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## Factors associated with the human papillomavirus (HPV) vaccination across three countries following vaccination introduction

Brooke Nickel<sup>a,b</sup>, Rachael H. Dodd<sup>a,d</sup>, Robin M. Turner<sup>c</sup>, Jo Waller<sup>d</sup>, Laura Marlow<sup>d</sup>, Gregory Zimet<sup>e</sup>, Remo Ostini<sup>f</sup>, Kirsten McCaffery<sup>a,b,\*</sup>

- <sup>a</sup> Wiser Healthcare, Sydney School of Public Health, The University of Sydney, Sydney, New South Wales, Australia
- b Centre for Medical Psychology and Evidence-based Decision-making (CeMPED), The University of Sydney, New South Wales, 2006, Australia
- <sup>c</sup> School of Public Health and Community Medicine, University of New South Wales, New South Wales, Australia
- <sup>d</sup> Department of Behavioural Science and Health, Cancer Research UK Health Behaviour Research Centre, UCL, London, UK
- e Section of Adolescent Medicine, Indiana University School of Medicine, Health Information & Translational Sciences, Indianapolis, IN, USA
- f Rural Clinical School Research Centre, Faculty of Medicine, The University of Queensland, Toowoomba, Queensland, Australia

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#### ABSTRACT

Direct international comparisons which aim to understand how factors associated with human papillomavirus (HPV) vaccine initiation and attitudes towards the HPV vaccination in parents differ are scarce. Parents (n = 179) of daughters aged 9-17 years in the US, UK and Australia completed an online survey in 2011 with questions measuring daughters' HPV vaccination status, HPV knowledge, HPV vaccination knowledge, and statements assessing attitude towards the HPV vaccine. The strongest factor associated with vaccination status across all countries was parental HPV knowledge (p < 0.001). Parents with both very low and very high knowledge scores were less likely to have vaccinated their daughters. Parents with higher HPV vaccination knowledge scores intended to vaccinate their daughters (if not already vaccinated) for protective reasons (p < 0.001), while those whose daughters were already vaccinated understood that vaccination protection was not 100% and that their daughters may still be at risk of getting HPV (p < 0.05). Compared to the UK and Australia, a higher proportion of parents with unvaccinated daughters from the US were worried about the sideeffects of the HPV vaccination (US: 60.5%, UK: 36.4%, AUS: 15.4%; p < 0.05), believed that getting the vaccination might be a hassle (US: 21.1%, UK: 0%, AUS: 7.7%; p < 0.05), and that the vaccine was too new (US: 44.7%, UK: 22.7%, AUS: 7.7%; p < 0.05). This study adds to the understanding of how parents may influence vaccination uptake by demonstrating the effect of knowledge and the parental attitudes towards HPV vaccination across three countries.

#### 1. Introduction

High-risk types of human papillomavirus (HPV), the most common sexually transmitted infection (STI) internationally, can lead to development of cervical cancer as well as genital warts, anal, penile and oropharyngeal cancers (Forman et al., 2012). In 2006, the United States Food and Drug Administration (FDA) approved the quadrivalent vaccine for the prevention of HPV types 6, 11, 16 and 18 (U.S. Food and Drug Administration, 2006) associated with over of 70% of all cervical cancer cases and 90% of genital warts cases (Munoz et al., 2004). In 2008, the FDA further approved the bivalent HPV vaccination which prevents HPV types 16 and 18 protecting against cervical cancer but not strains of HPV that cause genital warts (U.S. Food and Drug

Administration, 2006, 2009a). Recently, a nonavalent vaccine has been licensed for use in the European Union and the United States (US), providing protection against five additional high-risk types of HPV (Forster & Waller, 2016). Widespread use of this vaccine has not yet begun in the United Kingdom (UK), however, it is currently the only vaccine being administered in the US. Now, almost all high-income countries have one of the HPV vaccines available to girls and young women, although the choice of vaccine, the cohorts it is offered to, the way it is administered and the cost, varies. In the US, the HPV vaccine is predominantly available through physicians' clinics and medical centres, while in the UK and Australia, publically funded school-based programs offer the vaccine free to girls age 12–13. In 2007, Australia was the first country internationally to launch publically funded school-

Abbreviations: HPV, Human papillomavirus; US, United States; UK, United Kingdom; AUS, Australia

<sup>\*</sup> Corresponding author at: Wiser Healthcare, Sydney School of Public Health, The University of Sydney, New South Wales, 2006, Australia. E-mail address: kirsten.mccaffery@sydney.edu.au (K. McCaffery).

based programs, with the UK launching their program a year later in 2008. Australia also had catch-up programs targeting young women in schools and the community, and the UK had a similar catch-up program from 2008 to 2010.

Given that the primary target population for HPV vaccination programs is girls aged 9–13 years, typically before the initiation of sexual activity (World Health Organisation, 2013), parental knowledge and attitudes play an important role in the success of vaccination as consent is usually required for their adolescent children to be vaccinated. Research aimed at understanding HPV vaccine uptake has demonstrated that uptake of the HPV vaccine is generally high, however parents and girls often have insufficient knowledge and understanding about and have varying attitudes towards vaccination (Hendry et al., 2013). Alongside this, several studies conducted across different settings have aimed to examine factors influencing HPV vaccine uptake. Findings from these studies are wide-ranging, however, parental intentions have been shown to consistently be a strong predictor of their children's HPV vaccine uptake (Alberts et al., 2017; Mupandawana & Cross, 2016).

