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Letter-to-the-Editor in response to "Tanton C, et al. Human papillomavirus (HPV) in young women in Britain: Population-based evidence ofthe effectiveness of the bivalent immunisation programme and burden of quadrivalent and 9-valent vaccine types. Papillomavirus Res. 2017 Jun;3:36-41.doi: 10.1016/j.pvr.2017.01.001."

In their recent publication, Tanton et al. present the type-specific Human Papillomavirus (HPV) prevalence in urine samples from sexually-experienced women aged 16–44 years enrolled in the National Survey of Sexual Attitudes and Lifestyle-3 (Natsal-3; 2010–2012). Impact of the AS04-HPV-16/18 vaccine on HPV prevalence is estimated from a comparison with the results from the Natsal-2 survey (1999–2001) in the age group 18–20 years. The authors observed a nearly 50% reduction in the prevalence of HPV-16/18 in 18–20 year olds post-vaccine introduction, but no change in the prevalence of the non-vaccine types including HPV-31, −33 and −45 for which the AS04-HPV-16/18 vaccine has shown cross-protection in clinical trials and other post-licensure studies [1].

We would like to explore some limitations in the methodology used in the current analysis of the Natsal surveys that may explain why the current observations differ from those made in other settings.

It is recognized that individual HPV-type prevalence can change over time in a population [2]. Changes in epidemiology unrelated to vaccination during the long time span between sample collection for Natsal-2 (1999–2001), vaccination program implementation in 2008 and sample collection for Natsal-3 (2010–2012) could therefore bias the vaccine impact assessment.

As acknowledged in the discussion, the Natsal-3 survey was neither powered to assess prevalence estimates in subgroups and for rare HPV types nor to make comparisons with previous surveys. The prevalence comparison in the 18–20 year olds is based on 140 and 331 participants from Natsal-2 and −3, respectively and the provided prevalence rates indicate that case counts for non-vaccine types were rather small. Furthermore, weighting seems to have a very different effect in the Natsal-2 and −3 surveys. While weighting in Natsal-2 slightly increases the denominator (from 140 to 150), weighting in Natsal-3 resulted in an important reduction of the denominator size (331 to 199). This suggests different baseline characteristics in both survey populations. The paper does not present in detail the weighting algorithm and does not discuss the potential baseline differences impacting the estimation of the weighted denominator in both surveys.

Samples in Natsal-2 were collected in a urine collection cup, whereas samples in Natsal-3 were collected with a specific device (*Firstburst*) that collects the first-void urine. It has been shown that Chlamydia organism load is 6 times higher in the *Firstburst* collected first-void urine compared to urine collected in a regular cup [3]. As the use of different collection techniques may impact the HPV load, we wish to understand whether a validation of the *Firstburst* versus the urine cup sample collection has been conducted prior to the analysis.

The discussion puts into perspective the Natsal survey results with the HPV-prevalence data in England in women attending the Chlamydia screening program, as well as early observations (2009–2013) in 20–21 year olds that were vaccinated in the context of the catch up program and attended the Scottish cervical screening program. A more recent follow-up study of Scottish women vaccinated with the AS04-HPV-16/18 vaccine at target age 13 years now demonstrates vaccine effectiveness of 85·1% (CI95% 77·3 to 90·9) against infections with HPV-31, −33 and −45 [4]. The strength of the Scottish analysis lies in the large size of the population screened with high uptake, the ability to link individual vaccination status to screening and HPV genotyping outcomes and the availability of data for successive birth cohorts before and after implementation of the HPV vaccination program. The results have been acknowledged as a confirmation of sustained cross protection that should be taken into full consideration for future cost-effectiveness calculations [5].

While the Natsal survey data may provide some insight on HPV prevalence in the general female population at specific time points, it is however important to provide a clear view on its limitations for the prevalence comparisons and vaccine impact calculations. Furthermore, it is necessary to consider all available scientific evidence, as well as the individual quality of the evidence in order to inform HPV vaccination policy.

Disclosures

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