Connecticut Epidemiologist

In this issue...

Special Edition: CT HPV-Impact Project

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States and the primary cause of cervical cancer. Vaccination is recommended in early adolescence (ages 11–12) before exposure to the virus via sexual activity. [1]

HPV types 16 and 18 (HPV-16/18) are responsible for approximately 70% of cervical cancers and 50% of precancerous cervical lesions; all HPV vaccines that have been administered in the U.S. protect against these types.

The Connecticut Human Papillomavirus Vaccine Impact Monitoring Project (CT HPV-IMPACT) is one of five sites in the CDC-funded Emerging Infections Program network that conduct surveillance for precancerous cervical lesions. In Connecticut, HPV-IMPACT is an active, statewide surveillance program which has been collecting data since 2008. HPV-IMPACT defines precancerous lesions as cervical intraepithelial neoplasia grades 2–3 and adenocarcinoma in situ, collectively referred to as CIN2+.

The first two articles that follow used data from the CT HPV-IMPACT surveillance system to examine trends in CIN2+ incidence in CT and HPV vaccine effectiveness at preventing CIN2+ by age at vaccination. The third article summarizes data from a survey conducted by the CT HPV-IMPACT Program. The survey assessed clinician awareness of the 2019 ACIP recommendation for clinicians to engage in the practice of shared clinical decision-making regarding HPV vaccination with women 27–45 years of age Collectively, the results presented in these three articles can be used to inform public health and clinical practice to increase HPV vaccination coverage for greater individual and population-level protection against these oncogenic viruses.

[1] Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* Aug 16 2019;68(32):698-702. doi:10.15585/mmwr.mm6832a3

Trends in Precancerous Cervical Lesions, Connecticut, 2008–2022

M Brackney, MS, K Higgins, BA, L Niccolai, PhD
Emerging Infections Program, Yale School of Public Health

Background

Precancerous cervical lesions are a common HPV-associated occurrence and a necessary precursor to invasive disease, making this outcome a useful endpoint in evaluating early impact of HPV vaccination. The objective of this analysis was to examine trends in CIN2+ in the Connecticut population during 2008–2022.

Methods

HPV-IMPACT receives CIN2+ case reports from 26 pathology laboratories that diagnose the condition among CT residents. CIN2+ incidence rates by age group were calculated using population census data from the American Community Survey. [1,2]

Over the period of analysis, cervical cancer screening recommendations changed, with increases in age at first screening and longer time intervals between screenings. Therefore, we also calculated incidence rates using yearly estimates of the screened population derived from CT Behavioral Risk Factor Surveillance System (BRFSS) data. [3] The survey included questions on cervical cancer screening behaviors every other year (even years) from 2008–2020. We generated estimates for odd years by averaging the results of the preceding and following even year. In 2022, the BRFSS changed questions regarding cervical cancer screening and they were no longer comparable to previous years. As a result, we did not generate estimates for 2021–2022.

Joinpoint Regression Software [4] was used to model incidence rates, detect joinpoints, and generate annual percent change (APC) and average annual percent change (AAPC) estimates. A joinpoint indicates a given time point when there is a change in the trend. The APC is the annual percent change over specific years in which a trend was detected within the overall study period. The AAPC is a weighted average of (annual) percent change over the entire study period. Figures show both the observed and modeled CIN2+ incidence rates.

Trends in Precancerous Cervical Lesions, Connecticut, 2008–2022 *(continued)*

Results

From 2008–2022, substantial declines occurred in the incidence of CIN2+ in the three younger of the four age groups analyzed (Figure 1). Among 20–24 year olds, the AAPC was -16.0% (95% CI -18.0, -14.4). The greatest declines for this age group were observed in the middle time period during 2011–2016 (APC = -22.2% (95% CI -29.4, -19.3)) (Table 1). Among 25–29 year olds, the AAPC was -5.7% (95% CI -6.6, -5.1). One joinpoint was detected for those 25–29 in 2010, with larger declines in the later period (APC = -6.9% (95% CI -8.5, -6.3) during 2010–2022) (Table 1). Among 30–34 year olds, the AAPC was -1.9% (95% CI -3.6, -0.6). In this age group, one joinpoint was detected in 2012 (APC = -3.1% (95% CI -13.6, -1.6) during 2012–2022) (Table 1). No significant declines were detected in persons ages 35–39 years.

