Evaluation of Long-Term Effectiveness of Human Papillomavirus (HPV) Vaccine: Interim Analysis from QUEST-ADVANCE Study

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Background

- Approximately 99% of all squamous cell carcinomas of the cervix are caused by high-risk HPV including type 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68.
- To achieve elimination of cervical cancer, optimization of current HPV vaccination programs and improvement of vaccination coverage are of key importance.
- Few studies have provided robust comparison between 1-, 2-, 3-doses, and unvaccinated population.
- In British Columbia (BC), 2-dose schedule was currently adopted whereas 3-dose schedule was previously adopted, which provides unique cohorts to compare across different dosing schedules.
- Quadrivalent vaccine that includes the high-risk HPV types 16 and 18 and the low-risk HPV types 6 and 11 has been used in both 2- and 3-dose schedules.

Objective of the Present Analysis

Examine long-term quadrivalent vaccine effectiveness (VE) against prevalent HPV infection for 1, 2, and 3 doses of HPV vaccine compared to unvaccinated.

Methods

- QUEST-ADVANCE (**Qu**adrivalent HPV Vaccine **E**valuation **St**udy with **Ad**dition of the Nona**va**le**n**t Va**c**cin**e**) examines the requirement and effectiveness of HPV vaccine schedules in long-term (>= 10 years).

Enrollment

BC Provincial Immunization Registry

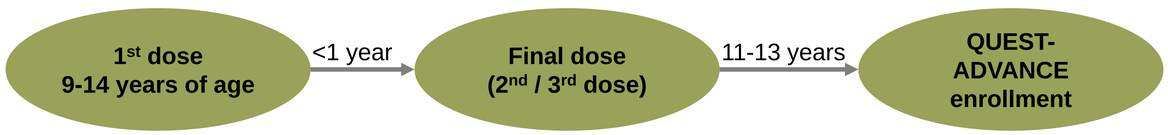
Inclusion Criteria

- Female sex at birth
- Vaccinated/ eligible for vaccination at 9-14 years of age
- 2-dose and 3-dose cohorts received the 1st dose at 9-14 years of age and the final dose no longer than 12 months after the first.
- It had been 11-13 years since first dose

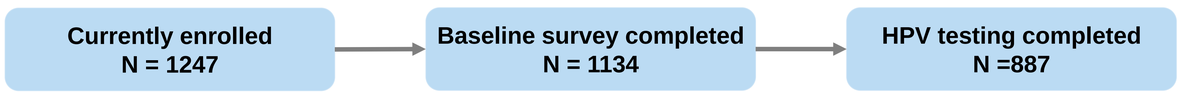
Measurements

- Baseline Survey
- HPV DNA testing using self-collected vaginal swab (type 16, 18, and "other' high-risk (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68).

Timeline



Analytic sample



Results

- As of October 2023, total of 1247 eligible females were invited to participate, among which 887 completed the first round of HPV testing.
- Smoking did not differ between dosing groups. Unvaccinated females reported significantly less medical condition compared with 1-, 2-, and 3-dose females.
- Unvaccinated females had their first sexual intercourse at a significantly older age compared with 1-, 2-, and 3-dose females (Ps<0.001).
- High long-term protection against HPV16 and HPV18 was found in all dosing groups.

Survey completed N (%)	Total N = 1134	3-dose N =649	2-dose N=348	1-dose N=30	Unvaccinated N=107
Ever had sexual intercourse					
No	43 (3.8)	20 (3.1)	18 (5.2)	0 (0.0)	5 (4.7)
Yes	946 (83.4)	557 (85.8)	285 (81.9)	25 (83.3)	79 (73.8)
Missing	145 (12.8)	72 (11.1)	45 (12.9)	5 (16.7)	23 (21.5)
Age of 1st intercourse (Med, IQR)	17 (16-19)	17 (16-19)	16 (16-18)	18 (16-20)	19 (17-21)
# of sexual partner (Med, IQR)	4 (2-10)	4 (2-10)	4 (2-8)	5 (2-10)	3 (1-8)
Ethnicity					
Asian	284 (25.0)	166 (25.6)	65 (18.7)	6 (20.0)	47 (43.9)
Indigenous	52 (4.6)	25 (3.9)	24 (6.9)	1 (3.3)	2 (1.9)
Latin	33 (2.9)	11 (1.7)	7 (2.0)	2 (6.7)	13 (12.1)
White	651 (57.4)	384 (59.2)	221 (63.5)	16 (53.3)	30 (28.0)
Multiethnic/ other	107 (9.4)	59 (9.1)	29 (8.3)	5 (16.7)	14 (13.1)
Missing	7 (0.6)	4 (0.6)	2 (0.6)	0 (0.0)	1 (0.9)
Smoking					
No	982 (86.6)	567 (87.4)	302 (86.8)	24 (80.0)	89 (83.2)
Yes	150 (13.2)	81 (12.5)	45 (12.9)	6 (20.0)	18 (16.8)
Missing	2 (0.2)	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)
Medical condition					
No	819 (72.2)	467 (72.0)	245 (70.4)	19 (63.3)	88 (82.2)
Yes	291 (25.7)	164 (25.3)	101 (29.0)	10 (33.3)	16 (15.0)
Missing	24 (2.1)	18 (2.8)	2 (0.6)	1 (3.3)	3 (2.8)

HPV test positive N (%)	Total N = 887	3-dose N = 515	2-dose N=273	1-dose N=20	Unvaccinated N=79
HPV-16	4 (0.5)	1 (0.2)	0	0	3 (3.8)
HPV-18	1 (0.1)	0	0	0	1 (1.3)
HPV-other high risk	178 (20.1)	104 (20.2)	58 (21.2)	1 (5.0)	15 (19.0)
Total	183 (20.6)	105 (20.4)	58 (21.2)	1 (5.0)	19 (24.1)

Conclusion

- The interim results suggest very high long-term effectiveness of the HPV vaccine against HPV16 and HPV18 in all groups, with evidence of ongoing exposure to HPV,
- The findings need to be examined in complete study cohorts to evaluate VE of different numbers of doses compared to unvaccinated with adjustment for potential confounders.
- Recruitment and follow-up are ongoing.