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Associations between prior HPV4 vaccine doses and cervical cancer screening participation

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ABSTRACT

Background: Cervical cancer screening, regardless of HPV vaccination, is a cornerstone of cancer prevention. This study evaluated associations between prior HPV vaccine doses and initiation and continued participation of screening by age at vaccination.
Methods: Using electronic medical records for a safety net healthcare system (Truman Medical Center), women aged 14–26 y vaccinated (n = 1123) between 07/01/2006 and 10/1/2009 were randomly selected and matched on birth year and health campus to unvaccinated (n = 1123) women. Frequency of screening was determined through 07/01/2013. Hazard ratios (HR) for screening were estimated using Cox proportional hazards regression.
Results: Screening rates were higher after vaccination: unvaccinated (53%), first (62%), second (59%) or third (61%) doses. Women who initiated screening were less likely to complete the vaccine series, regardless of age. Women receiving one dose were more likely than unvaccinated women to initiate screening (HR = 2.98 95% Confidence Interval (CI):2.45–3.61) and were more likely to screen than those receiving two (1 vs. 2, HR = 2.94 95% CI:2.09–4.14) or three doses (1 vs. 3, HR = 3.15 95% CI:2.21–4.48). Compared to unvaccinated women, women <21 y who completed 3-doses were 1.8-times more likely to screen at ≥21 y, whereas vaccinated women ≥21 y were more likely to screen regardless of number of doses ($p < 0.0001$).
Conclusions: Women who were vaccinated were more likely to screen than unvaccinated women; screening rate was highest after and occurred closest to the first vaccine dose. Research evaluating the efficacy of a one-dose vaccine is warranted and may provide both higher vaccination and screening rates.

1. Introduction

Cervical cancer screening, regardless of HPV vaccination, is the cornerstone of cancer prevention [1]. Although vaccination against the most commonly associated cervical cancer-HPV strains (16/18) could prevent the majority (70%) of cervical cancers worldwide, vaccines do not cover all high-risk HPV types, and racial/ethnic minorities are characterized by differential HPV type distribution [2–5]. Additionally, those who seek healthcare in the safety net systems for the underserved and uninsured have lower participation rates in cervical cancer screening and are at increased risk for cervical cancer [6,7]. Hence, participation in cervical cancer screening must be monitored and encouraged regardless of HPV vaccination.

Previous literature indicates that recent cervical cancer screening is associated with initiating HPV vaccination [8,9] and

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that the 'intent to participate' in future screenings is higher among vaccinated women [10–12]. The American Cancer Society recommends that cervical cancer screening should not change based on HPV vaccination status [13]. However, there is concern that women <21 years who are vaccinated may not adhere to recommended screening guidelines as adults [14,15], because they believe that vaccination provides complete protection from cervical cancer [15,16].

Several reports indicate women's participation in cervical cancer screening differs by vaccine status, ranging from 24% [17] to 90% [9], and age of vaccination [9,17–21]. This may be due partly to socioeconomic disparities reported to be associated with failure to complete the HPV vaccination series and to attend routine screenings [17,20]. A better understanding of the relationship between vaccination and screening may lead to programs that integrate HPV vaccination with cervical cancer screening programs.

Using data from an underserved U.S. population, the primary study aims were: to determine if HPV vaccination influences the rate of participation in routine screening over time; to evaluate the association between the number of HPV4 vaccine doses and participation in screening after vaccination; and to evaluate whether age at first vaccine dose, age of initial screening, and race modify the associations.

