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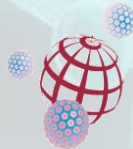
Rates of Cervical Intraepithelial Neoplasia in Women in British Columbia: a Data Linkage Evaluation of the School-based HPV Immunization Program

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Michael Smith Foundation for Health Research Trainee

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**Global Control of
HPV Related Diseases
and Cancer**

Disclosure Statement

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Background

- The BC school-based human papillomavirus vaccination (HPVV) program began in 2008 for girls born in 1994.
 - A “catch up” program for girls in grade 9 was also launched & active until 2011
- The immunization schedule has changed over time, moving from 3 → 2 doses for girls 9 – 14 yrs
- There are 2 vaccination registries covering the 5 Health Authorities in BC:
 - Panorama (NHA, IHA, VIHA, FHA)
 - PARIS (VCHA)

Cervical Screening in BC

- The BC Cancer Agency maintains one central registry of cytology and histology results, and treatment history
- In June 2016, the screening recommendations changed: screening to commence at age 25 (regardless of sexual debut)
 - Prior to June 2016, guidelines recommended women commence cervical cancer screening at age 21, or 3yrs after sexual debut

Objective

To evaluate the impact of the school-based quadrivalent HPV immunization program on rates of high-grade squamous intraepithelial lesion (HSIL) and cervical intraepithelial neoplasia (CIN) in BC.

The first cohort of young women to receive HPV vaccination in the school immunization program are now reaching age eligibility for the cervical screening program in BC.

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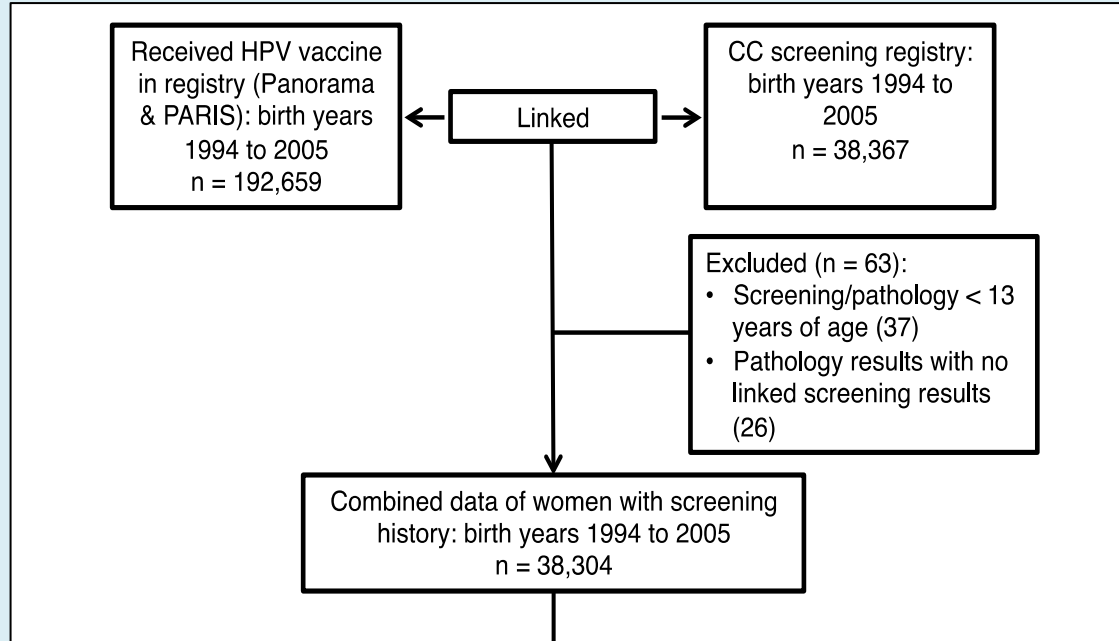
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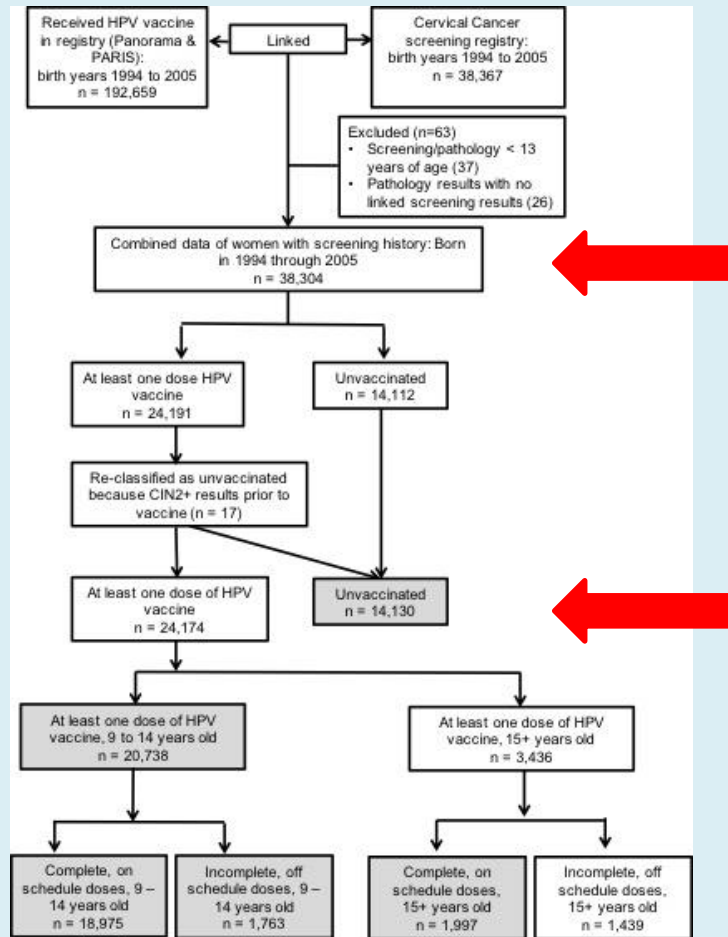
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Methods – Data Linkage

