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Assessing genital human papillomavirus genoprevalence in young Australian women following the introduction of a national vaccination program

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ABSTRACT

Objectives: Following the implementation of Australia's National HPV Vaccination Program in April 2007, this study evaluated the prevalence of vaccine-targeted human papillomavirus (HPV) genotypes (HPV 6, 11, 16, 18) amongst vaccine-eligible young women.
Methods: Between September 2011 and August 2013, women from Victoria, Australia aged 18–25 were recruited through targeted advertising on the social networking website Facebook. Participants completed an online questionnaire, and sexually active women were asked to provide a self-collected vaginal swab for HPV deoxyribonucleic acid (DNA) detection and genotyping. Samples positive for HPV were genotyped using the Linear Array HPV genotyping test (Roche Diagnostics). Self-reported HPV vaccination details were verified with the National HPV Vaccination Program Register (NHVPR).
Results: Of 431 vaginal swabs, 24.8% were positive for HPV DNA. Vaccine-targeted HPV genotypes were detected in only seven (1.6%) samples; all HPV 16 (of the six HPV 16 positive vaccinated women, all had received the vaccine after sexual debut). There were no cases of HPV 6, 11 or 18 identified. HPV types 51, 59, 73, 84, and 89 were the most prevalent genotypes. Vaccination rates were high, with 77.3% of participants having received all three doses of the vaccine, and there was an 89.8% concordance between self-reported and registry-reported HPV vaccination status. Strong associations were observed between vaccination status, age, language spoken at home and country of birth, as well as between HPV detection and the number of male sexual partners.
Conclusion: Preliminary data from this study demonstrate a very low prevalence of vaccine-related HPV genotypes amongst vaccine-eligible women from Victoria, Australia. We were able to use Facebook to effectively reach and recruit young women to participate in the assessment of the impact of Australia's HPV vaccination program.

Abbreviations: CI, confidence interval; DNA, deoxyribonucleic acid; HPV, human papillomavirus; NHVPR, National HPV Vaccination Program Register; OR, odds ratio; Pap, Papanicolaou; SEIFA, SocioEconomic Index for Areas; SD, standard deviation; VACCINE, Vaccine Against Cervical Cancer Impact and Effectiveness.

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1. Introduction

Persistent infection with a high-risk human papillomavirus (HPV) is a necessary pre-requisite for the development of cervical cancer [1,2]. HPV genotypes 16 and 18 are recognised as the most oncogenic of the high-risk HPV types and collectively account for 70% of cervical cancers worldwide [3]. Persistent infection, though a pre-requisite, is not sufficient to cause cancer. This outcome is rare and only occurs when HPV infection fails immunological clearance and control and various mutagenic events occur [4].

HPV has an estimated pre-vaccine global prevalence of 12% in women across the age range with normal cytological findings [5]. The development of cervical cancer is a process that typically progresses over years of persistent HPV infection with a high-risk genotype, however approximately 90% of women clear a specific HPV type within one to two years [6]. Despite the rarity of progression to cancer, an estimated 266,000 women died of cervical cancer worldwide in 2012, with 87% of these deaths occurring in resource poor countries [7]. In contrast, due to the success of Australia's National Cervical Screening Program, cervical cancer ranks as the 12th most common cancer in Australian women [8].

In addition to the screening program, in April 2007, Australia became the first country to introduce a fully government-funded National HPV Vaccination Program using the prophylactic quadrivalent HPV vaccine Gardasil®. The vaccine was offered to all females aged 12–26 years in a catch-up program delivered through schools and the community until the end of 2009. Vaccination of girls aged 12–13 is ongoing under the National Immunisation Program, with boys included since 2013. The uptake of the vaccine in the targeted population in Australia has been high, with the national coverage rate for three doses of the vaccine reported at 73% in school-aged girls [9]. While the long-term effect of the vaccine on reducing the incidence of cervical cancer will not be seen for decades, a decline in prevalence of vaccine-targeted HPV infection will be one of the earliest measures of the vaccine's impact. Potentially any replacement of prevalent oncogenic vaccine-targeted HPVs with other oncogenic non-vaccine HPV types could diminish the vaccine's effectiveness; however, the current genetic and evolutionary understanding of HPV types is that they are exceptionally genetically-stable and evolve very slowly [10].