2. Materials and methods

2.1. Study population

This retrospective matched-pair cohort study includes HPV vaccinated and unvaccinated women aged 14–26 years (y) randomly selected from the electronic medical record (EMR) database for 27,786 women in the Missouri Truman Medical Center (TMC) safety net healthcare system between July 1, 2006 and October 1, 2009 [22]. Vaccinated women were those who received at least one dose of HPV4 vaccination and had at least one healthcare visit post-vaccination. Unvaccinated women had no record of HPV vaccination during the baseline period, had at least one healthcare visit at TMC post-study entry, and were matched on a 1:1 ratio to vaccinated women by birth year and healthcare system campus. Entry into the study was defined as the date of first vaccination for the vaccinated woman in a matched pair. A total of 2308 women (1154 vaccinated; 1154 unvaccinated) were enrolled. Those eligible for the present study (N = 2,246: 1123 vaccinated; 1123 unvaccinated) had complete data for vaccination, screening, and race. Frequency of screening was determined through July 1, 2013, when the youngest vaccinated woman (14 y, enrolled in 2007) would be of recommended screening age (21 y) [23], with the exception of five individuals (0.22%) who were enrolled at 15 y in 2008 or 16 y in 2009 who did not reach 21 y by 2013. The study was designed to have 80% power to detect an absolute difference of 6% between screening rates among vaccinated and unvaccinated women. This study was approved by the University of Missouri-Kansas City Adult Health Sciences Institutional Review Board (#12-351).

2.2. Data collection

Vaccination status was ascertained from patient logs maintained for vaccine accountability, billing records, and EMR searches for quadrivalent HPV vaccine, HPV4, or Gardasil®. The cytology screening nomenclature followed the 2001 Bethesda system [24], which includes "negative for intraepithelial lesion or malignancy" (NILM). Cervical cancer screening was based on the 2009 recommendation [23] for screening initiation at age 21 y followed by 3-year intervals, if NILM; allowing dichotomization of screening age at 21 y. Screenings occurring prior to age 21 y were also recorded.

2.3. Statistical analysis

Descriptive statistics were calculated for age at study entry (<21, ≥21 y), age at initial screen (<21, ≥21 y), race/ethnicity (Black, Hispanic, non-Hispanic White, Other), body mass index

Table 1
Descriptive characteristics, stratified by total number of HPV4 vaccine doses received.

	All women	Unvaccinated	1 Dose	2 Doses	3 Doses
Total N N *(%)*	*2246*	*1123 (50.0%)*	*475 (21.2%)*	*284 (12.6%)*	*364 (16.2%)*
Characteristics[a]	N (%)	N (%)	N (%)	N (%)	N (%)
Age at study entry[b]					
<21 years	879 (39.1)	417 (37.1)	183 (38.5)	118 (41.6)	161 (44.2)
≥21 years	1367 (60.9)	706 (62.9)	292(61.5)	166 (58.4)	203 (55.8)
Race/ethnicity					
Black	1196 (53.2)	625 (55.7)	239 (50.3)	139 (48.9)	193 (53.0)
Hispanic	148 (6.6)	73 (6.5)	37 (7.8)	28 (9.9)	10 (2.8)
non-Hispanic White	794 (35.4)	358 (31.9)	187 (39.4)	106 (37.3)	143 (39.3)
Other	108 (4.8)	67 (6.0)	12 (2.5)	11 (3.9)	18 (4.9)
Body mass index, kg/m^2					
<18.5 (Underweight)	55 (2.4)	32 (2.8)	7 (1.5)	4 (1.4)	12 (3.3)
18.5–24.9 (Normal)	623 (27.7)	288 (25.6)	124 (26.1)	94 (33.1)	117 (32.1)
25–29.9 (Overweight)	508 (22.6)	252 (22.4)	102 (21.5)	64 (22.5)	90 (24.7)
≥30 (Obese)	779 (34.7)	386 (34.4)	184 (38.7)	98 (34.5)	111 (30.5)
Missing	281 (12.5)	165 (14.7)	58 (12.2)	24 (8.5)	34 (9.3)
Pregnancy history					
0 live births	522 (23.2)	215 (19.2)	100 (21.1)	62 (21.8)	145 (39.8)
≥1 live births	1341 (59.7)	583 (51.9)	347 (73.0)	205 (72.2)	206 (56.6)
Missing	383 (17.1)	325 (28.9)	28 (5.9)	17 (6.0)	13 (3.6)

Note: column percentages may not equal 100% due to rounding.
[a] Chi square p-value is significant ($p < 0.05$) for the difference in distribution of characteristics between unvaccinated and HPV4 vaccination dose groups for all variables.
[b] Age at study entry (vaccination) among those who were vaccinated. Unvaccinated participants were matched to vaccinated participants by year of birth and campus. Current age at the start date into the study is the date of first vaccination for the matched pair.