



Comparison of colposcopic appearances between HPV-vaccinated and unvaccinated women with high-risk HPV infections



Foley GM, Leng M, Hwang L, Moscicki AB

David Geffen School of Medicine at UCLA, Department of Pediatrics, Department of Adolescent Medicine

Study Aim

To determine whether HPV vaccination status impacts the severity of colposcopic features in women with high-risk HPV infections.

Background

- Human papillomavirus (HPV) is the leading cause of cervical cancer (CC) in women; most infections are transient and only persistent high-risk HPV (hrHPV) infections are at risk for the development of invasive cervical cancer [1]. Consequently, HPV testing is now an integral part of CC screening.
- Abnormal CC screening is followed up with colposcopy. Certain criteria have been developed based on lesion characteristics to aid the clinician in targeting lesions at high risk for pre-cancer/cancer for biopsy.
- HPV types 16 and 18, the most common types associated with CC, have also been associated with more severe colposcopic features compared to other hrHPV types [2]. With the introduction of HPV vaccines, there has been concern that colposcopy may be less sensitive for identifying lesions with potential pre-cancer/cancer in HPV vaccinated women [3].

Methods

Subject Population:

- Women were enrolled in the UCSF HPV natural history study (1990–2004), which included healthy women ages 13–21 who received colposcopy with colposcopy and HPV DNA testing every 4–6 months [4].

Methods:

- All colposcopic photographs (range of 3 to 30 per woman) for 60 vaccinated and 56 unvaccinated women were reviewed by author GF, blinded to HPV and vaccination status; photos were excluded if uninterpretable.
- Colposcopic photographs were included in final analysis only if hrHPV testing was positive at that visit date.
- Only colposcopic photographs taken after date of first vaccine dose were included in analysis for vaccinated group.
- Outcomes included 1) colposcopic impression (normal vs. abnormal, Figure 1) and 2) colposcopy severity score (derived from 0 – 7 point scale for each lesion based on vascular changes, size, acetowhitening, and demarcation).
- Chi-squared analysis and Fischer's Exact Test were used to test for associations between vaccination status, hrHPV genotype, and colposcopic findings for all colposcopic photographs and separately for individual women using colposcopic photograph with highest colposcopy score.

