

# No effect of human papillomavirus vaccination on sexual debut of school children

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## ABSTRACT

**INTRODUCTION:** We aimed to describe sexual behaviour and knowledge about sexually transmitted infections (STI) among Danish adolescents stratified by gender and human papillomavirus (HPV) vaccination status.

**METHODS:** We conducted a questionnaire study in Viborg Municipality, Denmark. A validated questionnaire was sent to all ninth-grade pupils without prior notice to either teachers or pupils.

**RESULTS:** In 2014, 776 pupils attended the ninth grade, 685 (88%) of whom participated in the study. A total of 376 (55%) reported having received the HPV vaccine. HPV-vaccinated girls ( $p = 0.03$ ) and boys ( $p = 0.04$ ) had more knowledge about STI than those who were unvaccinated. A total of 157 (23%) pupils reported having had intercourse, with a mean age at debut of 14.4 (standard deviation  $\pm 1$ ) years and no significant difference by gender or vaccination status. From first to latest intercourse, we found a significant decline in total condom use among all pupils ( $p < 0.001$ ), with the most significant decline being observed among HPV-vaccinated pupils ( $p < 0.001$ ), in particular among HPV-vaccinated girls ( $p < 0.001$ ). In addition, a non-significant increase was observed in the lack of use of contraception (16% versus 27%) from first to latest intercourse, with no difference being observed by gender or vaccination status.

**CONCLUSIONS:** Overall, no difference in the proportion of pupils with sexual debut or mean age at sexual debut was observed between HPV-vaccinated and unvaccinated adolescents in Denmark. However, HPV-vaccinated adolescents were more likely to stop using a condom despite their higher STI awareness.

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**TRIAL REGISTRATION:** not relevant.

Human papillomavirus (HPV) is the most common sexually transmitted infection (STI) with an 80% lifetime risk of infection [1]. Low-risk HPV types may cause formation of anogenital warts, whereas high-risk types may cause cancer of the cervix, anus, vulva, vagina, penis, and of the head and neck [2]. In Denmark, the quadrivalent HPV vaccine was implemented in the Danish childhood vaccination programme in 2009, recommending vaccination of girls aged 12 years, with

catch-up programmes targeting women in the 1985-1997 birth cohorts [3]. Since the implementation of the HPV vaccine, the incidence of anogenital warts has declined significantly in Denmark [4], and studies have reported a significantly lower risk of cervical neoplasia among HPV-vaccinated than among unvaccinated individuals [5]. However, some parents may decide not to vaccinate their children because of a perceived low-infection risk, lack of knowledge about HPV and the vaccine, or because of concerns about vaccine safety [6, 7]. The latter concern caused a dramatic decline in vaccine uptake in Denmark, from 82% in the 1998-2000 birth cohorts to 18% in the 2003 birth cohort [3]. Other studies have reported parental concerns about earlier sexual debut and risky sexual behaviour following HPV vaccination [8, 9]. A previous Danish study found no association between HPV vaccination and early sexual debut or risky sexual behaviour among women who had been HPV-vaccinated as part of the catch-up programme [10]. However, to our knowledge, research on sexual behaviour among Danish adolescents who have been HPV-vaccinated under the childhood vaccination programme is limited. Thus, the aim of the present study was to describe characteristics of sexual behaviour and knowledge about STI among adolescents stratified by gender and HPV vaccination status.

## METHODS

This cross-sectional study was conducted in 2014 in Viborg Municipality, Denmark. Viborg Municipality is located in the Central Denmark Region and has approximately 95,000 inhabitants, with an average income and age distribution that is similar to that of the average population in Denmark [11, 12]. A questionnaire was distributed to all pupils in the ninth grade without giving prior notice to either teachers or pupils. Upon receipt, the pupils completed the questionnaire anonymously in class. The initial questionnaire was developed in 1986 with the main purpose of evaluating sex education in all public schools in Viborg Municipality and subsequently the questionnaire has been distributed to all pupils in ninth grade every seven years. The validation process of the initial questionnaire has been reported elsewhere [12], and several papers have been published in the intermediate period. Over time, add-

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itional questions have been added to the initial questionnaire. The questionnaire used in the present study contained 33 items, including questions about gender, age, age at sexual debut, knowledge about STI, HPV vaccination, use of contraceptives, etc. (supplementary information).

