	1.539	0.305
Educational Level (High)	0.31	0.096	0.969	0.041
Educational Level (Low)	0.65	0.230	1.961	0.425
Age	1.26	1.137	1.417	<0.001
EHPI	0.86	0.780	0.957	0.005
Unmarried	0.97	0.925	1.022	0.270
Educational Level (High)	0.96	0.905	1.011	0.118
Educational Level (Low)	0.97	0.914	1.036	0.388
Age	1.01	1.008	1.018	<0.001
RPI	0.06	0.007	0.494	0.011
Unmarried	0.67	0.259	1.682	0.389
Educational Level (High)	0.29	0.090	0.937	0.036
Educational Level (Low)	0.60	0.209	1.823	0.347
Age	1.28	1.150	1.446	<0.001

Tab. V. Results from Bayesian Weighted Quantile Sum (bWQS) regression 3.2. Figures, Tables and Schemes

	OR	CI-lower	CI-higher
beta1	0.05	0.005	0.405
Age	1.29	1.186	1.448
Educational Level	0.54	0.310	0.880
Marital Status	0.63	0.247	1.538
W-EHPI	0.476	0.089	0.849
W-HRPI	0.229	0.010	0.584
W-HPI	0.295	0.009	0.654

statistical significance (OR=0.27; 95% CI: 0.048, 1.313; $p=0.113$), while the RPI showed a statistically significant association (OR=0.06; 95% CI: 0.007, 0.494; $p=0.011$), indicating that higher overall risk perception was also related to increased likelihood of HPV vaccination. Age was consistently associated with higher vaccination probability across all models ($p<0.001$). Marital status (unmarried vs. married) and low educational level were not significantly associated with vaccination in most models; however, higher educational level was negatively associated with HPV vaccination in the models including HRPI (OR=0.31; $p=0.041$) and RPI (OR=0.29; $p=0.036$), suggesting that individuals with higher education were less likely to be vaccinated.

To assess the combined effect of risk perception on HPV vaccination, we applied Bayesian Weighted Quantile Sum (bWQS) regression, incorporating the three risk perception indices as exposures. Given the high collinearity among the indices, bWQS provided an appropriate framework for estimating their joint contribution while accounting for inter-correlation (Fig. S1). The model was adjusted for potential confounders, including age, educational level and marital status (Tab. V). Results from bWQS analysis showed a negative association between the weighted mixture of risk perception indices and the likelihood of HPV vaccination (OR=0.05; 95% CI: 0.005; 0.405). Age and educational level confirmed the same trend observed for regressions with single indices (age: OR=1.29; 95% CI: 1.186; 1.448 - educational level: OR=0.54; 95% CI: 0.310; 0.880). Among the three indices, EHPI contributed the highest weight to the mixture ($w=0.476$), followed by HPI ($w=0.295$) and HRPI ($w=0.229$) (Fig. S2), suggesting it may play a more prominent role in shaping vaccination decisions. These findings underscore the importance of aggregated risk perception in influencing vaccine uptake behaviour.

Discussion

The findings of this study provide a comprehensive analysis of socio-demographic and behavioural factors associated with HPV vaccination coverage before pregnancy among women enrolled during pregnancy. Understanding these associations is crucial for developing targeted public health strategies to increase

vaccine coverage, particularly amidst challenges such as vaccine hesitancy and inequitable access to preventive healthcare. Vaccination behaviours are shaped by a complex interplay of individual, social, and cultural factors, and this study offers valuable insights into barriers and facilitators that influence health decision-making.

One key observation was the significant age disparity between vaccinated and unvaccinated individuals, with vaccinated participants being notably younger. This difference likely reflects greater exposure to vaccination campaigns during adolescence and early adulthood, critical periods for establishing preventive health behaviours, as well as a cohort effect related to the relatively recent introduction of the HPV vaccine. Indeed, younger women were more likely to be targeted by organised vaccination programmes, whereas older women may not have been offered vaccination in their youth and may have subsequently been lost to follow-up by the healthcare system. Moreover, younger individuals are often better informed about HPV and vaccination benefits [44] and are more receptive to new information due to higher cognitive adaptability [45]. Notably, age was a significant predictor across all risk perception indices in our regression analyses, suggesting that perceived vulnerability and awareness of health risks increase with age.

Marital status also emerged as a significant factor, with unmarried individuals demonstrating higher vaccination rates than married ones. This finding aligns with previous research indicating lower HPV vaccine uptake among married women compared to unmarried women [46-8]. Married women may perceive a lower risk of HPV due to assumptions of monogamy, reducing their perceived need for vaccination [46]. However, it is important to emphasize that even women with only one sexual partner face an 85% lifetime risk of HPV infection [49].