Figures/Tables

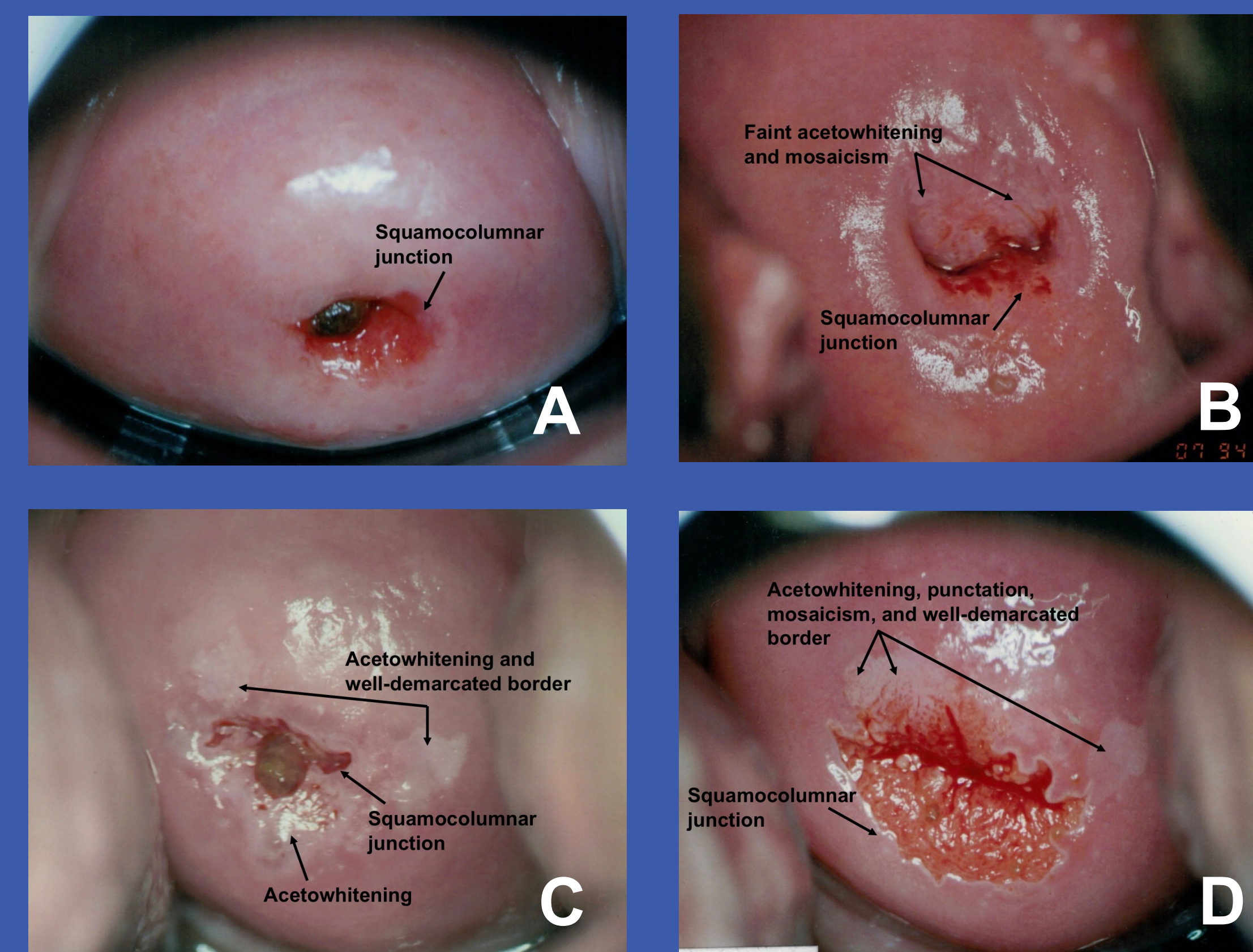


Figure 1. A: Example of colposcopic photograph given colposcopic impression of "normal/benign". B-D: Examples of colposcopic photographs given colposcopic impression of "abnormal".

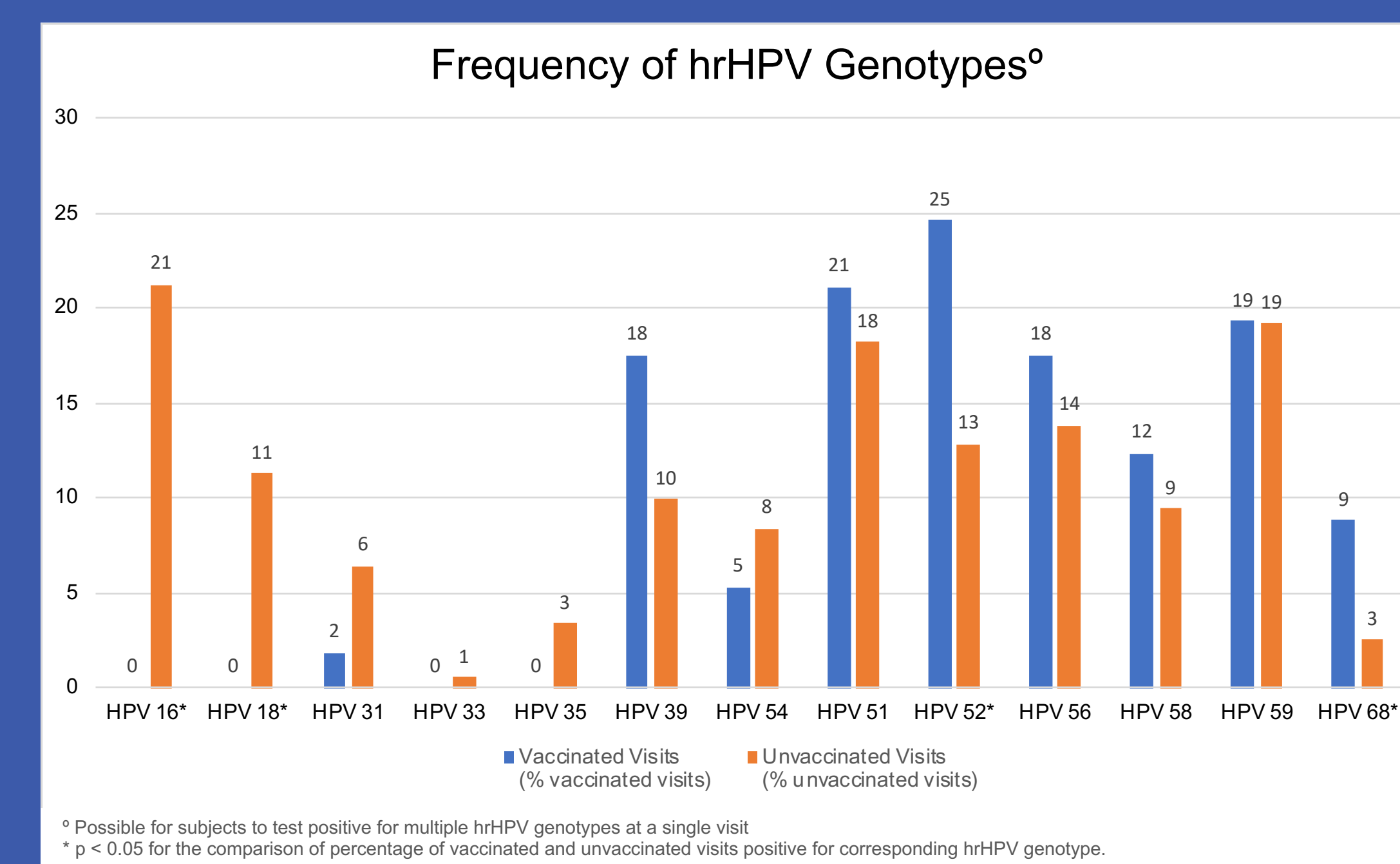


Figure 2: Percent of visits included in final analysis that were positive for each hrHPV genotype by vaccination status.