We categorised knowledge about STI as low, fair, and good if two-three, four-five, or six or more STIs were known, respectively. STI knowledge and sexual debut are reported for all pupils, whereas the remaining variables (e.g., number of partners and intercourses, use of contraceptives, etc.) are reported for students with sexual debut only.

For statistical analysis of categorical data, we applied the chi-squared test and Fisher's exact test, as ap-

propriate. Differences in mean age were analysed using Student's t-test or the Wilcoxon Mann-Whitney test. The level of significance was set to  $p < 0.05$ . All statistical analyses were conducted using SPSS IBM Statistics 20. According to Danish legislation, ethical approval is not required for questionnaire studies. Approval was granted from the board of each participating school, the Municipal School Commission and the Municipal Children and Adolescents Section.

*Trial registration:* not relevant.

## RESULTS

In 2014, 776 pupils were registered in the ninth grade in Viborg Municipality, 738 of whom returned a questionnaire (95%). Among the returned questionnaires, 53 (7%) were blank and 685 (88%) were deemed sufficient for analysis. The mean age  $\pm$  standard deviation (SD) of the pupils was  $15.3 \pm 0.5$  years (Table 1). Of all pupils, 365 (53%) were boys and 55% reported having been HPV-vaccinated (90% of the girls and 24% of the boys) (Table 1).

The majority of pupils had a fair or good knowledge about STI, with minor differences by gender and vaccination status (Table 2). Of note, HPV-vaccinated girls ( $p = 0.03$ ) and boys ( $p = 0.04$ ) had greater knowledge about STI than those who were unvaccinated. Most students ( $\sim 70\%$ ) recognised HPV as an STI. Compared with unvaccinated boys, HPV-vaccinated boys had greater knowledge about HPV ( $p = 0.016$ ), whereas no significant difference on HPV knowledge was observed between unvaccinated and HPV-vaccinated girls. Overall, most pupils attained their information about sex and sexually transmitted infections from friends (63%), the internet (59%), a teacher (55%), the TV (42%), or from a doctor or nurse (40%). HPV-vaccinated pupils were more likely to have received their information from more credible sources, such as a teacher ( $p < 0.01$ ) or a doctor/nurse ( $p < 0.01$ ) than unvaccinated pupils were.

A total of 157 (23%) pupils had previously had intercourse (Table 1), with a mean age  $\pm$  SD at the sexual debut of  $14.4 \pm 1$ . Overall, no difference was observed in the proportion of pupils with sexual debut by gender or vaccination status; however, HPV-vaccinated girls were significantly younger at their sexual debut than unvaccinated girls were ( $p < 0.01$ ). No difference in mean age at sexual debut was observed between HPV-vaccinated and unvaccinated boys or when comparing boys and girls (Table 2). Among pupils with sexual debut, the majority reported having had a single sex partner, and most reported having had sex more than four times (Table 2). Of note, HPV-vaccinated girls were more likely to have had more than one sex partner than unvaccinated girls were ( $p = 0.02$ ), but when

**TABLE 1**

Basic characteristics on the 685 pupils in ninth grade who completed the questionnaire.

	Boys (n = 365)	Girls (n = 320)	All (N = 685)
Age, yrs, mean $\pm$ SD	15.3 $\pm$ 0.5	15.2 $\pm$ 0.5	15.3 $\pm$ 0.5
Non-Danish parents, n (%)	31 (8)	48 (15)	79 (12)
HPV-vaccinated, n (%)	88 (24)	288 (90)	376 (55)
Sexual debut, n (%)	82 (22)	75 (23)	157 (23)
Age at sexual debut, years $\pm$ SD	14.4 $\pm$ 1.1	14.4 $\pm$ 1	14.4 $\pm$ 1
Sex partners, n (%)			
1	56 (68)	50 (67)	106 (68)
2-5	19 (23)	24 (27)	43 (27)
> 5	7 (9)	1 (5)	8 (5)
All	82 (100)	75 (100)	157 (100)
Intercourses, n (%)			
1	18 (22)	8 (11)	26 (22)
2-4	19 (23)	12 (16)	31 (20)
> 4	45 (55)	55 (73)	100 (64)
All	82 (100)	75 (100)	157 (100)

HPV = human papillomavirus; SD = standard deviation.

comparing all HPV-vaccinated to unvaccinated pupils, no difference was observed.

Contraception was used at the first intercourse by

most pupils (84%), with condom being the most commonly used contraceptive method (76%) (Table 3).