Educational attainment showed an inverse relationship with vaccination status. A larger proportion of vaccinated individuals had lower educational levels compared to the unvaccinated group. While higher education often correlates with better health literacy and vaccine uptake [50], this finding may reflect the success of targeted interventions that effectively reached lower-educated populations. Nevertheless, lower educational attainment is frequently associated with reduced HPV knowledge [51], underscoring the need for ongoing, inclusive public health campaigns. Moreover, logistic regression models revealed that higher educational level was significantly associated with lower odds of vaccination in the presence of certain risk perception variables, such as HRPI and RPI, suggesting that educational attainment may interact with cognitive risk evaluations in complex ways. This finding suggests a more complex relationship between education and vaccination behaviours. Individuals with higher education typically possess enhanced knowledge, superior information-processing skills, and greater risk awareness [52], which generally enable them to better assess threats and adopt effective preventive

strategies [53]. One possible interpretation is that among individuals with higher education, greater knowledge and information-processing skills may prompt more critical evaluation of vaccine-related information or diminished perceived personal risk, leading to lower acceptance of HPV vaccination despite awareness of potential risks. These findings imply that while higher educational attainment often facilitates access to health information, it does not necessarily translate into increased risk perception or consistent preventive action. Additionally, the younger age of vaccinated individuals may partly explain this inverse association, as younger participants often present lower educational levels due to ongoing studies.

Risk perception indices revealed vaccinated individuals had higher scores for HPI and EHPI, indicating the importance of personal health risk appraisal in vaccine decision-making. Though differences in HRPI and RPI were not statistically significant, trends suggested vaccinated individuals generally had greater awareness of HPV risks and the effectiveness of prevention measures. These findings are consistent with research showing that vaccinated individuals tend to perceive higher risks of cervical cancer and demonstrate greater engagement in preventive behaviours [54] and non-vaccinated women often cite a low perceived risk of HPV, influenced by factors such as lack of sexual activity or reliance on alternative prevention methods [42, 55, 56]. These associations were further supported by regression analysis: higher HPI, EHPI, and RPI scores were significantly associated with increased likelihood of HPV vaccination, reinforcing the relevance of perceived hazard and exposure in motivating preventive action.

An unexpected result was the association between smoking habits and vaccination status. Smokers were more prevalent among vaccinated individuals compared to non-smokers. This contrasts with literature suggesting smokers are less likely to engage in preventive health measures [57, 58]. The observed trend may reflect unique socio-behavioural dynamics within our population and highlights the importance of further research to clarify underlying mechanisms.

Other lifestyle factors, such as alcohol consumption, folate supplementation, physical activity, and breastfeeding duration, did not show statistically significant differences between vaccinated and unvaccinated individuals. While these variables are not directly related to HPV vaccination, their inclusion underscores the multifaceted nature of health behaviours in this specific phase of life. Indeed, many women tend to modify their habits before and during pregnancy, often reducing smoking, caffeine, and alcohol intake, and increasing their consumption of fruits and vegetables [59, 60]. However, a significant proportion continues to engage in unhealthy behaviours, despite available evidence and clinical recommendations promoting a healthy lifestyle. These behavioural patterns are shaped not only by medical advice but also by non-medical influences, including social, cultural, and psychological factors. In particular, psychosocial variables such as anxiety and stress have been negatively

associated with pregnancy outcomes [61], and may also influence adherence to preventive measures like vaccination.

Participants' beliefs regarding health protection responsibility showed relevant associations with HPV vaccination status. Vaccinated individuals were more likely to attribute responsibility for health protection to industry leadership and national institutions, suggesting that trust in these entities may positively influence vaccine uptake. Conversely, no significant differences emerged regarding local institutions, individual citizens, or local health services. However, trends indicated a higher attribution of responsibility to local institutions and individual citizens among vaccinated participants, although these did not reach statistical significance. This pattern nonetheless highlights the broader relevance of institutional trust in shaping vaccine acceptance [62].

Regarding sources of information on health risks, vaccinated participants reported a stronger reliance on factory workers, suggesting that, within this industrial-area population, informal workplace communication may serve as a significant channel for health information dissemination. This pattern likely reflects the strong social ties and trust-based relationships common in industrial work environments, where peer-to-peer dynamics and supportive workplace cultures – characterized by encouragement from both colleagues and supervisors – have been shown to foster healthier behaviours among employees [63]. No significant associations were found for other sources such as national media, local media, health professionals, scientists, internet, or personal networks. Nonetheless, a non-significant trend suggested greater reliance on national media and health professionals among vaccinated individuals, warranting further investigation.