When using screened population estimates to calculate rates, significant declines were detected in the two youngest age groups. Among 20–24 year olds, the AAPC was -13.7% (95% CI -17.4, -11.3) with no joinpoints detected (Table 1). Among 25–29 year olds, the AAPC was -2.3% (95% CI -4.4, -0.7). One joinpoint was detected in 2014 with an APC of -5.2% during the later period of 2014–2022 (95% CI -17.0, -2.5). No significant decreasing trends were noted in the older screened population age groups (30–34 and 35–39 years).

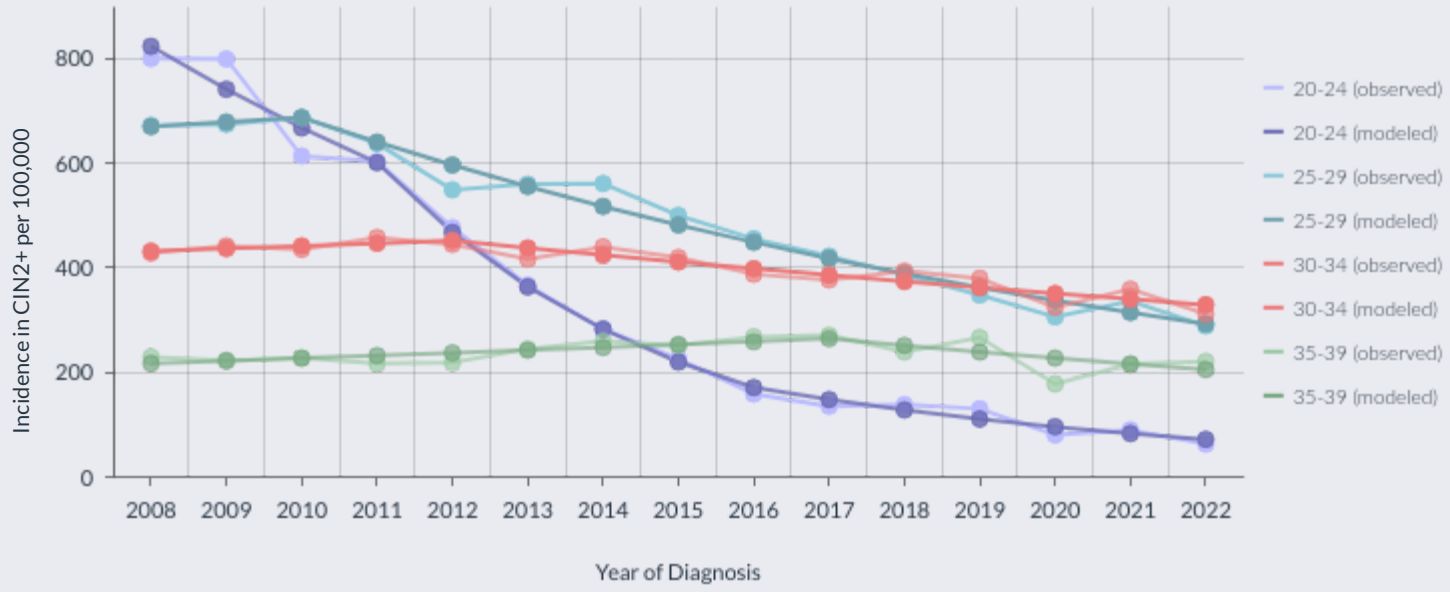
Discussion

The results of this analysis provide evidence of ongoing HPV vaccination impact and contribute to the growing body of global research that has shown decreases in HPV prevalence and precancerous cervical lesions since the introduction of vaccination.[5]

This analysis demonstrated large declines in the incidence of CIN2+ in persons ages 20–34 years during 2008–2022 when considering the total population model. These declines were greater and occurred in earlier time periods in younger age groups. This trend is consistent with vaccine impact because younger age cohorts had greater opportunity for vaccination before exposure to HPV. However, screening guidelines which increased both the age of initiation and the interval between screenings over the study period likely contributed to reduced detection of transient lesions. Therefore, we also examined incidence trends using estimates of screened women. These results demonstrated significant decreasing trends in CIN2+ for those aged 20–29 years but not in the 30–34 year old age group. This suggests that some of the declines observed in the total population estimates may be due to reduced detection of lesions as a result of changes in cervical cancer screening practices.