Compared with unvaccinated pupils, HPV-vaccinated

**TABLE 2**

Knowledge of the 685 pupils in ninth grade on sexually transmitted infections and sexual activity by sex and human papillomavirus vaccination status.

	Boys			Girls			Boys and girls		
	HPV-unvaccinated (n = 277)	HPV-vaccinated (n = 88)	all (N <sub>9</sub> = 365)	HPV-unvaccinated (n = 32)	HPV-vaccinated (n = 288)	all (N <sub>9</sub> = 320)	HPV-unvaccinated (n = 309)	HPV-vaccinated (n = 376)	total (N <sub>tot</sub> = 685)
<i>Knowledge on STI, n (%)</i>									
Low	13 (5)	3 (3)	16 (4)	5 (16)	10 (3)	15 (5)	18 (6)	13 (3)	31 (5)
Fair	116 (42)	26 (30)	142 (39)	14 (44)	128 (44)	142 (44)	130 (42)	154 (41)	284 (41)
Good	148 (53)	59 (67)	207 (57)	13 (41)	150 (52)	163 (51)	161 (52)	209 (56)	370 (54)
<i>Knowledge on HPV, n (%)</i>									
Sexual debut, n (%)	60 (22)	22 (25)	82 (22)	10 (31)	65 (23)	75 (23)	70 (23)	87 (23)	157 (23)
Age at sexual debut, yrs, mean ± SD {n}	14.6 ± 1.2 {60}	14.6 ± 0.8 {22}	14.4 ± 1.1 {82}	15.2 ± 0.6** {10}	14.3 ± 0.9 {65}	14.4 ± 0.9 {75}	14.4 ± 1.1 {70}	14.4 ± 0.9 {87}	14.4 ± 1 {157}
<i>Sex partners, n (%)</i>									
1	41 (68)	15 (68)	56 (68)	10 (100)	40 (62)	50 (67)	51 (73)	55 (63)	106 (68)
2-5	14 (23)	5 (23)	19 (23)	0	24 (37)	24 (32)	14 (20)	29 (33)	43 (27)
> 5	5 (8)	2 (9)	7 (9)	0	1 (2)	1 (1)	6 (7)	3 (3)	8 (5)
<i>Intercourses, n (%)</i>									
1	15 (25)	3 (14)	18 (22)	2 (20)	6 (9)	8 (11)	17 (24)	9 (10)	26 (17)
2-4	13 (22)	6 (27)	19 (23)	2 (20)	10 (15)	12 (16)	15 (21)	16 (18)	31 (20)
> 4	32 (53)	13 (59)	45 (55)	6 (60)	49 (75)	55 (73)	38 (54)	62 (71)	100 (64)

HPV = human papillomavirus; SD = standard deviation; STI = sexually transmitted infection.

\*\* p < 0.01, unvaccinated vs vaccinated, non-parametric test.

**TABLE 3**

Use of contraception at first and latest intercourse among pupils with sexual debut. The values are n (%).

