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Surveillance of type-specific HPV in sexually active young females in England, to end 2018

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Key points

- PHE has conducted surveillance of type-specific HPV infections in sexually active 16-24 year-old females (undergoing chlamydia screening) since prior to the start of the national HPV vaccination programme (with the HPV16/18 vaccine)

- the prevalence of HPV16/18 in sexually active 16-18 year-old females who were offered vaccination at age 12-13 years has been less than 2% (compared to over 15% prior to the vaccination programme in 2008). In the most recent year, 2018, 10 years after vaccination was introduced, we detected no HPV16/18 infections in 16-18 year-olds (0% of n=584): this shows the programme has succeeded in delivering both direct and indirect protection

- the prevalence of HPV6/11 in 16-18 year-olds did not decrease until 2018, from 7-10% during 2010-2017 to 4.1 in 2018

- the prevalence of HPV31/33/45 has also declined during the post-vaccination years, to the end of 2018, suggesting evidence of substantial cross-protection

- there has been no evidence of increases in any other high-risk HPV types, ie of type replacement.

Background

Persistent infection with high-risk human papillomavirus (HPV) is a necessary cause of cervical cancer [1]. Prior to vaccination, 2 high-risk types, HPV16 and HPV18, were present in approximately 80% of cervical cancers in the UK [2]. The national HPV vaccination programme began offering vaccination to females in England in September 2008 and has recently extended the offer to include males (from September 2019). This programme offers HPV vaccination routinely to males and females entering year 8 of school (aged 12-13 years) and is almost exclusively delivered in schools. There was a catch-up programme in the first 2 years of the programme to offer vaccination to all females aged up to 18 years in 2008.

The programme initially used the bivalent (HPV16/18) vaccine (Cervarix®) [3,4]. In 2012, the programme changed to using the quadrivalent (HPV16/18/6/11) vaccine (Gardasil®), which additionally offered protection against 2 low-risk HPV types, HPV6/11, that cause approximately 90% of genital warts [5,6]. In 2014, the programme changed from a 3-dose course to a 2-dose course.

Vaccination coverage has been consistently high, above 80% for routine cohorts. We have previously reported evidence of substantial declines in the prevalence of HPV types included in the vaccine and in other closely related types in young, sexually-active females since the introduction of the programme [7].

Methods

Residual vulvovaginal swab (VVS) specimens were collected from 16-24 year-old females attending for opportunistic chlamydia screening in selected primary care settings. Over the years 2010-2018, specimens have been sent from 10 laboratories in seven regions across England to PHE's Virus Reference Department (VRD) for type-specific HPV testing using an in-house multiplex PCR and Luminex®-based genotyping test. Demographic data reported to PHE were linked to specimens received: data were anonymised prior to HPV testing.

HPV prevalence and 95% confidence intervals (CI) were calculated for 3 age groups (16–18, 19–21, and 22–24 year-olds) and 5 post-vaccination periods (2010–2011, 2012–2013, 2014–2015, 2016-2017, and 2018). For HPV16/18, previously published prevalence estimates from 2008 (ie prior to introduction of HPV vaccination) were included in trend analyses [8]. For all other HPV types, trend analyses considered changes within the post-vaccination period only, due to differences in detection rates for certain types by the assay used in the pre-vaccination period [7]. Findings were analysed for HPV16/18, the closely related types HPV31/33/45, other high-risk HPV types (HPV35/39/51/52/56/58/59/68) [1] and the low-risk types HPV6/11.

Individual vaccination status was collected where available for earlier post-vaccination periods in previous analyses, but a high proportion of missing vaccination status data led to the pragmatic decision to not collect vaccination status during the 2017-2018 post-vaccination survey period. Individual-level vaccination coverage (where available; ie prior to 2017) and published national HPV vaccination programme coverage figures (where individual vaccination status was unavailable) were combined to estimate vaccination coverage by year and age group, as described in previous analyses [7].

Results

A total of 18,780 specimens were included in this analysis, 1,353 and 1,754 of which were collected in 2017 and 2018, respectively (representing new data since the last report) [7]. These specimens are broadly representative of sexually-active young females undergoing chlamydia screening offered opportunistically in primary care settings.

The estimated vaccination coverage in the population, the age at which vaccination would have been offered, and the vaccine offered are shown by age group and year/period of collection in Table 1.

