Performance of HPV tests in screening of young vaccinated women- insights from the SHEVa study.

PERFORMANCE OF HPV TESTS IN SCREENING OF YOUNG VACCINATED WOMEN- INSIGHTS FROM THE SHEVA STUDY

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Introduction

HR-HPV based primary cervical screening is now being implemented in several countries. HPV vaccination is changing the extent and distribution of HPV genotypes in the population. Consequently, **it is important for clinically validated HPV tests to be tested in vaccinated population to understand the impact of immunisation on their performance.**

Scotland is well placed to achieve this as girls vaccinated with the bivalent vaccine as part of “catch-up” immunisation programme have been entering the cervical screening programme since 2010. The Scottish HPV prevalence in vaccinated women (SHEVa) studies are designed to provide insight into the performance of clinically validated HPV tests in vaccinated women (Bhatia *et al*, 2016, IJC).

The present analysis focuses on the clinical performance of a DNA and RNA based HPV test in vaccinated women attending their first cervical screen.

Methods

Samples- Cervical samples from women attending their first routine screen at age 20 were collected for national immunization surveillance and residual samples stored in Scottish HPV Archive.
For this analysis, samples were collected from 993 unvaccinated and 1007 vaccinated women between 2010 and 2012. To enrich for disease cases in vaccinated women, a further 459 samples from vaccinated women with abnormal cytology results were collected between 2013 and 2014.
HPV testing- All samples were tested using the rTHPV test (Abbott) and APTIMA HPV test (Hologic) according to manufacturers instructions.
Outcome measures- Clinical performance of assays (sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the detection of CIN2+

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References: Bhatia R *et al*. Use of HPV testing for cervical screening in vaccinated women-Insights from the SHEVa (Scottish HPV Prevalence in Vaccinated Women) study. Int J Cancer. 2016 Jun 15;138(12):2922–31.

Results

Population distribution
Follow-up (average 17.1 months) was available for 943 women. Cases were defined as histologically confirmed >=CIN2 with controls as either <=CIN1 or two sequential negative cytology results (Table 1)

Population	Cases (CIN2+)	Controls (<=CIN1 or cytology normal)
Total (N=943)	119 (35.60%)	352 (37.33%)
Unvaccinated (N= 337)	63 (18.69%)	140 (41.54%)
Vaccinated (N=606)	56 (9.47%)	212 (34.98%)

Table 1: Overview of population

Clinical performance of the HPV tests
Table 2 shows the performance of rtHPV and Aptima tests in vaccinated women compared to unvaccinated women from SHEVA cohort. The sensitivity and NPV of the tests remain high but the specificity and PPV have reduced for both assays in vaccinated women.

	rTHPV Test		APTIMA HPV Test	
	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
Sensitivity	98.4 (90.3 - 99.9)	94.6 (84.2 - 98.6)	100 (92.8 - 100)	94.7 (84.4 - 98.6)
Specificity	30.0 (22.7 - 38.4)	22.7 (17.4 - 29.1)	31.4 (24.0 - 39.9)	20.3 (15.2 - 26.5)
Positive Predictive Value (PPV)	38.8 (31.3 - 46.8)	24.5 (19.1 - 30.9)	39.6 (32.1 - 47.7)	24.2 (18.9 - 30.5)
Negative Predictive Value (NPV)	97.7 (86.2 - 99.9)	94.1 (82.8 - 98.5)	100 (90.0 - 100)	94.5 (81.1 - 98.3)

Table 2: Clinical performance of HPV tests stratified by vaccination status

Conclusions

Clinically validated HPV tests maintain high sensitivity and NPV but the specificity and PPV of HPV testing as a primary screen is reduced in young vaccinated women. This has implications for the appropriate management of HPV screen-positive vaccinated women and underlines the importance of robust triage strategies.