Vaccination, screening and treatment for cervical disease can greatly reduce the incidence of cervical cancer. The World Health Organization has declared that cervical cancer elimination, defined as less than four cases per 100,000 women, should be a goal for all nations. In Connecticut, HPV vaccine is provided by the Vaccines for Children Program and is available at no cost for all children aged 9–18 if not covered through health insurance. Cervical cancer screening is available through the Cervical Cancer Early Detection Program for those who are eligible. Given these prevention tools, ongoing monitoring of precancerous lesions and invasive carcinoma is needed until cervical cancer elimination is achieved.

Figure 1: Trends in diagnosed cases of CIN2+ among women aged 20–39 years, Connecticut, 2008–2022



Trends in Precancerous Cervical Lesions, Connecticut, 2008–2022 *(continued)*

Table 1: Changes in incidence among women diagnosed with CIN2+, by age group, Connecticut, 2008–2022

Total Population (2008–2022)				
Age group	Years	APC (95% CI) [1]	AAPC (95% CI) [2]	Joinpoint(s) [3]
20–24	2008–2011	-10.0* (-14.9, -0.3)	-16.0* (-18.0, -14.4)	2011, 2016
	2011–2016	-22.2* (-29.4, -19.3)		
	2016–2022	-13.4 (-18.6, 4.0)		
25–29	2008–2010	1.3 (-5.3, 6.3)	-5.7* (-6.6, -5.1)	2010
	2010–2022	-6.9* (-8.5, -6.3)		
30–34	2008–2012	1.2 (-2.5, 13.5)	-1.9* (-3.6, -0.6)	2012
	2012–2022	-3.1* (-13.6, -1.6)		
35–39	2008–2017	2.2* (0.5, 11.3)	-0.4 (-2.2, 1.4)	2017
	2017–2022	-4.9* (-18.3, -1.0)		
Screened Population (2008–2020)				
Age group	Years	APC (95% CI) [1]	AAPC (95% CI) [2]	Joinpoint(s) [3]
20–24	2008–2020	-13.7* (-17.4, 11.3)	-13.7* (-17.4, 11.3)	None
25–29	2008–2014	0.7 (-1.8, 10.8)	-2.3* (-4.4, -0.7)	2014
	2015–2020	-5.2* (-17.0, -2.5)		
30–34	2008–2014	3.2* (1.6, 6.4)	1.4* (0.3, 2.4)	2014, 2017
	2014–2017	-7.2* (-10.5, -2.5)		
	2017–2020	7.0* (1.7, 16.6)		
35–39	2008–2020	1.4* (0.3, 2.4)	3.5* (0.9, 6.0)	None

1 APC = annual percent change, the annual percent change over specific years in which a trend was detected within the overall study period
2 AAPC = average annual percent change, the weighted average of the percent change over the entire study period
3 Joinpoint = indicates a change in the trend at a given time point
* Statistically significant ($p < 0.05$)

References

1 US Census Bureau. 2010–2021 American Community Survey 5-year estimates, demographic and housing estimates. 2021. Accessed February 20, 2023.

2 US Census Bureau. 2022 American Community Survey 1-year estimates, demographic and housing estimates. 2022. Accessed November 17, 2023.

3 Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System Survey Data. Atlanta, Georgia: US Department of Health and Human Services, Centers for Disease Control and Prevention 2008–2020.