HPV16 and/or HPV18 infection

Declines in HPV16/18 infection were seen within the post-vaccination period across all age groups (Figure 1), with greater declines in the age groups and years with higher coverage. The prevalence of HPV16/18 declined within the post-vaccination period between 2010/11 and 2018 from 8.2% (95% CI 6.7-10.0) to 0.0% (95% CI 0.0-0.006) in 16-18 year-olds (p value for trend <0.001) and from 14.0% (95% CI 12.4-15.8) to 0.7% (95% CI 0.3-1.4) in 19-21 year-olds (p value for trend <0.001). In the oldest age group (22-24 year-olds), the prevalence declined from 16.4% (95% CI 14.4-18.6) in 2010/11 to 2.6% (95% CI 0.7-6.5) in 2018 (p value for trend <0.001).

HPV31, HPV33 and/or HPV45 infection, and other high-risk infections

In the younger age groups, there was evidence of a decrease in HPV31/33/45 infection within the post-vaccination period overall. The prevalence of HPV31/33/45 decreased from 6.5% (95% CI 5.1-8.1) in 2010/11 to 1.9% (95% CI 0.9-3.3) in 2018 in 16-18 year-olds (p value for trend <0.001) and from 8.6% (95% CI 7.3-10.1) to 2.8% (95% CI 1.8-4.0) in 19-21 year-olds (p value for trend <0.001). In 22-24 year-olds, the prevalence of HPV 31/33/45 declined from 7.8% (95% CI 6.4-9.5) to 5.2% (95% CI 2.3-9.9; p value for trend 0.957) (Figure 2). Infection with other high-risk HPV types did not increase (Table 1).

HPV6 and/or HPV11 infection

There was no decrease in HPV6/11 prevalence until 2018 in 16-18 year-olds, and then a decline from 7.0-10.0% during 2010-2017 to 4.1 (95%CI 2.7-6.1) in 2018. Declines have not been seen yet in older age groups. This fits with use of the quadrivalent vaccine (including HPV6/11 protection) since 2012 (Table 1).

