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Human papillomavirus vaccine uptake, knowledge and attitude among 10th grade students in Berlin, Germany, 2010

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Purpose: Since March 2007, the Standing Committee on Vaccination (STIKO) recommends HPV vaccination for all 12–17 y-old females in Germany. In the absence of an immunization register, we aimed at assessing HPV-vaccination coverage and knowledge among students in Berlin, the largest city in Germany, to identify factors influencing HPV-vaccine uptake.

Results: Between September and December 2010, 442 students completed the questionnaire (mean age 15.1; range 14–19). In total 281/442 (63.6%) students specified HPV correctly as a sexually transmitted infection. Of 238 participating girls, 161 (67.6%) provided their vaccination records. Among these, 66 (41.0%) had received the recommended three HPV-vaccine doses. Reasons for being HPV-unvaccinated were reported by 65 girls: Dissuasion from parents (40.2%), dissuasion from their physician (18.5%), and concerns about side-effects (30.8%) (multiple choices possible). The odds of being vaccinated increased with age [Odds Ratio (OR) 2.19, 95% Confidence Interval (CI) 1.16, 4.15] and decreased with negative attitude toward vaccinations (OR = 0.33, 95% CI 0.13, 0.84).

Methods: Self-administered questionnaires were distributed to 10th grade school students in 14 participating schools in Berlin to assess socio-demographic characteristics, knowledge, and statements on vaccinations. Vaccination records were reviewed. Multivariable statistical methods were applied to identify independent predictors for HPV-vaccine uptake among female participants.

Conclusions: HPV-vaccine uptake was low among school girls in Berlin. Both, physicians and parents were influential regarding their HPV-vaccination decision even though personal perceptions played an important role as well. School programs could be beneficial to improve knowledge related to HPV and vaccines, and to offer low-barrier access to HPV vaccination.

Introduction

Persisting human papillomavirus (HPV) infections, especially with HPV high-risk types 16 or 18, are prerequisites for cervical precancer and cancer. At the end of 2006 a quadrivalent HPV-vaccine became available in Germany providing protection against the HPV-types 6, 11, 16, and 18. The primary vaccination series consists of 3 separate doses administered at 0, 2, and 6 mo. If an alternate vaccination schedule is necessary, the second dose should be administered at least one month after the first and the third at least 3 mo after the second dose. The primary vaccination series should be completed within a 1-y period, according to the German summary of product characteristics (SPC). In 2007, a bivalent vaccine was approved for immunisation against HPV-types 16 and 18. For this vaccine, the German SPC recommends a vaccination schedule of 0, 1, 6 mo. HPV vaccination is free of charge in Germany. In clinical trials, the HPV-vaccines demonstrated > 90% efficacy against HPV 16- and 18-related precancerous lesions among women aged 15–26 y.[1,2] Since March 2007, the German Standing Committee on Vaccination (STIKO) recommends HPV vaccination for all 12–17 y-old females, preferable before sexual debut.

In Germany, a structured program for the evaluation and assessment of the impact of HPV vaccination is missing. Furthermore, HPV vaccination coverage at the national level is estimated only based on sales data since an immunization register is lacking and coverage data for routine vaccinations is only collected at school entry.[3,4] We aimed at assessing HPV vaccination coverage and knowledge among students of 10th grade in Berlin, with 3.5 million inhabitants the largest city in Germany, to identify factors influencing HPV-vaccine uptake. We also sought to understand where adolescents receive vaccine information, whether male and female adolescents are informed about HPV, and if so, to which extent.

Barriers to vaccine adoption are multifactorial.[5-7] An understanding of the perceptions and characteristics of vaccinated and

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non-vaccinated persons can inform communication activities and vaccine delivery strategies. Previous studies indicate poor knowledge about HPV and the vaccine in the target group but also in public.[8,9]

Few studies explored the influence of migration history on beliefs about HPV infection and HPV vaccination and identified ethnical disparities in this regard.[10,11] Also in Germany, a national Health Interview and Examination Survey for Children and Adolescents (KiGGS) showed a significant difference in the uptake of specific vaccines (e.g., against tetanus, diphtheria, or HiB) according to migration background.[12] In our study we evaluated this variable in correlation with HPV vaccination in Germany to promote strategies that address all populations.

Appropriate measures for health promotion, disease prevention and screening (regarding cervical cancer) can only be taken with actual knowledge about the characteristics, awareness, and beliefs of the population toward this disease and the vaccination against it.[13,14] A recent population-based study in the Netherlands gives insight in determinants of HPV vaccine uptake on a national level, which showed the complexity involved in the decision making process of the target population as to whether or not getting vaccinated, as well as the influence of the media and professionals on this process.[15] As determinants and barriers may differ between nations, it is important to perform studies which can account for national disparities. Barriers to vaccination might also differ by vaccine and the respective target population for vaccination. Therefore, the identification of vaccination-specific barriers on a country-level is needed to design and adopt tailored public health activities.

Results

Participants. Of 65 initially contacted schools in Berlin, a total of 14 (22%) participated in the study. The schools were distributed over 9 of the 12 (75%) city districts and comprised of six high-level and eight low-level schools with a total 35 10th grades classes. Between 17th of September and 8th of December 2010 the investigation team visited schools either once (n = 5, all low-level schools) or twice (n = 9), depending on the preference to have information materials distributed by the investigation team or by the school itself.