This study underscores the complex interplay of socio-demographic and behavioural factors influencing HPV vaccination uptake. Identifying these patterns provides valuable insights into factors associated with HPV vaccination uptake and may help inform tailored, population-specific interventions aimed at addressing barriers to vaccination. The results highlight the importance of addressing misconceptions about HPV risk, particularly among married women and those with lower educational attainment. Importantly, our findings also demonstrate that individual cognitive risk perception – particularly regarding environmental hazards, perceived exposure, and overall risk – plays a significant role in vaccination decisions. Furthermore, exploring unique trends, such as the association between smoking and vaccination, can inform more effective, targeted public health strategies. Notably, participants' beliefs about who holds responsibility for health protection revealed important trends that may shape vaccination behaviours. Vaccinated individuals tended to place greater trust in industry leadership and national institutions as responsible for safeguarding public health, suggesting that confidence in authoritative bodies could enhance vaccine acceptance. Conversely, trust in local institutions, individual citizens, and local health services

did not significantly differ between groups, indicating these may be perceived as less influential or less relevant in vaccination decisions. Similarly, while various sources of health risk information such as national and local media, healthcare professionals, scientists, the internet, and personal networks showed no significant differences in trust levels, vaccinated participants reported a notably higher reliance on factory workers as informants. This unexpected finding points to potentially unique community dynamics or communication channels that could be leveraged to improve vaccine outreach. Ultimately, these findings contribute to the broader goal of reducing HPV-related morbidity and mortality through improved vaccination coverage and equitable access to preventive healthcare.

Strengths and Limitations

This study has several strengths. By leveraging data from the NEHO cohort, which includes a well-defined sample of women of reproductive age residing in areas with varying environmental and socio-demographic characteristics, the study provides a nuanced understanding of factors influencing HPV vaccination uptake. Although pregnant women are not a target group for HPV vaccination, this population represents a well-defined and accessible subgroup of young women, allowing a retrospective assessment of HPV vaccination status and its determinants in a public health-relevant population. The use of validated indices to measure risk perception (HPI, EHPI, HRPI, and RPI) further strengthens the reliability of the findings by capturing multidimensional aspects of participants' perceptions. Additionally, the study fills critical gaps in the literature by focusing on a population often overlooked in vaccine-related research and by exploring associations between sociodemographic factors, risk perceptions, and vaccination status.

However, the study is not without limitations. First, although the overall sample size was relatively robust (567 participants), only 42 women (7.4%) were vaccinated against HPV, which limits the statistical power to detect certain associations, reduces the precision of some estimates, and requires that the findings be interpreted with caution. The particularly low HPV vaccination rate observed in our sample compared to national and regional estimates cannot be fully explained by the available data and may reflect unmeasured contextual or population-specific factors. Therefore, caution is warranted when comparing these findings with broader surveillance data.

Second, the cross-sectional design prevents establishing causal relationships between the observed factors and HPV vaccination uptake.

Third, data on lifestyle habits and vaccination status were self-reported and may therefore be subject to recall bias or social desirability bias. In addition, the lack of information on several variables that could act as relevant confounders in the analysis of HPV vaccination uptake, such as household income, accessibility to nearby vaccination hubs, sexual activity and related habits, previous HPV infections or HPV-related cancers,

and adherence to routine cervical cancer screening, represents a further limitation. These variables were not included in the questionnaire because the NEHO cohort was originally designed to investigate environmental exposures and health risk perception rather than vaccination behaviours. Their absence may have limited our ability to fully capture the complexity of factors influencing HPV vaccination decisions.

Furthermore, the observed inverse association between educational level and HPV vaccination uptake may be partially influenced by a cohort or confounding effect related to age, as younger women are more likely both to be vaccinated and to have lower educational levels due to ongoing studies. This should be taken into account when interpreting the relationship between education and vaccination behaviour.

Finally, the study sample, while robust, may not fully generalize to populations outside the specific geographic and social contexts investigated. In particular, most participants resided in SInS and their corresponding LRAs, mainly involving medium-small sized urban areas. This environmental burden may have influenced participants' cognitive risk assessments, increasing their sensitivity toward environmental health risks and potentially affecting both their perceptions and reported behaviours. Consequently, findings regarding risk perception and vaccination decisions may not be entirely generalizable to populations living in larger cities or in less polluted or differently perceived environments.