A recent Australian study documented a significant decline in vaccine-targeted HPV prevalence from 28.7% to 6.7% in Australian women presenting for Papanicolaou (Pap) testing at family planning clinics [11]. A fall in cervical abnormalities has also been observed in young women eligible for the HPV vaccination program within five years of the program's introduction [12,13]. These studies, in addition to reports of dramatic falls in genital wart prevalence in Australia [14], indicate the early effects of HPV vaccination in reducing vaccine-targeted HPV infection, as well as disease.

In this paper, we present an interim analysis of one component of the VACCINE (Vaccine Against Cervical Cancer Impact and Effectiveness) Study, which was designed to evaluate the effectiveness and impact of the HPV vaccination program in an Australian setting [15]. The aim of the present study is to report the prevalence of HPV genotypes among young women in vaccine-offered cohorts recruited via social media. We also describe the factors associated with HPV prevalence and vaccination status within the cohort.

2. Materials and methods

Detailed methods for this study have been published previously [15]. The study protocol was approved by the Royal Women's Hospital Human Research and Ethics Committee. Inclusion criteria for participation in the study were (1) female, (2) aged 18–25 years, (3) living in the State of Victoria, Australia and (4) provision of verbal and written consent. The sample size is indicative of the number of participants recruited at the time data was prepared for the interim analysis.

2.1. Recruitment

Participants were recruited through advertisements on the social networking site Facebook. This method of recruitment was piloted previously [16]. Briefly, advertisements appeared randomly on the Facebook profiles of users matching the inclusion criteria. Prospective participants who clicked on an advertisement were then directed to the secure VACCINE Study website which provided a brief introduction to the study and prompted respondents to visit the registration page. Participants were telephoned on the contact number provided in their expression of interest and screened for inclusion in the study. Following verbal consent to participate, women completed an online questionnaire hosted on SurveyMonkey®.

The survey captured information including their sexual and cervical screening history, as well as attitudes and experiences with HPV and the HPV vaccine. Participants self-reported their HPV vaccination status and provided consent to verify their vaccination details with the National HPV Vaccination Program Register (NHVPR). Where a matching record was not located on the register, registry staff contacted the vaccination provider in order to verify doses if the participant had provided these details. Additionally, women who were sexually active were asked to self-collect a vaginal swab and return it by mail. Participants who completed all requirements of the study were sent a $10 gift voucher, to compensate for the time and inconvenience involved in participating.

2.2. HPV DNA genotyping

All sample processing and HPV DNA genotyping was performed at the Royal Women's Hospital Microbiology and Infectious Diseases Department molecular microbiology laboratory. In brief, swabs were swirled in 400 μL phosphate-buffered saline and stored in a −80 °C freezer until ready for DNA extraction using an automated MagNAPure 96 isolation and purification system (Roche Diagnostics®). A qualitative beta-globin test was then performed using a LightCycler (Roche Diagnostics®) to assess whether the sample DNA had been successfully extracted [17]. Samples were subsequently amplified for the HPV L1 gene using consensus primers PGMY09–PGMY11 [18], and amplicons were detected using PCR enzyme-linked immunosorbent assay (ELISA; Roche Diagnostics GmbH) [19]. Briefly, a generic probe for detection of the presence of any HPV sequences in the sample was employed using biotin-labelled probes able to detect all mucosal HPV types [19,20]. Samples that were HPV positive by PCR-ELISA were genotyped using LINEAR ARRAY® HPV Genotyping Test (Roche Diagnostics®), for which the hybridisation and washing steps were modified by using an automated blot processor (BeeBlot, Bee Robotics) [21–23].

Genotyping profiles were interpreted manually using the HPV reference guide provided with each kit. This genotyping test allows for the simultaneous detection of up to 37 HPV genotypes (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84, IS39 (82v) and CP6108 (HPV 89)). Where the HPV 52/33/35/58 band was present in the presence of HPV 33, 35 and/or 58, a HPV 52-specific real-time PCR assay was performed to confirm the presence or absence of HPV 52 [24]. DNA samples that were negative for both beta-globin and HPV were considered unassessable and excluded from the analysis.