Long-term Impact of Human Papillomavirus (HPV) Vaccination on Pre-invasive and Invasive Cervical Neoplasia

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Ana M. Rodriguez[1], MD, MPH, Burak Zeybek[1], MD, Deepak Adhikari[2], MS, Yong-Fang Kuo[2], PhD
[1]Department of Obstetric & Gynecology, [2]Department of Preventive Medicine and Community Health
The University of Texas Medical Branch, Galveston, TX

INTRODUCTION

- Since mid-2006 the HPV vaccine has been available, and efforts have been directed toward vaccinating today's younger generation despite significant barriers
- Guidelines recommend HPV vaccination for girls and boys aged 11–12 (ideally), with catch-up doses for ages 13–26
- A randomized clinical trial of a 2-dose HPV vaccine schedule showed noninferiority of immune responses in girls up to 24 months compared with women aged 15 to 25 years receiving 3 doses. Long-term effectiveness of this regimen is unknown
- It is incompletely understood the long-term impact of HPV vaccination on associated HPV-genital diseases, treatment and cervical cancer screening schemes in vaccinated women

OBJECTIVES

To investigate the incidence of pre-cancerous cervical lesions and invasive cervical cancer among HPV vaccinated women

METHODS

Data Source

- Health insurance claim data from Clinformatics™ DataMart, a product of OptumInsight Life Sciences, Inc. (Eden Prairie, MN). Years: 2006-2015
- Institutional Review Board approval was not required

Study Cohort

- 11,335 women (age 9-26 years) with at least one dose of the HPV vaccine within 3 years period
- Followed at least 4 years from last dose of vaccine (age>=21) or once reach 21, and without history of previous diagnosis of cervical dysplasia or cervical cancer

Statistical Analysis

- Categorical outcomes were analyzed by Chi-square test
- Continuous outcomes were analyzed by ANOVA
- Time to event analyses were conducted by KM Survival method
- Data extraction and analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA)

RESULTS

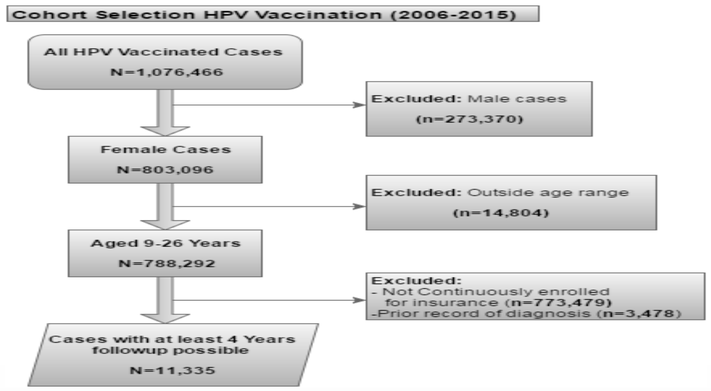


Table 1: Patient characteristics and HPV dose

Characteristics	Dose 1 (N=1,975)	Dose 2 (N=2,089)	Dose 3 or More (N=7,271)	P-value
Time(months) to complete doses, mean(SD)	--	5.25(4.85)	8.04(4.07)	<0.0001
Age at first dose , mean(SD)	21.51(2.67)	20.94(2.85)	20.33(2.85)	<0.0001
Age group				<0.0001
<19	268(8.49)	483(15.3)	2,405(76.20)	
19-20	536(15.96)	633(18.85)	2,189(65.19)	
21-23	621(27.56)	445(19.75)	1,187(52.69)	
>23	550(21.42)	528(20.56)	1,490(58.02)	
Region				<0.0001
Midwest	516(16.38)	517(16.41)	2,117(67.21)	
Northeast	215(13.72)	302(19.27)	1,050(67.01)	
South	894(18.79)	917(19.27)	2,947(61.94)	
West	350(18.82)	353(18.89)	1,157(62.20)	
Follow up length (months), mean(SD)	62.71(12.85)	61.84(12.34)	61.75(11.63)	0.0062
No. PAP tests*, mean (SD)	2.00(1.54)	2.06(1.52)	2.29(1.60)	<0.0001

*=fixed 4 year follow up applied

Table 2: Incidence Rate of High Grade Cytology, CIN-II or III and High Risk Group