POLICIES

This study underscores the critical role of socio-demographic and behavioural factors in shaping HPV vaccination coverage before pregnancy in women enrolled during pregnancy, providing valuable insights for targeted policy and public health interventions. Health behaviours are deeply influenced by individuals' perceptions of susceptibility, severity, benefits, and barriers related to a disease [64, 65]. Perceived benefits and barriers significantly impact decision-making processes [42]. To encourage early vaccination, it is crucial to widely disseminate information about the higher effectiveness of the HPV vaccine when administered at a young age.

Pregnant women have been recognized as an ideal target population for developing interventions aimed at promoting vaccinations. The antenatal period represents a pivotal time when attitudes and beliefs about vaccines first take shape [66] and serves as a strategic "teachable moment" for health promotion and behaviour change [67-69]. Efforts should be intensified to improve the availability of unbiased data on the safety and efficacy of vaccines, including studies from non-industry-sponsored sources [70, 71], and to strengthen vaccine reporting and pharmacovigilance systems [72].

By addressing these barriers through targeted education, improved data transparency, and enhanced healthcare provider engagement, policymakers can foster greater trust in vaccination programmes. Ultimately, these strategies can contribute to higher HPV vaccination

coverage, reduced disease burden, and improved maternal and child health outcomes globally.

Conclusion

This study highlights the critical interplay between socio-demographic and behavioural factors influencing HPV vaccination coverage before pregnancy in women enrolled during pregnancy. The findings underscore the need for targeted public health strategies to address disparities in vaccination coverage and reduce barriers to access. Younger age, marital status, and specific risk perception indices emerged as significant factors associated with HPV vaccination, revealing opportunities for tailored interventions. The unexpected association between smoking and vaccination status suggests areas for further research to understand population-specific dynamics. By enhancing education, promoting equitable access to vaccines, and leveraging the antenatal period as a strategic opportunity for health promotion, these insights can inform policies aimed at improving HPV vaccination coverage and reducing the burden of HPV-related diseases. Future studies specifically designed to investigate HPV vaccination behaviours should incorporate these variables in order to better disentangle structural, behavioural, and socioeconomic determinants of vaccine uptake and to inform more targeted public health interventions.

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Institutional Review Board Statement

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the three Ethics Committees responsible for the involved NPCSS: the Ethics Committee of the University Hospitals of Messina for the NPCSS of Milazzo (18 September 2017, no. 9/2017), the Ethics Committee "Catania 2" for the NPCSS of Augusta-Priolo (11 July 2017, no. 38/2017/CECT2), and the Ethics Committee of Calabria Region for the NPCSS of Crotone (20 July 2017, no. 173).

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Data availability statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Conflicts of interest statement

The authors declare that they have no competing interests.

Authors' contributions

FC, CF equally contributed to this work and share the first authorship. GD, SR contributed equally as last authors; FC, CF: Conceptualization; IC, GD, SR: Methodology; FC, GD, SR: Acquisition of data; FC, CF, FB, IC, GD, SR, PC, VL, NA: Writing - original draft preparation; FC, CF, IC, GD, SR, PC, VL, NA: Writing - review and editing; IC: Statistical analysis; GD, SR: Supervision and project administration.

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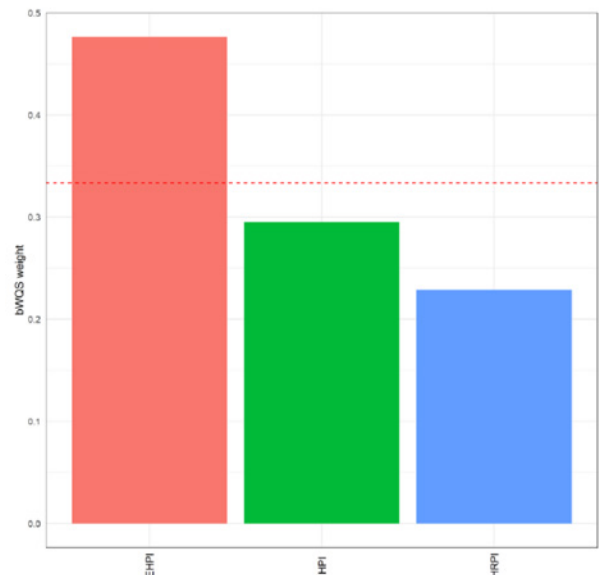
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Supplementary materials

Fig. S1. Correlation plot of the four risk perception indices.



Fig. S2. Weights of the risk perception indices according to the bWQS model.



The dotted red line indicates the threshold above which an index weight is considered relevant.

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