4 Joinpoint Regression Program, Version 5.0.2 - May 2023; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute.

5 Drolet M, Bénard É, Pérez N, Brisson M. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. *Lancet*. Aug 10 2019;394(10197):497–509. doi:10.1016/s0140–6736(19)30298-3

HPV Vaccine Effectiveness by Age at Vaccination in Women, New Haven County, Connecticut, 2008–2019

C Hijiya, MPH, M Brackney, MS, K Higgins, BA, L Niccolai, PhD
Emerging Infections Program, Yale School of Public Health

Background

Vaccination against HPV is recommended to prevent HPV infections and subsequent HPV-associated disease. In the U.S., the Advisory Committee for Immunization Practices (ACIP) recommends the HPV vaccine for children aged 11–12 years (and as early as 9 years), with catch-up vaccination from 13–26 years.[1] Since 2006, three HPV vaccines became licensed for use in the U.S.: quadrivalent (protects against HPV-6, 11, 16, and 18), introduced in 2006; bivalent (protects against HPV-16 and 18), introduced in 2009; and 9-valent (protects against HPV-6, 11, 16, 18, 31, 33, 45, 52, and 58), introduced in 2016.[1] Vaccination against HPV at younger ages is recommended because it is most effective when given before first exposure to the virus through sexual activity and because each new sexual partner increases the risk of new HPV infection.[1] Thus, with increasing age and exposure to HPV, the benefit of vaccination may be diminished.

There is limited data on the extent to which vaccine effectiveness (VE) differs by age at vaccination in real-world populations. Delays in administration beyond ACIP-recommended ages may be reducing the real-world effectiveness of HPV vaccination. Here, we aim to estimate differences in HPV VE against CIN2+ by age at vaccination using HPV-IMPACT data including surveillance data from laboratory reports, patient medical records, and patient interview reports for women in New Haven County, Connecticut from 2008–2019.

Methods

HPV-IMPACT conducts enhanced surveillance for women residing in New Haven County, Connecticut aged 18–39 years old diagnosed with CIN2+ and reported by pathology laboratories. This includes medical record review and telephone interviews to determine vaccination status, cervical cancer screening history, and demographic information. Residual biopsy tissue from diagnostic specimens were requested from pathology laboratories and sent to the CDC for HPV DNA typing for 37 HPV types, including all vaccine types.[2]

We estimated HPV VE by age at vaccination using a case-control analytic approach. If an individual's biopsy tissue was positive for HPV types 16 and/or 18 (HPV-16/18) DNA, the individual was categorized as a case; if negative for HPV-16/18 DNA, the individual was categorized as a control. We chose HPV 16/18 for this analysis because nearly all vaccinations administered to individuals during the study period were given before 2014 when the quadrivalent vaccine was the predominant vaccine used in the United States. Cases that received the 9-valent vaccine were removed from the analysis (n=5).

Cases and controls who received at least one dose of HPV vaccine prior to their CIN2+ diagnosis were considered vaccinated and stratified into two age categories: first vaccination at less than 18 years of age (≤18 years), and first vaccination after 18 years of age (>18 years). Unvaccinated cases and controls received no vaccine prior to their CIN2+ diagnosis.

The adjusted odds ratio (aOR) was used to evaluate the association between vaccination status (including age at vaccination) and the outcome of HPV-16/18 CIN2+. The aOR was estimated using a multivariate logistic regression model and controlled for race/ethnicity and insurance type. HPV VE was estimated using the formula VE = (1-aOR)*100%.

Results

A total of 5,497 women were diagnosed with CIN2+ in New Haven County from 2008–2019 and reported to HPV-IMPACT. The analysis included 1,748 women with known vaccination status, age at vaccination, and HPV type. Of these women, 621 (35.5%) had HPV-16/18 CIN2+ (cases), and 1127 (64.5%) had non-HPV-16/18 CIN2+ (controls). Furthermore, 1,365 women (77.9%) were unvaccinated, 155 (8.9%) were vaccinated at ≤18 years, and 228 (13.0%) had been vaccinated at >18 years. The distribution of age at vaccination for this sample is shown in Figure 1.

The estimated ORs for HPV-16/18 CIN2+ by age at vaccination are presented in Table 1. After adjusting for race/ethnicity and insurance type, aORs for individuals vaccinated at ≤18 years and >18 years were 0.21 (95% CI: 0.13, 0.35) and 0.61 (95% CI: 0.45, 0.83) respectively. The corresponding VE estimates for being vaccinated at ≤18 years and >18 years compared with being unvaccinated were 79% (95% CI: 65%, 87%) and 39% (95% CI: 17%, 55%) respectively.