	Vaccinated non-16/18 hrHPV n = 57	Unvaccinated hrHPV (all) n = 203	Unvaccinated non-16/18 hrHPV n = 141	Unvaccinated 16/18 ± other hrHPV n = 62
Colposcopic Impression n (column %)				
Normal/Benign	24 (42.1)	94 (46.3)	79 (56.0)	15 (24.2)
Abnormal	33 (57.9)*	109 (53.7)	62 (44.0)*	47 (75.8)*
Colposcopy Score mean ± SD	3.77 ± 2.71*	3.40 ± 2.67	2.86 ± 2.58**	4.65 ± 2.46*
Individual Women n	25	60	40	20
Colposcopic Impression n (column %)				
Normal/Benign	13 (52.0)	25 (41.7)	20 (50.0)	5 (25.0)
Abnormal	12 (48.0)	35 (58.3)	20 (50.0)	15 (75.0)
Colposcopy Score mean ± SD	3.48 ± 2.45	3.63 ± 2.41	3.20 ± 2.42*	4.50 ± 2.21*

* p < 0.05 between marked comparison groups in each corresponding row

** p < 0.05 between marked comparison groups in each corresponding row

Table 1: Colposcopic findings by vaccination status and HPV genotype for all colposcopic photographs and for individual women.

Results

- Of 1427 colposcopic photographs reviewed by author GF, 260 met criteria for inclusion in final analysis (i.e. hrHPV positive at that visit); 203 colposcopic photographs from 60 women were included in the unvaccinated group and 57 colposcopic photographs from 25 women were included in the vaccinated group.
- Visit for vaccinated women had higher rates of HPV types 52 and 68 compared to visits for unvaccinated women (p = 0.03, 0.04 respectively, Figure 2).
- Colposcopic photographs from women with 16/18 hrHPV had significantly higher rates of abnormal colposcopic impressions as well as higher colposcopy scores compared to those from women with non-16/18 hrHPV.
- Colposcopic photographs from vaccinated women with non-16/18 hrHPV had significantly higher colposcopy scores compared to those from unvaccinated women with non-16/18 hrHPV infections; there were no significant differences between these groups in analysis including each woman once (Table 1).
- Sixty-three percent of cervical lesions in vaccinated women originated prior to date of first vaccination. The mean colposcopy score for lesions originating prior to date of first vaccination was 5.39, compared to 1.00 for new lesions arising after date of first vaccination.

Discussion

- Our study supports prior findings that HPV types 16 and 18 are associated with more severe colposcopic features compared to other hrHPV types [2].
- Surprisingly, we observed that vaccinated women with non-16/18 hrHPV infections had more severe-appearing cervical lesions compared to unvaccinated women with non-16/18 hrHPV.
- These differences are explained by the high number of cervical lesions with severe colposcopic features pre-dating first vaccination. One possibility for the high number of lesions with severe colposcopic features observed in vaccinated women is related to provider bias in promoting vaccinations for those considered "highest risk" for HPV infection [5].
- The disappearance of these differences in sub-analysis of individual women also suggests that a few vaccinated women with severe cervical disease were primarily driving these differences.
- In contrast, new cervical lesions appearing post-vaccination had very low colposcopy scores— lower than unvaccinated women with non-16/18 hrHPV, therefore underscoring the likely poor performance of colposcopy in women who were vaccinated before the onset of sexual activity.

Limitations

- We utilized a select group of healthy women with mostly normal cytology, unlike real-life scenarios in which abnormal cervical cancer screening drives referral to colposcopy.
- Although we only included visits with positive hrHPV to mimic primary HPV screening, the lack of abnormal cytology in the majority of women may reflect smaller lesions than otherwise expected.
- The design of our parent study did not allow us to assess the actual risk of CIN 2,3 at each visit since biopsies were not routinely performed.

Conclusion

- Our study suggests that HPV vaccination will diminish colposcopic findings associated with hrHPV infections, primarily due to the eradication of HPV 16/18 lesions.
- However, women vaccinated after the onset of sexual activity remain at high risk for cervical lesions, especially if these lesions existed prior to vaccination. Consequently, colposcopy is likely to remain an important part of cervical cancer screening in this population.
- The role of colposcopy in women vaccinated at appropriate target ages is yet to be established.

References

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