The understanding of parental psychosocial determinants that influence HPV vaccine initiation is a growing area of research (Allen et al., 2010; Krawczyk et al., 2015a; Krawczyk et al., 2015b; Trim et al., 2012), although no studies have directly compared countries that use different methods of administering the vaccine, such as school-based or non-school-based programs. Using online survey data collected across three countries, this study examined parents of 9–17 year-old girls in the US, UK and Australia to identify country-specific factors which are associated with their daughters' vaccination status (HPV vaccine initiation). It also compared attitude differences between countries and by HPV vaccination knowledge by using identical knowledge and attitude variables in order to help better identify how parents' attitudes and knowledge play a role in vaccination participation internationally.

#### 2. Material and methods

#### 2.1. Participants

Participants (n = 12,259) from the US, UK and Australia were directed to a web-based survey by Survey Sampling International (SSI). SSI has existing online panels of participants who sign up to take part in market research for points which go towards a small reward (e.g. coupons and discounts). Quotas were set to ensure adequate representation of different age-groups and genders. The initial target sample for the survey was 2400 participants aged 18-70 years with approximately 800 participants from each country, including an equal number of men and women. Participants meeting these criteria were recruited to the survey. Participants were asked additional demographic questions including whether they had a daughter aged 9-17 years of age (the HPV vaccination age-range). From this information, survey data was analysed from participants who indicated they had at least one daughter in the HPV vaccination age-range. Ethical approval was obtained from human research ethics committees at Indiana University, USA, University College London, UK and the University of Sydney, Australia.

#### 2.2. Measures

Participants were given information which included the purpose of the study, confidentiality and anonymity information and contact details for researchers in their country. Initially participants were asked their age, gender and country of residence to determine if they were eligible to take part in the survey, based on the quota of n=400 men and n=400 women from each country. Before participants began the questions on HPV knowledge they were asked 'how many daughters do you have between the ages of 9 and 17'. If participants had a daughter or daughters in this age-range they were asked for their daughters' specific age(s) and how many of those had received at least one dose of

the HPV vaccine. If at least one of the participant's daughters had been vaccinated, the parent was classified as "vaccinated" for the outcome variable. All participants were then asked questions on their knowledge of HPV (16 questions) and HPV vaccination (7 questions), which were later validated (Waller et al., 2013). Response options for the two sets of knowledge questions were True/False/Don't know, and data on knowledge of HPV, HPV vaccination and HPV testing were analysed and results published (Dodd et al., 2014; Marlow et al., 2013).

If participants answered that they had a daughter in the vaccination age-range they were further directed to a set of purposely designed attitude statements on HPV and HPV vaccination (Supplementary Table 1) which were derived from a UK survey (Marlow et al., 2007). Statements were directed specifically to either participants with at least one unvaccinated daughter eligible for HPV vaccination (14 attitude statements) or participants with at least one daughter who had received one or more doses of vaccine (8 attitude statements), with both sets of parents receiving the same eight attitude statements (with the wording only differing slightly based on context). Parents with at least one unvaccinated daughter were given an additional six attitude statements. Response options for the attitude statements were given as a 5-point Likert scale (Strongly disagree, Disagree, Neither disagree nor agree, Agree, Strongly agree). Data analysis on attitudes to HPV and to HPV vaccination was performed on the responses of participants who indicated that they had a daughter who was of vaccination age.

Participants were removed from the final analysis if they did not know whether their daughter had received the HPV vaccination, if they had never heard of the HPV vaccination or if they did not answer any of the parental attitude statements on HPV or the HPV vaccination (n = 146).

#### 2.3. Statistical analysis

Responses to attitude items were collapsed into three categories: Disagree (Strongly disagree and Disagree), Neither disagree nor agree, and Agree (Agree and Strongly agree). Parental HPV vaccination knowledge scores (ranging from 0 to 7) were combined into three categories: low (0-2 correct responses), medium (3-4), and high (5+). Chi-square tests were conducted initially to investigate the association between knowledge, attitudes and daughters' vaccination status.

The association between the proportion with daughters "not vaccinated" and the demographic, knowledge (as a continuous measure) and attitude variables were investigated using logistic regression with odds ratios reported from these models. Initially all variables were fitted univariately with the outcome and then a multivariable model was constructed. We decided a priori on the most important variables to be included in the model and included all the attitude variables regardless of significance because of the small sample size. For the model building, all demographic factors were fitted and then backwards elimination applied. The knowledge measures were then included and backwards elimination used. Finally, all attitude variables were added to produce the final model. The attitude regarding genital warts was only measured in two countries so it was fitted separately where the data was available and adjusted for all factors in the final model. This is because at the time of data collection the US and Australia offered Gardasil which protects against genital warts and the UK offered Cervarix which did not protect against genital warts. Fractional polynomials were used to assess the linearity of the association between the continuous knowledge scores and vaccination status. Likelihood ratio p-values were used to assess statistical significance with p < 0.05 considered significant.

Data were analysed using SPSS V.21 (IBM, Armonk, NY). The logistic regression models were conducted in Stata 14 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station).

#### 3. Results

The survey had a 62% response rate, as a total of 12,259 men and

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