Discussion

The higher HPV VE against CIN2+ for younger ages in this study supports administration of the HPV vaccine at younger ages to confer the greatest protection. Estimates of HPV VE were higher for those who were vaccinated at ≤18 years (79%) compared to those vaccinated at >18 years (39%). This lower protection when given at older ages is in agreement with previous studies evaluating vaccine effectiveness by age at vaccination.[3,4] For example, in one study of CIN3 from the United Kingdom, there were marked differences in VE even within the range of 12–18 years, with VE estimates for protection against CIN3 of 39%, 75%, and 97% for those offered the vaccine at 16–18 years, 14–16 years, and 12–13 years respectively.[4]

There are some limitations to this study. Of women diagnosed with CIN2+, 68.1% were excluded due to incomplete information. Because we categorized HPV types as 16/18 and non-16/18, women with CIN2+ caused by other HPV types protected against by vaccination would have been classified as controls, which may have resulted in the VEs calculated to be underestimated. Due to sample size constraints, we were unable to examine narrower age groups. Continued surveillance will provide more data for further evaluation of VE at younger ages that are closer to the ACIP recommendations. This may provide further support to current age recommendations for HPV vaccination in the U.S. Finally, residual age confounding and unmeasured confounding (e.g., due to sexual behaviors) might be present.

HPV Vaccine Effectiveness by Age at Vaccination in Women, New Haven County, Connecticut, 2008–2019 *(continued)*

In conclusion, this analysis of women diagnosed with CIN2+ identified through population-based surveillance provides support for initiating HPV vaccination at younger ages. Higher VE estimates in those who were vaccinated at younger ages highlights the importance of vaccination before exposure to HPV. Ongoing surveillance will provide updated estimates for the additional oncogenic types included in the current 9-valent HPV vaccine.

Figure 1: Distribution of age at vaccination for women with CIN2+ with known HPV vaccination status and typed specimens, New Haven County, CT: 2008–2019 (n=383)