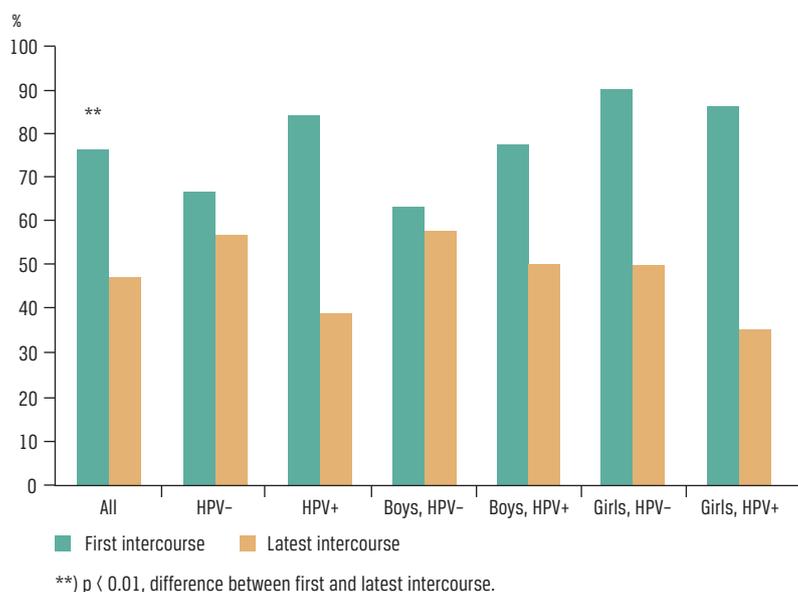
	Boys			Girls			Boys and girls		
	HPV-unvaccinated (n = 60)	HPV-vaccinated (n = 22)	all (N <sub>9</sub> = 82)	HPV-unvaccinated (n = 10)	HPV-vaccinated (n = 65)	all (N <sub>9</sub> = 75)	HPV-unvaccinated (n = 70)	HPV-vaccinated (n = 87)	total (N <sub>tot</sub> = 157)
<i>Use of contraception at 1st intercourse</i>									
No contraception	15 (25)	3 (14)	18 (22)	1 (10)	6 (9)	7 (9)	16 (23)	9 (10)	25 (16)
Condom	36 (60)	16 (73)	52 (63)	8 (80)	46 (71)	54 (72)	44 (63)	62 (71)	106 (68)
Oral contraceptive	7 (12)	2 (9)	9 (11)	0	3 (7)	3 (4)	7 (10)	5 (6)	12 (8)
Condom and oral contraceptive	2 (3)	1 (5)	3 (4)	1 (10)	10 (15)	11 (15)	3 (4)	11 (13)	14 (9)
Other <sup>a</sup>	0	0	0	0	0	0	0	0	0
<i>Use of contraception at latest intercourse</i>									
No contraception	15 (25)	7 (32)	22 (27)	5 (50)	16 (25)	21 (28)	20 (29)	23 (26)	43 (27)
Condom	30 (50)	11 (50)	41 (50)	3 (30)	17 (26)	20 (27)	33 (47)	28 (32)	61 (39)
Oral contraceptive	10 (17)	4 (18)	14 (17)	0	23 (35)	23 (31)	10 (14)	27 (31)	37 (24)
Condom and oral contraceptive	5 (8)	0	5 (6)	2 (20)	6 (9)	8 (11)	7 (10)	6 (7)	13 (8)
Other <sup>a</sup>	0	0	0	0	3 (5)	3 (4)	0	3 (3)	3 (2)

HPV = human papillomavirus.

a) Included use of contraception implant (n = 1), intrauterine device (n = 1), and progesterone injection in combination with condom (n = 1).

**FIGURE 1**

Total condom use at first and latest intercourse by gender and human papillomavirus (HPV) vaccination status.



pupils were more likely to have used condom at their first intercourse (67% versus 84%,  $p = 0.03$ ) but not at their latest intercourse (57% versus 39%,  $p = 0.12$ ) (Table 3, **Figure 1**). Total condom use declined significantly from first to latest intercourse among all pupils (77% to 47%,  $p < 0.001$ ), which was mainly a result of a significant decline in condom use among HPV-vaccinated pupils (84% versus 39%,  $p < 0.001$ ), in particular HPV-vaccinated girls (86% versus 35%,  $p < 0.001$ ). Contrary hereto, a non-significant increase in the use of oral contraceptives was observed among HPV-vaccinated girls (22% versus 44%,  $p = 0.17$ ). Of note, a non-significant increase in the lack of contraception was observed, from 16% at the first intercourse to 27% at latest intercourse, with no major differences by vaccination status or gender.

## DISCUSSION

Since the introduction of the HPV vaccine, concerns have been raised that HPV vaccination may lead to an earlier sexual debut and risky sexual behaviour [7, 8]. Using self-reported data from nearly 700 ninth-graders, we found no significant difference in the proportion of adolescents with sexual debut by gender and HPV vaccination status. Additionally, we found no major differences in the mean age at sexual debut or the number of sex partners between HPV-vaccinated and unvaccinated adolescents (both genders combined). These results are in agreement with the findings of a previous Scandinavian study including 44,052 women aged 18-45 years of age [10].

The mean age at sexual debut in the current study was lower than that reported in previous studies [13]. This finding likely reflects a difference in the mean age of the study population between the studies and does not suggest a trend towards an earlier sexual debut. This differentiation is important, particularly because young age at sexual debut is known to be associated with risk-taking behaviour such as binge drinking, smoking and a higher number of sex partners [14].