Figure 1: Prevalence of HPV16 and/or HPV18 infection by year and age group

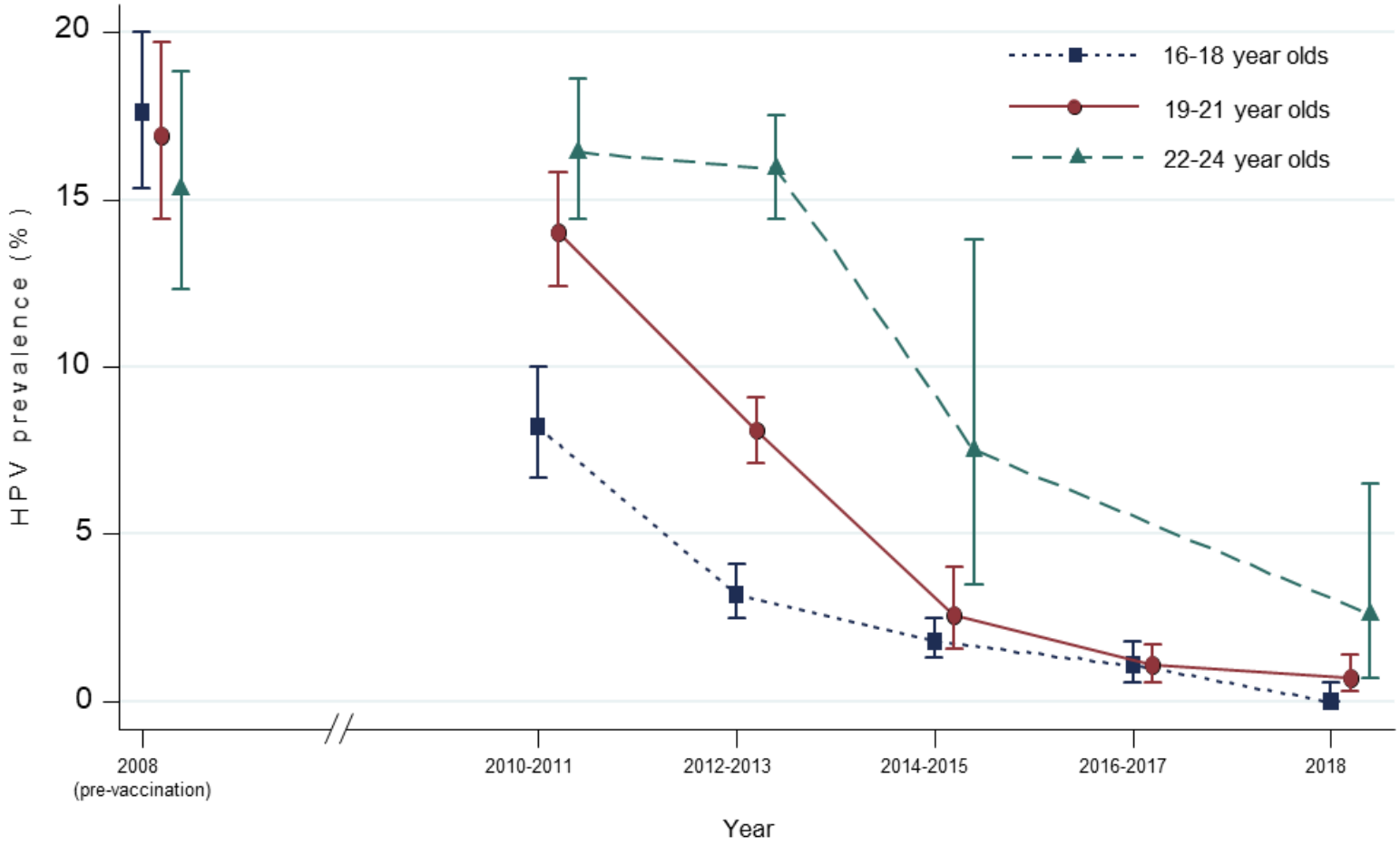

Figure 2: Prevalence of HPV31, HPV33 and/or HPV45 infection by year and age group