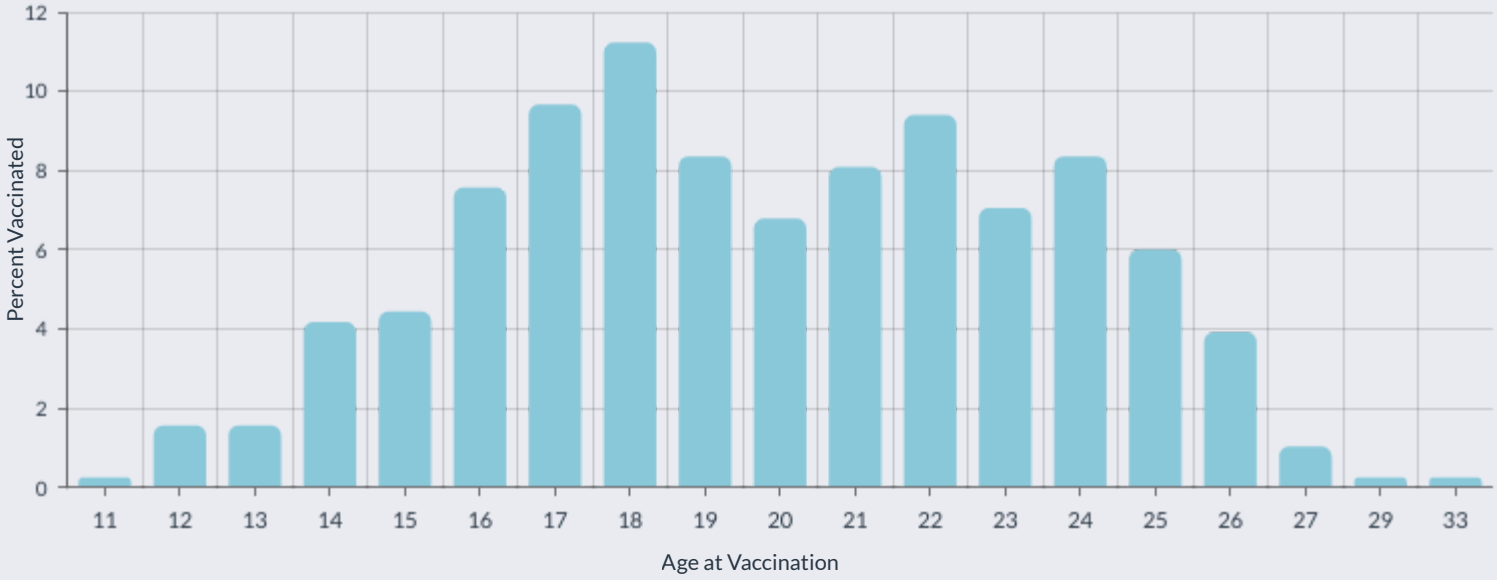


Table 1: Estimated odds ratios for HPV-16/18 CIN2+, by age at vaccination (n=1,748)

Vaccination Status	Adjusted OR (95% CI)	VE
Unvaccinated	1	-
Vaccinated ≤18 years	0.21 (0.13-0.35)*	79%
Vaccinated >18 years	0.61 (0.45-0.83)*	39%

* $p < 0.05$
1 Calculated using the formula (1-aOR)*100

References

1 Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* Aug 16 2019;68(32):698–702. doi:10.15585/mmwr.mm6832a3

2 Hariri S, Unger ER, Powell SE, Bauer HM, Bennett, NM, Bloch KC, Niccolai LM, Schafer S, Markowitz LE; HPV-IMPACT Working Group. The HPV vaccine impact monitoring project (HPV-IMPACT): assessing early evidence of vaccination impact on HPV-associated cervical cancer precursor lesions. *Cancer Causes Control.* 2012 Feb;23(2):281–8. doi 10.1007/s10552-011-9877-6. Epub 2011 Nov 23. PMID: 22108842.

3 Markowitz LE, Drolet M, Lewis RM, et al. Human papillomavirus vaccine effectiveness by number of doses: Updated systematic review of data from national immunization programs. *Vaccine.* Sep 2 2022;40(37):5413–5432. doi:10.1016/j.vaccine.2022.06.065

4 Falcaro M, Castañon A, Ndlela B, et al. The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study. *Lancet.* Dec 4 2021;398(10316):2084–2092. doi:10.1016/s0140-6736(21)02178-4

Provider Awareness and Practices for HPV Vaccine Administration for Patients Ages 27–45 Years, Connecticut, 2023

L Koshy, BPH, K Higgins, BA, M Brackney, MS, L Niccolai, PhD
Emerging Infections Program, Yale School of Public Health

Introduction

Infection with certain types of HPV can lead to the development of cervical and other cancers, however, the HPV vaccine helps to protect individuals from cancer causing strains of the virus.[1,2] Recommendations for adolescents and young adults have evolved since licensure in 2006, and in 2019, the Advisory Committee on Immunization Practices (ACIP) recommended that physicians engage in shared clinical decision-making about HPV vaccination with patients 27–45 years that currently have low coverage.[2,3] In 2023, the CT Emerging Infections Program (EIP) at Yale School of Public Health conducted a survey to understand provider awareness of the ACIP recommendations and practice of HPV vaccine administration to adults aged 27–45 years in Connecticut.

Methods

The Connecticut Department of Public Health practitioner licensing database was utilized to identify healthcare providers (MDs, DOs, PAs, and NPs) from the following specialties who perform cervical biopsies: internal medicine, family medicine and obstetrics/gynecology. A computer-generated random sample of healthcare providers were selected to participate in our study, with oversampling conducted for the EIP catchment area of New Haven County. The surveys were faxed to providers with the option of completing the survey online (Qualtrics survey), over the telephone or on paper. Surveys completed on paper were returned by email or fax.

Results

A total of 211 potentially eligible providers were identified. Of these, 100 eligible providers successfully received the survey (111 were deemed ineligible because of retirement, no longer practicing at the listed facility, or had incorrect fax numbers). The response rate among eligible providers who received and completed the entire survey was 22% (22/100). All but one of the healthcare providers (21/22, 95.5%) that participated in the survey were OB/GYNs.