- The cohort of interest: women born in 1994 to 2005, and received HPVV recorded in Panorama/PARIS and a matched cohort of unvaccinated women from cervical screening registry
- Outcomes: cytology (HSIL) or histology (CIN2, CIN3 and CIN2+)





Methods – vaccine status

At least one dose of HPV vaccine, All: All women who have at least one dose of HPVV on immunization record, with vaccine recorded at least 6 months after any CIN/HSIL diagnosis, for all women born in 1994 to 2005.

Unvaccinated: No doses of HPVV on immunization record, or vaccine was recorded after or up to 6 months prior to CIN/HSIL diagnosis, for all women born in 1994 to 2005.

At least one dose, 9-14 years old: All women who received at least one dose of HPVV between 9-14 years of age, which includes both complete on-schedule doses and incomplete doses.

At least one dose, 15 + years: All women who received at least one dose of HPVV at 15 years or older, which includes both complete on-schedule doses and incomplete doses.

Complete on-schedule doses, 9-14 years old:
Full course of doses (either 2 or 3 doses based on birth cohort), on-schedule, with first dose between 9-14 years of age.

Incomplete, off schedule doses, 9-14 years old:
>one dose received at 9-14 years of age, but less than full course, or was off-schedule, based on birth cohort.

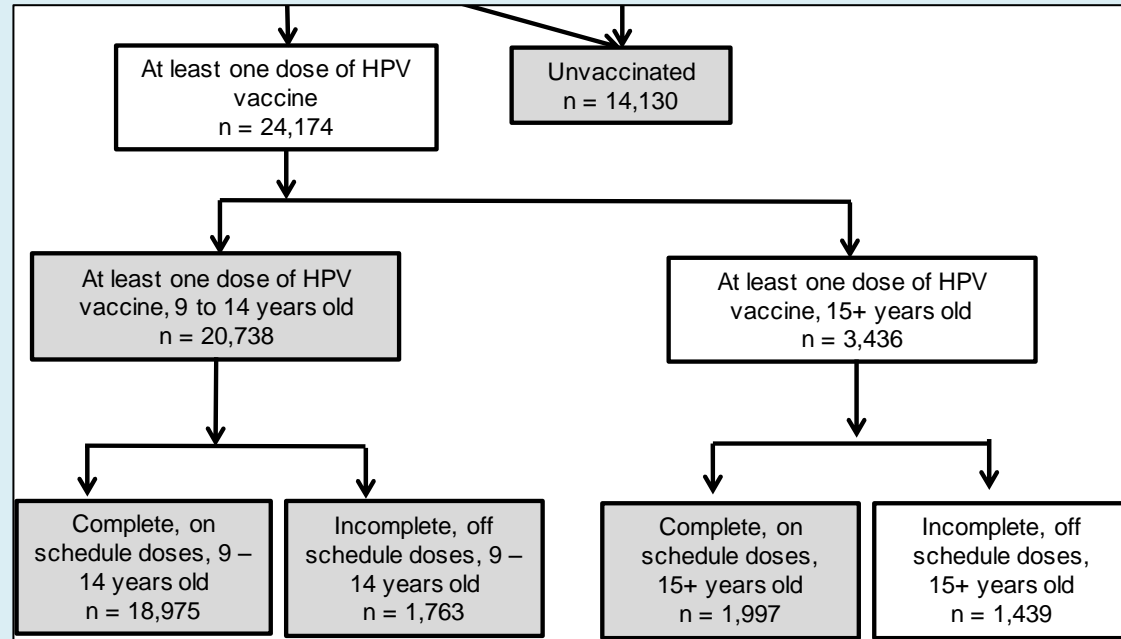
Complete on-schedule doses, 15+ years: 3 doses, on-schedule, with first dose at 15 years of age or older

Incomplete off schedule, 15+ years: >one dose received at 15 years or older, but less than full course, or was off-schedule, based on birth cohort.

Methods - Comparisons

3 comparison:

- 1) At least 1 dose at 9-14 years of age vs. Unvaccinated
- 2) Complete, on schedule 9 – 14 years vs. Incomplete 9 – 14 years of age vs. Unvaccinated
- 3) Complete 9 – 14 years vs. Complete 15+ years