No. doses	High grade cytology Failed N, %, CI			CIN-II or CIN-II histology Failed N, %, CI			High Risk Group Failed N, %, CI		
	Year 1	Year 3	Year 5	Year 1	Year 3	Year 5	Year 1	Year 3	Year 5
1	16 0.8 (0.5,1.3)	41 2.1 (1.5,2.8)	57 3.0 (2.3,3.8)	9 0.5 (0.2, 0.9)	25 1.3 (0.9,1.9)	43 2.3 (1.7,3.1)	21 1.1 (0.7, 1.6)	52 2.6 (2.1, 3.4)	82 4.3 (3.5, 5.4)
2	7 0.3 (0.2,0.7)	35 1.7 (1.2,2.3)	46 2.2 (1.7, 3.0)	7 0.3 (0.2,0.7)	20 1.1 (0.6,1.5)	32 1.5 (1.1, .2)	12 0.6 (0.3, 1.0)	45 2.2 (1.6, 2.9)	62 3.0 (2.4, 3.9)
>=3	40 0.5 (0.4,0.8)	134 1.8 (1.6,2.2)	199 2.8 (2.5, 3.3)	26 0.3 (0.2, 0.5)	88 1.2 (1.0, 1.5)	129 1.8 (1.5, .2)	58 0.8 (0.6, 1.0)	190 2.6 (2.3, 3.0)	280 3.9 (3.5, 4.4)

Definitions:

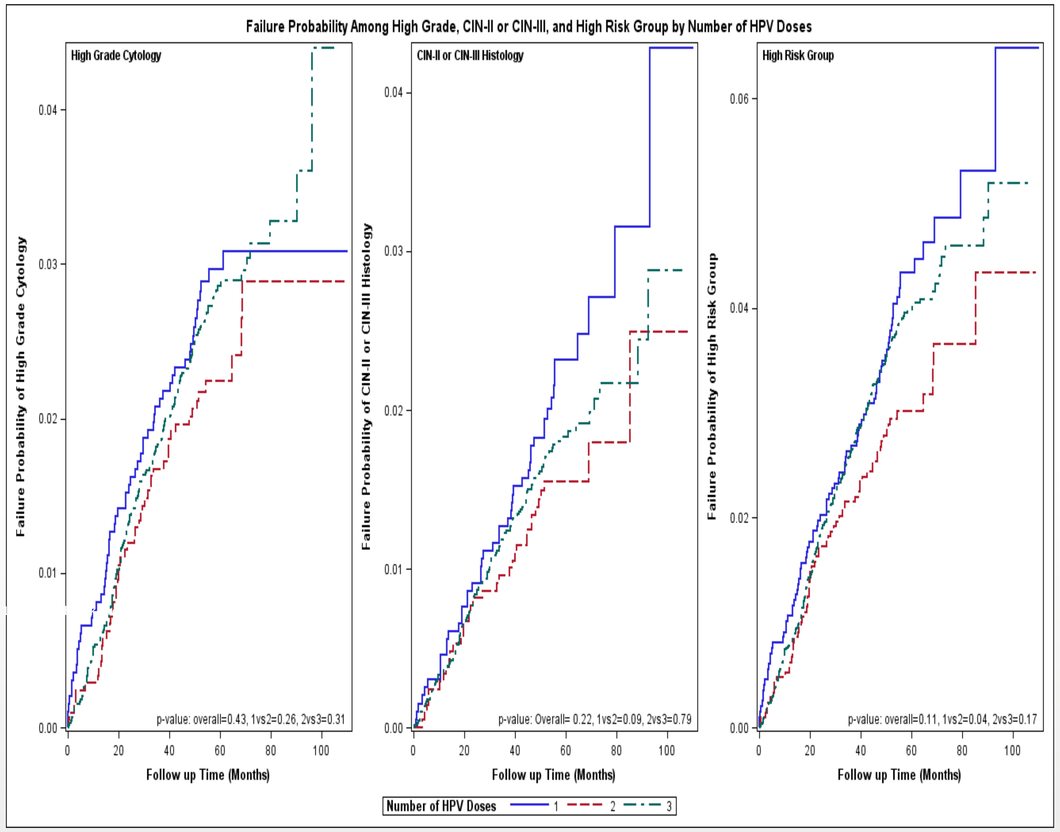
High grade of Cytology: ASC-H or HGSIL

High risk group: any of ASC-H, HGSIL, CIN-II, CIN-III, adenocarcinoma in situ, and invasive cancer

Table 3: High Risk Group*

Characters	HR(95% CI)	p-value
Dose 2vs1	0.74(0.54,1.02)	0.07
Region South vs West	1.29(0.97, 1.72)	0.08
Age at first Vaccine	1.07(1.03, 1.15)	<0.01

*Only marginally significant are shown-adjusted for age, region and dose



CONCLUSIONS

- Our preliminary results show that in the total vaccinated cohort, single dose HPV-vaccinated women had a higher cumulative incidence of high grade cytology/histology, adenocarcinoma in situ, and cervical cancer
- Pairwise comparison showed that women who received two doses of the HPV vaccine exhibited higher prophylactic efficacy against abnormal high grade cytology, high grade histology, adenocarcinoma in situ and invasive cervical cancer when compared to receiving a single HPV dose (p-value 0.04)
- No additional protective effect was found with getting a third dose of the HPV vaccine (p-value 0.17)
- Effect of doses has marginal trend toward significance (p-value 0.07) for higher number of doses - dose 2vs1 HR 0.74 (0.54, 1.02) in High Risk outcomes

LIMITATIONS

- The used data for this study contains claims that are collected for payment purposes, not research

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