All providers (22/22, 100%), were aware of the ACIP recommendation to engage in shared clinical decision making. Many providers (17/22, 77.3%) reported they have administered HPV vaccine to patients 27–45 years, a group that currently has low coverage. Among providers who reported having administered HPV vaccine in this age group, 35.3% (6/17) reported that they have conversations about the HPV vaccine with all their patients, 47.1% (8/17) reported having conversations about the vaccine with patients they believe might benefit from the vaccine or with those who inquire about it and 17.6% (3/17) of providers shared that they only have conversations about the vaccine with patients who they think might benefit from it. Furthermore, 70.6% (12/17) reported that 'some' of their patients in the 27–45 year age group receive the HPV vaccine after discussing it, 17.6% (3/17) reported that 'most' of their patients in this age group get the HPV vaccine after discussing it, and 11.8% (2/17) reported 'very few' of their patients get the HPV vaccine after discussing it (Figure 1). Providers reported barriers to vaccinating patients in this age group including vaccine cost, mistrust of the vaccine, lack of information and patients' fears of the negative vaccine impact on their health (Figure 2). In addition, providers reported that many of their patients aged 27–45 years did not feel that the vaccine was relevant to them because they had normal pap smear results, or they were in monogamous relationships.

Discussion

Participating clinicians reported being aware of the ACIP recommendations for shared clinical decision making with persons 27–45 years of age regarding HPV vaccination. However, only a third of providers report having discussions about the HPV vaccine with all unvaccinated patients in this age group. Efforts to facilitate discussions with all patients in this age group about the benefits of HPV vaccine are needed.

These results support incorporating shared clinical decision-making engagement into medical education and professional development opportunities for healthcare providers. In addition, alternative options such as potentially bundling recommendations for HPV vaccine with other vaccines or medical procedures such as the flu vaccine or cervical cancer screenings should be considered to increase discussion with patients in this age-group. A bundling intervention like this resulted in increased vaccine coverage among adolescents in a California study when the influenza and MenACWY (meningococcal) vaccines were offered as a bundle along with the HPV vaccine.[4] Lastly, public health awareness campaigns can help to increase awareness of the ACIP recommendation among age-eligible individuals and debunk misconceptions that providers mentioned their patients might have about the vaccine.

This study may provide insight into current provider practices concerning clinicians' conversations about the HPV vaccine with their patients aged 27–45 years. However, the low response rate and the resulting small sample size could have caused bias, a lack of precise estimates and limited generalizability.

Opportunities remain to increase vaccination rates for all age-eligible persons. Cervical cancer elimination is now possible with combined vaccination, screening, and treatment. Increased efforts to vaccinate all eligible women will accelerate progress toward this important public health goal.

Provider Awareness and Practices for HPV Vaccine Administration for Patients Ages 27–45 Years, Connecticut, 2023 *(continued)*

Figure 1: How likely are healthcare providers' patients aged 27–45 years to get the HPV vaccine after discussing it? (n=17)