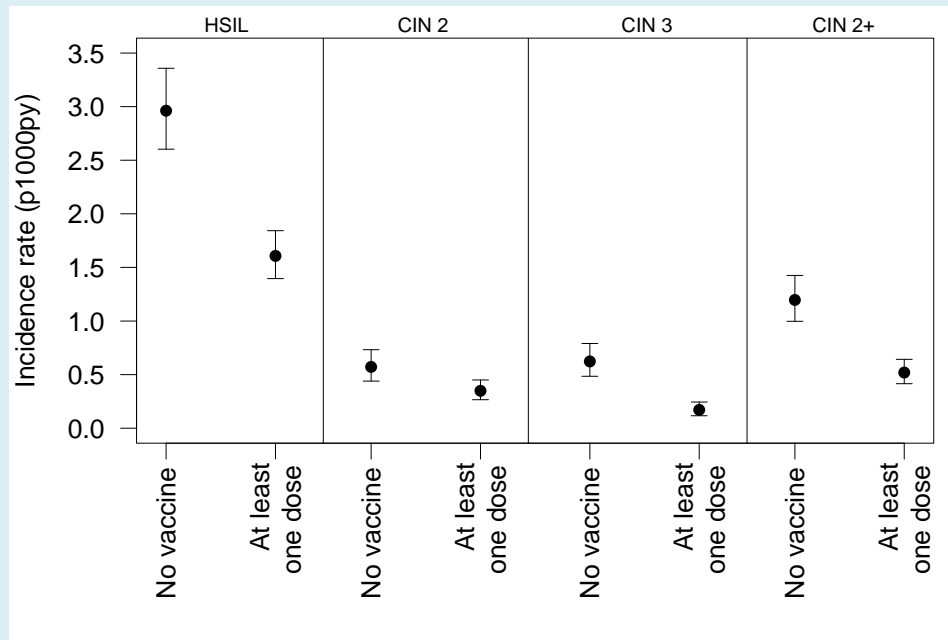


Methods - Analysis

- Incidence Rates (IRs) (1000 person-years)
 - Individual years-at-risk was based on years between first screen minus 3 years, and either the date of the outcome (HSIL/CIN2+), or the last date in the data set (July 31, 2018).
- Relative Rate (RR)
 - RR and 95% CI for each of cytology (HSIL) or histology (CIN2, CIN3 and CIN2+) outcome were modelled using adjusted Poisson regression
 - Model adjustment: birth year and age at first screening test less 3 years, as an approximation for sexual debut.

Results: IRs

Figure 1: Incidence rates per 1000 women per year (p1000py) and 95% CI for unvaccinated vs. at least 1 dose administered between 9 – 14 yrs. HSIL, CIN 2, CIN 3, and CIN 2+ shown separately.



Results – RR Estimates

	HSIL			CIN2+		
	n	RR* (95%CI)	P-value	n	RR* (95%CI)	P-value
Unvaccinated (n=14, 130)	229	ref		115	ref	
At least 1-dose, 9 – 14 yrs. (n=20,738)	191	0.54 (0.44 -0.65)	<0.0001	76	0.43 (0.32 – 0.58)	<0.0001

- **Rate of CIN 2+ was approximately 50% lower in women with a least 1 dose administered at 9 – 14 yrs relative to the unvaccinated group.**

Results – RR Estimates

	HSIL			CIN2+		
	n	RR* (95%CI)	P-value	n	RR* (95%CI)	P-value
Unvaccinated (n= 14, 130)	229	ref		115	ref	
Incomplete doses, 9 – 14 yrs (n= 1,763)	20	0.61 (0.37 – 0.94)	0.03	9	0.57 (0.27 – 1.06)	0.1
Complete doses, 9 – 14 yrs (n=18,975)	171	0.53 (0.43 – 0.64)	<0.0001	67	0.42 (0.31 – 0.57)	<0.0001

- There was no significant difference in the RR of CIN2, CIN3, or CIN2+, in young women with incomplete HPV vaccine series administered 9 – 14 yrs of age compared to unvaccinated women.

Results – RR Estimates

	HSIL			CIN2+		
	n	RR* (95%CI)	P-value	n	RR* (95%CI)	P-value
Complete doses, 9 – 14 yrs (n= 18, 975)	171	ref		67	ref	
Complete doses, 15 years+ (n=1,997)	32	1.58 (1.06 – 2.27)	0.02	13	1.56 (0.82 – 2.74)	0.15

- There was a trend for increased CIN2+ in women who received complete doses at 15 years or older compared to girls who had complete dose at 9 – 14 years of age, but significance was not reached.

Conclusions

- **Limitations:** Potential misclassification of vaccine status if vaccine received out of province. Additional confounders were not available in registry data.
- Women who received at least 1 dose of HPV vaccine at 9-14 years of age had half the rate of high-grade cervical lesions compared to unvaccinated women.
- Observed no significant difference in high-grade lesions in women with incomplete HPV vaccine series administered 9 – 14 yrs of age compared to unvaccinated women.
- There was a trend for increased high-grade cervical lesions in women who received complete doses at 15 years or older compared to girls who had complete dose at 9 – 14 years of age. Immunization, as per the provincial schedule, should be encouraged.
- Continued program monitoring will be important for measuring long-term population impact.