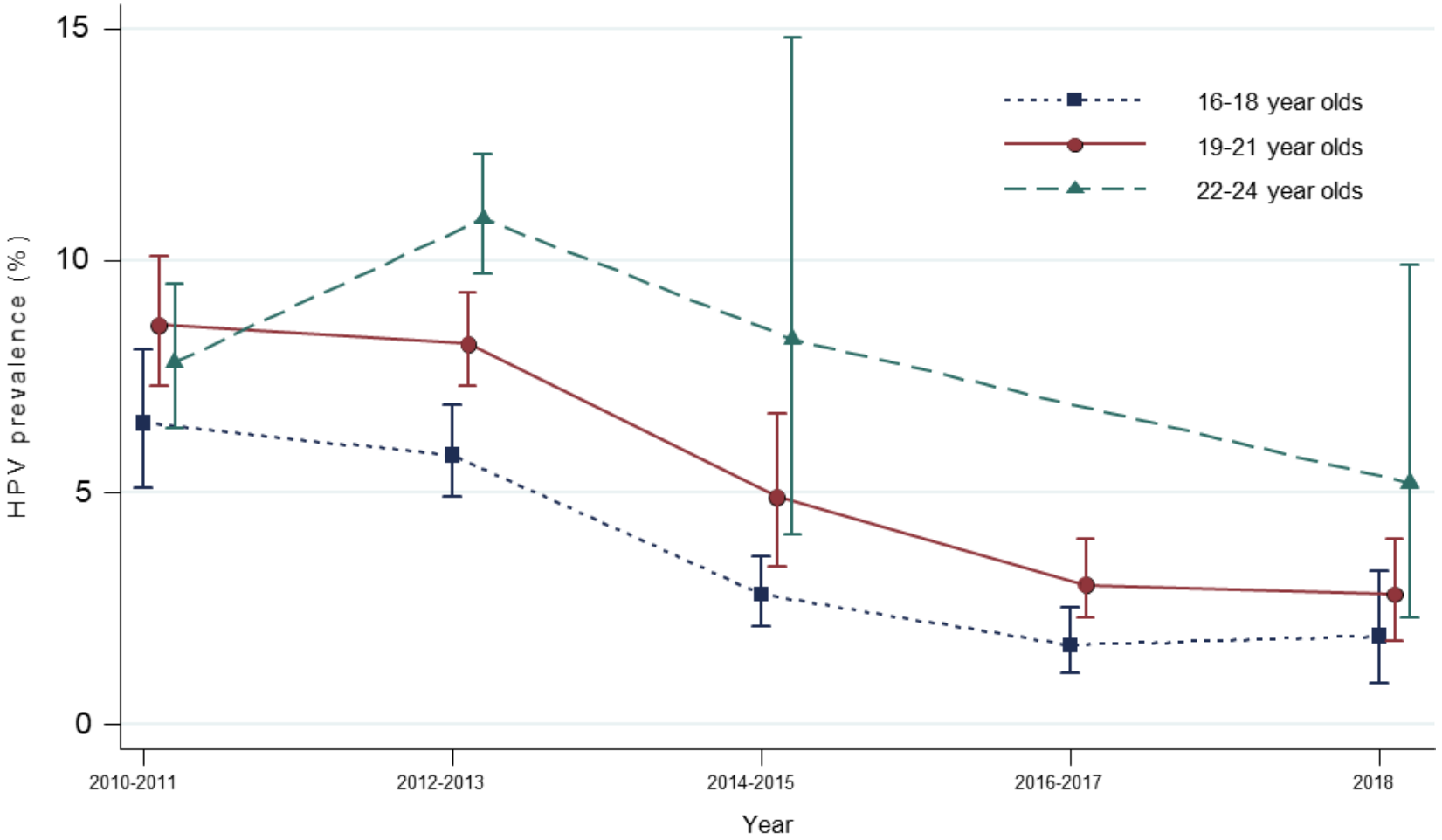

Table 1. Pre-vaccination and post-vaccination type-specific HPV prevalence by age group among all females

	Post-vaccination prevalence (95% CI[1])					
HPV type	**2010-2011**	**2012-2013**	**2014-2015**	**2016-2017**	**2018**	**p-value for trend**
16-18 years old	**n=1128**	**n=2094**	**n=1954**	**n=1311**	**n=584**	
[Estimated HPV vaccination coverage]	*[60%]*	*[77%]*	*[84%]*	*[85%]*	*[86%]*	
[Age at vaccination and vaccine offered]	*12-18yrs; 2V*	*12-18yrs; 2V*	*12-15yrs; 2V/4V*	*12-13yrs; 2V/4V*	*12-13yrs; 2V/4V*	
High-risk HPV types						
HPV16/18	8.2 (6.7,10.0)	3.2 (2.5,4.1)	1.8 (1.3,2.5)	1.1 (0.6,1.8)	0.0 (0.0,0.006)	<0.001
HPV16	6.4 (5.0,8.0)	2.4 (1.8,3.1)	1.5 (1.0,2.1)	0.9 (0.5,1.6)	0.0 (0.0,0.006)	<0.001
HPV18	2.8 (1.9,4.0)	1.0 (0.6,1.5)	0.4 (0.2,0.8)	0.2 (0.0,0.7)	0.0 (0.0,0.006)	<0.001
HPV31/33/45	6.5 (5.1,8.1)	5.8 (4.9,6.9)	2.8 (2.1,3.6)	1.7 (1.1,2.5)	1.9 (0.9,3.3)	<0.001
Other high-risk HPV (not 16/18/31/33/45)	34.2 (31.5,37.1)	34.3 (32.3,36.4)	32.7 (30.6,34.8)	25.9 (23.5,28.3)	25.5 (22.0,29.3)	<0.001
Low-risk HPV types						
HPV6/11	7.8 (6.3,9.5)	9.5 (8.3,10.8)	10.7 (9.4,12.2)	7.2 (5.8,8.7)	4.1 (2.7,6.1)	0.009
19-21 years old	**n=1704**	**n=2892**	**n=737**	**n=1607**	**n=1015**	
[Estimated HPV vaccination coverage]	*[25%]*	*[49%]*	*[79%]*	*[83%]*	*[84%]*	
[Age at vaccination and vaccine offered]	*12-18yrs; 2V*	*12-18yrs; 2V*	*12-18yrs; 2V*	*12-15yrs; 2V*	*12-13yrs; 2V/4V*	
High-risk HPV types						
HPV16/18	14.0 (12.4,15.8)	8.1 (7.1,9.1)	2.6 (1.6,4.0)	1.1 (0.6,1.7)	0.7 (0.3,1.4)	<0.001
HPV16	11.0 (9.5,12.6)	6.7 (5.8,7.7)	1.8 (0.9,3.0)	1.0 (0.6,1.6)	0.6 (0.2,1.3)	<0.001
HPV18	3.6 (2.7,4.6)	1.8 (1.3,2.3)	0.8 (0.3,1.8)	0.1 (0.0,0.3)	0.1 (0.0,0.5)	<0.001
HPV31/33/45	8.6 (7.3,10.1)	8.2 (7.3,9.3)	4.9 (3.4,6.7)	3.0 (2.3,4.0)	2.8 (1.8,4.0)	<0.001
Other high-risk HPV (not 16/18/31/33/45)	39.1 (36.8,41.4)	43.0 (41.2,44.9)	38.3 (34.7,41.9)	33.4 (31.0,35.7)	32.2 (29.3,35.2)	<0.001
Low-risk HPV types						
HPV6/11	8.0 (6.7,9.4)	9.0 (8.0,10.1)	9.1 (7.1,11.4)	7.8 (6.5,9.2)	9.5 (7.7,11.4)	0.391

[1] Exact 95% CI were calculated for zero numerators.