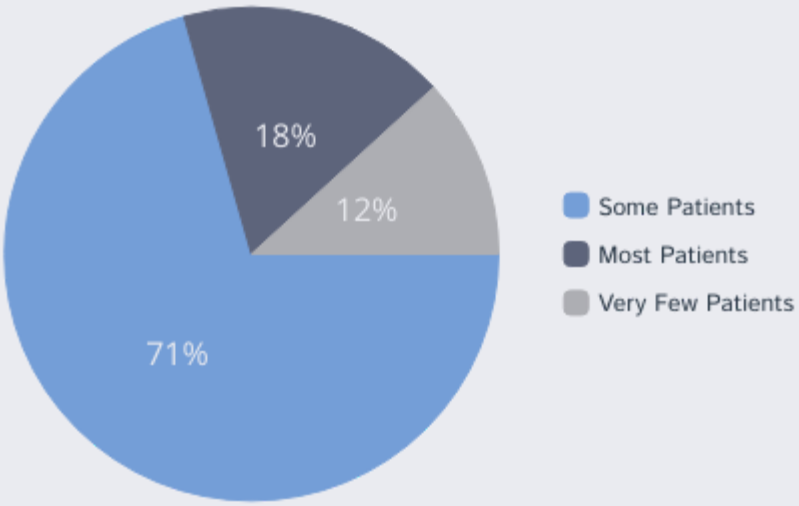
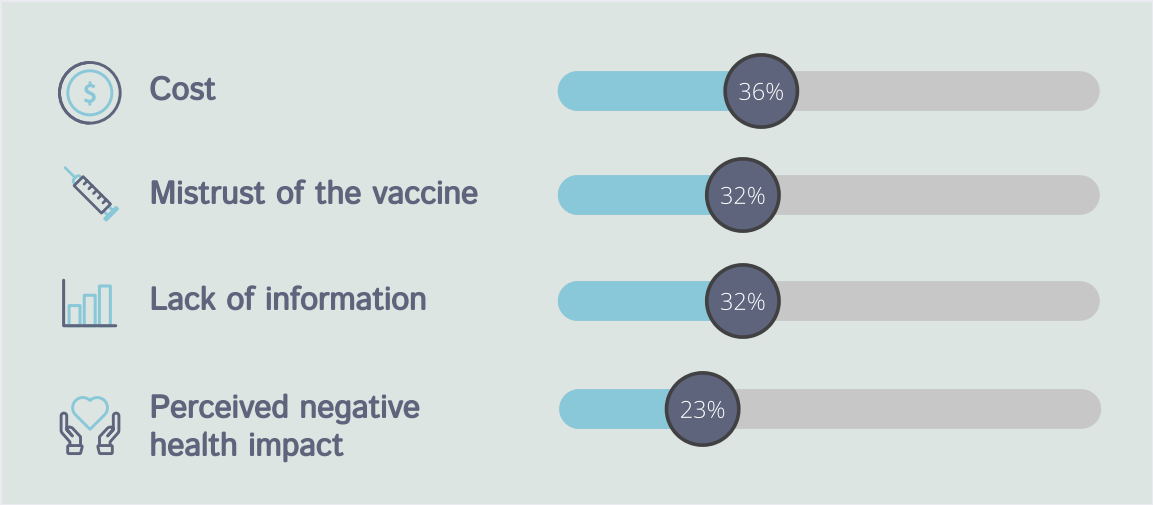


Figure 2: Barriers to vaccination reported in provider survey (% of providers)



References

1 Centers for Disease Control and Prevention. (2021, July 22). Human papillomavirus (HPV) infection - STI treatment guidelines. Centers for Disease Control and Prevention. https://www.cdc.gov/std/treatment-guidelines/hpv.htm

2 Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep*. Aug 16 2019;68(32):698–702. doi:10.15585/mmwr.mm6832a3

3 Kasting, M. L., Giuliano, A. R., Christy, S. M., Rouse, C. E., Robertson, S. E., & Thompson, E.L. (2020). Human papillomavirus vaccination prevalence among adults aged 19–45 years: An analysis of the 2017 national health interview survey. *American Journal of Preventive Medicine*, 59(6), 837–849. https://doi.org/10.1016/j.amepre.2020.05.031

4 Shah MD, Glenn BA, Chang LC, et al. Reducing Missed Opportunities for Human Papillomavirus Vaccination in School-Based Health Centers: Impact of an Intervention. *Acad Pediatr.* Nov–Dec 2020;20(8):1124–1132. doi:10.1016/j.acap.2020.04.002

Infectious Diseases Section Job Postings

Infectious Diseases Section - Assistant Director of Infectious Diseases

STD Control Program - Epidemiologist 1

Connecticut Department of Public Health

Manisha Juthani, MD
Commissioner

Lynn Sosa, MD
State Epidemiologist

Infectious Diseases Section Programs

Epidemiology & Emerging Infections	(860) 509-7994	HIV Healthcare and Support Services	(860) 509-7801
Healthcare Associated Infections	(860) 509-7995	Immunization Program	(860) 509-7929
HIV/HCV Prevention Program	(860) 509-7797	STD Control Program	(860) 509-7920
HIV/HCV Surveillance Program	(860) 509-7900	Tuberculosis Control Program	(860) 509-7722

Connecticut Epidemiologist Newsletter

Editor: Sue Petit, MPH Assistant Editor: Amanda Durante, PhD, MSc Content Design/Production: Heather Linardos, MPH