Most previous studies found no difference in self-reported sexual behaviour or clinical indicators of risky sexual behaviour among HPV-vaccinated and unvaccinated individuals [15-17]. Thus, previous studies found no difference in pregnancy rates, contraceptive counselling or STI testing and diagnosis between vaccinated and unvaccinated girls [15]. However, one Dutch study reported that HPV-vaccinated individuals were more likely to be sexually active than unvaccinated individuals (odds ratio = 1.19; range: 1.02-1.39) [18]. In the present study, we found no difference in the number of intercourse events overall, or by vaccination status or gender. However, HPV-vaccinated girls were significantly more likely to have had more than one sex partner compared to unvaccinated girls, suggesting risky sexual behaviour. While we found that HPV-vaccinated girls were significantly younger at their sexual debut than unvaccinated girls, these results should be interpreted with caution, particularly due to the low number of unvaccinated girls, risk of confounding, and because the majority of girls, regardless of their vaccination status, have not had sexual debut.

Our study found that use of contraception at first intercourse was common among Danish adolescents, and the majority reported use of a condom. These findings are in line with previous studies from Denmark and Sweden [12, 19]. Compared with unvaccinated individuals, we found that HPV-vaccinated individuals were more likely to use a condom at their first intercourse ( $p = 0.03$ ) (Figure 1). This association could be coincidental or due to the fact that HPV-vaccinated pupils had more knowledge about STI and were more likely to get information about sex and STIs from more credible sources. Paradoxically, compared to unvaccinated individuals, HPV-vaccinated individuals were less likely to use a condom at their latest intercourse. This trend may be driven by other causes such as the increased use of oral contraceptives, as observed in the present study, and the nature of the relationship. Importantly, we found a significant decline in total condom use, from 76% at the first intercourse to 47% at the latest intercourse ( $p < 0.001$ ), with the most significant decline among HPV-vaccinated individuals ( $p < 0.001$ ), girls ( $p < 0.001$ ), and HPV-vaccinated girls ( $p < 0.001$ ). Despite the significant decline in condom use, we cannot infer that the decline is attributed to

HPV vaccination, particularly due to the observational design of the present study and because we were unable to control for confounding.

The decreasing use of a condom is worrisome, particularly because not using a condom is associated with an increased risk of STI. Additionally, we found that one in four pupils did not use any contraception at their latest intercourse, which is in agreement with the findings by Höglund et al [19] but, importantly, we found no differences in the lack of contraception by vaccination status or gender. Historically, the proportion of adolescents reporting no use of contraception at their latest intercourse has increased slightly since 2000, from 18% in 2000 to 27% in 2014 [12], a finding that parallels the observed increase in the incidence of syphilis and gonorrhoea in recent years. Additionally, a low condom use may explain the consistently high incidence of chlamydia in Denmark, and the estimated approx. 17% prevalence who have had chlamydia at least once [20].

Our study has some limitations that must be addressed. First, the number of pupils with sexual debut is low, which warrants careful interpretation of the study results. Second, although the population of Viborg Municipality is similar to the average Danish population with respect to age distribution and income, differences in HPV vaccine uptake and sexual behaviour may exist across municipalities. Third, we had to rely on self-reported data, which is subject to recall bias. However, given the short time frame between possible HPV vaccination, sexual debut and the time of the questionnaire study, we estimate the impact of potential recall bias to be low. Fourth, information about sexual behaviour may have been subject to social desirability bias, which could have affected our results towards an over- or under-estimation depending on the social norms among boys and girls. Finally, we were unable to control for confounding. This is a major limitation as, e.g., unvaccinated girls and their parents may have different health beliefs and behaviours, which may have affected the probability of the outcome and the decision not to vaccinate. The strengths of the study include a high response rate and the fact that the questionnaire was distributed to all schools in Viborg Municipality, minimising any selection bias. Additionally, we used a questionnaire that has been distributed to the same schools since 1986.

## CONCLUSIONS

We found no difference in the proportion of adolescents with sexual debut or mean age at sexual debut among HPV-vaccinated and unvaccinated adolescents in Denmark when evaluating both genders combined. The decline in condom use from first to latest intercourse among all pupils, in particular HPV-vaccinated

individuals, warrants a clear understanding of the reasons why some pupils decide not to use a condom. This understanding is critical to initiate appropriate interventions such as improvements in sex education, especially given that HPV-vaccinated boys and girls had greater knowledge about STI and obtained their knowledge from more credible sources than those unvaccinated, but even so were more likely to stop using condom.

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