RESEARCH GRANT SCIENTIFIC REPORT – GRACI FOUNDATION

Impact of Human Papillomavirus Immunisation on High-Grade Cervical Intraepithelial Neoplasia Rates in Young New Zealand Women: A retrospective cohort study

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OBJECTIVE:

Determine whether the introduction of a quadrivalent human papillomavirus vaccination has led to a decrease in the rates of cervical cell abnormalities and cervical intraepithelial neoplasia reported in young New Zealand women (aged 20–24 years).

DESIGN:

Retrospective population-based cohort study.

POPULATION:

N=104,313 women born 1990–1994 with at least one cervical smear or biopsy recorded when aged 20–24 years during the Audit Period (1 January 2010 and 31 December 2015).

METHODS:

Data linkage was undertaken between the National Immunisation Register and the National Cervical Screening Programme Register. Women were classified as vaccinated (at least one quadrivalent HPV vaccination dose before 18 years), late vaccinated (first HPV vaccination after 18 years), or unvaccinated (no HPV vaccination recorded). Incidence of high grade cytology and histology per 1000 person years was calculated for each group.

RESULTS:

Eligible women included 42,435 (41%) vaccinated women, 14,595 (14%) late vaccinated women, and 47,283(45%) unvaccinated women. Incident rate analyses included 376,402 person years of follow up.

The incidence of high grade cytology was lower in vaccinated women than in unvaccinated women (8.5 vs 11.3 per 1,000 person years, incident rate ratio [IRR] 0.75, 95% CI 0.70 – 0.80, p<.001). The incidence of high grade cytology was also lower in late vaccinated women than in unvaccinated women (9.7 vs 11.3 per 1,000 person years, IRR 0.86, 95% CI 0.79 – 0.94, p<.001).

The incidence of high grade histology was lower in vaccinated women than in unvaccinated women (6.0 vs 8.7 per 1,000 person years, IRR 0.69, 95% CI 0.64 – 0.75, p<.001). However,

there was no difference in the incidence of high grade histology in late vaccinated vs unvaccinated women (8.1 vs 8.7 per 1,000 person years, IRR 0.93, 95% CI 0.84 – 1.02, p=. 122).

Maori and Asian women were less likely to be vaccinated than women of European descent (Maori women 38% vs 42%, X^2 =93.45 p< .001; Asian women 33% vs 42%. X^2 =212.30 p< . 001). However, taking vaccination status into account, there was no difference in the incidence of high grade histology between New Zealand European and Maori women (Cox proportional hazard ratio 0.93, 95% CI 0.84 – 1.03, p=.168). All other ethnicities had substantially lower rates of high grade histology (Cox proportional hazard ratio [range] 0.17–0.47, p<.001).

DISCUSSION:

Data indicates that, compared with unvaccinated women, receiving at least one quadrivalent HPV vaccine dose prior to age 18 years is associated with a 25% decrease in high grade cervical cytology rate and a 31% decrease in high grade histology rate in women aged 20-24 years. While there was also a 14% decreased incidence of high grade cytology in women vaccinated after 18 years compared with unvaccinated women, there was no decrease in high grade histology rates in late vaccinated women.

While Maori were less likely to be vaccinated than women of European descent, after taking vaccination status into account, there was no difference in the incidence of high grade histology between New Zealand European and Maori women. Asian women were also less likely to be vaccinated than women of European descent, however, after taking vaccination status into account, Asian women actually had lower rates of high grade histology.

We classified women as vaccinated if they had had at least one dose of the HPV vaccine prior to age 18. However, most vaccinated women (89%) did receive all three doses and there was no substantial difference in the results if we excluded women who had had fewer than three doses.

Due to the relatively recent introduction of the HPV vaccine, the length of follow up for vaccinated women is still quite limited. The women we have the most follow up data (i.e., those born in 1990-1991) were primarily 17 or 18 years old when vaccinated, meaning that a

significant proportion of those women may have already been exposed to HPV16/18 prior to vaccination. In addition, although HPV vaccination coverage in NZ has increased from 39% for the cohort born in 1990 to 67% for the cohort born in 2003, we are still lagging behind many countries such as Australia and Scotland (e.g., vaccination rates for women born in 1994 of 73% in Australia and 86% in Scotland compared with 54% in NZ).

A number of factors such as increased HPV vaccine uptake, decreased mean age of vaccination, the recent introduction of the nonavalent HPV vaccine, and inclusion of HPV vaccination for males in New Zealand, mean that it is possible that an even greater impact of HPV vaccination on rates of high grade cervical cell abnormalities may be observed over time.

In line with many other countries, the NCSP is signalling their intention to cease cervical screening in NZ women under 25 years in 2019. Thus, it is important that we continue to investigate the incidence of cervical cell abnormalities in young women. It will be important to continue to add follow up data over the next few years to determine the long term impact of the introduction of the vaccination programme on the incidence of high grade histologies in young women.

DISSEMINATION OF RESULTS:

This data was presented at the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) Annual Scientific Meeting in Auckland (29 October – 1 November 2017) and at an invited breakfast session at the Australian Society of Gynaecologic Oncologists (ASGO) Annual Scientific Meeting in Taupo (4-7 July 2018).

RANZCOG ASM Abstract

- Innes C, Sykes PH, Williman J, Simcock BJ, Dempster-Rivett K, Hider P, Lawton B (2017). Impact of HPV vaccination on rates of high grade cervical abnormalities in young NZ women: Register data matching study. Australian & New Zealand Journal of Obstetrics & Gynaecology, 57(Suppl. 1), 6.

An academic paper based on these results is in preparation and is expected to be submitted for publication soon.