Table 1 (continued). Pre-vaccination and post-vaccination type-specific HPV prevalence by age group among all females

22-24 years old	**n=1212**	**n=2267**	**n=120**	**n=0**	**n=155**	
[Estimated HPV vaccination coverage]	*[0%]*	*[7%]*	*[25%]*	*[>80%]*	*[83%]*	
[Age at vaccination and vaccine offered]	*N/A*	*12-18yrs; 2V*	*17-18yrs; 2V*		*12-16yrs; 2V*	
High-risk HPV types						
HPV16/18	16.4 (14.4,18.6)	15.9 (14.4,17.5)	7.5 (3.5,13.8)		2.6 (0.7,6.5)	<0.001
HPV16	14.6 (12.7,16.7)	13.4 (12,14.9)	5.8 (2.4,11.6)		1.9 (0.4,5.6)	0.012
HPV18	2.6 (1.8,3.7)	3.1 (2.4,3.9)	1.7 (0.2,5.9)		0.6 (0.0,3.5)	<0.001
HPV31/33/45	7.8 (6.4,9.5)	10.9 (9.7,12.3)	8.3 (4.1,14.8)		5.2 (2.3,9.9)	0.957
Other high-risk HPV (not 16/18/31/33/45)	31.9 (29.3,34.6)	39.1 (37.1,41.2)	35.0 (26.5,44.2)		36.1 (28.6,44.2)	0.002
Low-risk HPV types						
HPV6/11	3.5 (2.5,4.7)	6.0 (5.0,7.0)	1.7 (0.2,5.9)		12.3 (7.5,18.5)	<0.001

Discussion

Ten years after the introduction of the national HPV vaccination programme in adolescent females, population-based data continue to show dramatic declines in infections with HPV vaccine-types and closely related HPV types. The new data reported here show a continuation of previously reported trends [7,9,10]. Among females offered HPV vaccination, the most substantial reductions in infections with HPV vaccine-types were seen in the youngest age groups – who would have been offered vaccination at 12-13 years and have the highest coverage. Most notably, we detected no HPV16 and/or HPV18 infections in 2018 among 16-18 year-old females, who would have been vaccinated with a coverage of 86% aged 12-13 years.

We have previously observed declines in HPV31/33/45 within the post-vaccination period, indicating there is clear evidence of cross-protection from the bivalent vaccine [7]. These declines have been sustained to the end of 2018 across all age groups, indicative of continuing substantial cross-protective effects of vaccination.

The prevalence of HPV6/11 has decreased by approximately 50% in the youngest age group, most of whom would have received the quadrivalent vaccine aged 12-13 years, within the more recent post-vaccination period, strongly suggesting that we are beginning to see an impact of quadrivalent vaccination. This is consistent with recently published results from surveillance of genital warts diagnoses in young females in England to end of 2018 [11,12].

Results continue to show evidence of substantial effects of herd protection, as indicated by reductions in HPV types in excess of coverage. This is most clearly evident in data from 2018 for 16-18 year-old females where no HPV16 and/or HPV18 infections were detected, and where approximately 15% of the population is presumed not vaccinated as per coverage estimates. HPV16 and/or HPV18 prevalence has been <2% in this age group since 2014.

Concerns regarding whether reduction in HPV vaccine-types would lead to other HPV types becoming more common have thus far been unsubstantiated. If HPV vaccination was causing a selective advantage for non-vaccine HPV types, increases in these other types would be expected to show and strengthen over time as later post-vaccination periods include females vaccinated at a younger age and with higher vaccination coverage. Results to end of 2018 provide reassurance that prevalence of non-vaccine HPV types has not increased.

This analysis includes HPV results for over 18,000 specimens, allowing for precise estimates of the population-level impact of HPV vaccination in England. A limitation is the lack of vaccination status for each specimen, precluding the calculation of vaccine

effectiveness. Potential selection bias is a further limitation as changes in the population of females undergoing chlamydia screening could result in changes in HPV prevalence unrelated to vaccination.

Sustained declines in HPV infection among 16-24 year-old females are a further indication that the high-coverage HPV vaccination programme in England will almost certainly lead to large reductions in cervical cancer in the future. We will continue to monitor infections of HPV vaccine-types and other high-risk HPV types in this population. Additionally, surveillance is in place to evaluate the impact of vaccination on cervical cancers in due course.

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