Overall, 442 students completed the questionnaire: 238 (53.8%) girls and 204 (46.2%) boys. According to respective class lists these were 59.0% (442/749) of all registered students. Median age of female (range 14–18 y) and male (range 13–19 y) participants was 15 y with males being slightly older when compared with females (mean age 15.4 vs. 15.2 y; $p < 0.05$). Among participating females, 147/161 (91.3%) were 15 y old or older. Fifty-seven percent of the participating students visited high-level schools, and 94% were born in Germany. There were significantly more female students, who visited high-level schools when compared with male participants (63.9% vs. 51.5%, $p < 0.05$); Following our definition, 90 (20.4%) students were classified as first and 120 (27.2%) as second generation migrants. First generation migrants were statistically significant older compared with students with no migration background (15.6 vs. 15.3 y, $p = 0.012$). There was no significant difference in sex and age for the two defined migrant groups compared with students with no migration background.

For 294/442 (66.3%) students (161 female, 133 male) information on vaccination status was available from the vaccination cards. The majority was vaccinated against tetanus (99.3%, 292/294) and had received at least one vaccine dose against measles (95.6%, 281/294), mumps, or rubella (95.2%, 280/294 each). There were no statistical significant differences in the vaccination coverage by gender, migration status, or school type (for all, $p > 0.05$).

HPV vaccination status. Of 161 girls with vaccination cards, 96 (59.6%) individuals received at least one dose of HPV vaccine: 41.7% (40/96) in 2007, the year when the STIKO recommendation was launched, followed by 25.0% (24/96) in 2008, 14.6% (14/96) in 2009, and 18.7% (18/96) in 2010. Two-third (65/96) completed the recommended three-dose vaccine series, 89% (59/66) received the tetravalent HPV-vaccine. Of these 59 girls, 14 (24%) received all three vaccine shots within the recommended 6 mo, 40 girls (68%) completed the vaccine series within 12 mo. Only 5 girls (8%) did not receive the required three doses within one year. Six girls completed the three-dose vaccination series with the bivalent HPV-vaccine, 2 of them within the recommended six months.

Of 30 girls with incomplete HPV vaccination series, 14 (46.7%) received the first HPV vaccinations more than one year before our investigation: 3 had received only one and 11 two HPV-vaccine shots. The remaining girls with incomplete vaccination series (n = 16) received the first HPV vaccination in the year 2010 (5 one and 11 two vaccine doses).

The comparison of documented data from the vaccination card with self-reported HPV vaccine status showed that 139/161 (86.3%) girls remembered their HPV vaccination status accurately. Among those, 84.4% (81/96) with at least one HPV vaccination remembered this fact correctly, and 89.2% (58/65) knew that they have never been vaccinated against HPV.

Table 1 shows the number of HPV-vaccinated girls by documented HPV vaccination series (complete and incomplete) and school type. We could not detect a statistical significant difference in number of administered HPV-vaccine doses between students of high- and low- level schools taking no vaccination as reference.

Female students' characteristics by actual HPV vaccine status are presented in **Table 2** comparing those who had received at least one HPV vaccine dose to those who had received none. Compared with HPV-unvaccinated girls, HPV-vaccinated were more likely to be older (mean age 15.0 vs. 15.3; $p = 0.021$, range 14–16 y vs. 14 -18 y) but did not otherwise differ statistically significant by school type, migration background, and documented vaccinations other than against HPV. Additionally, major sources of information about routine vaccinations are presented by respondents' HPV vaccination status. Multiple answers were permitted. The majority of respondents reported that their source of information was the physician (83.2%), followed by parents (64.6%) and school-lessons (18.0%). When stratified by HPV vaccination status, none of the sources differed statistically significant.

Table 1. Number of vaccinated girls and vaccination coverage (%) among 161 female students with vaccination card by school type, Berlin, 2010

Vaccination series	Total	Vaccination coverage	High-level schools	Vaccination coverage	Low-level schools	Vaccination coverage	p-value**
	n	%	n	%	n	%	
None	65	–	43	–	22	–	ref.
Incomplete*	30	18.6	12	40.0	18	60.0	0.455
complete	66	41.0	21	31.8	45	68.2	0.601
Total	**161**	**59.6**	**76**	—-	**85**	—-	

Notes: * defined as HPV vaccination with less than 3 vaccine doses; ** compared with "no vaccination."

Table 2. Female students characteristics and major source of information for vaccination (in general) by HPV vaccination status, n = 161; Berlin 2010

	All females n = 161	Received HPV vaccine⁺ n = 96	No HPV vaccine receipt n = 65	p-value#
Median age [range]	15,21 (14–18)	15,82 (14–18)	15,13 (14–16)	0.021
High level school vs. low [%]	106 (65.8)	63 (65.6)	43 (66.2)	0.945
Migration background				
No migration background [%]	81 (50.3)	46 (47.9)	35 (53.8)	0.306
First generation migrant [%]	33 (20.5)	23 (24.0)	10 (15.4)	0.186
Second generation migrant [%]	47 (29.2)	29 (30.2)	18 (27.7)	0.730
Documented vaccinations against… (vs. no resp. vaccination)				
Measles [%]	154 (95.6)	91 (94.8)	63 (96.9)	0.702
Mumps [%]	153 (95.0)	91 (94.8)	62 (98.4)	1.000
Rubella [%]	153 (95.0)	91 (94.8)	62 (95.4)	1.000
Tetanus [%]	159 (98.8)	94 (97.9)	65 (100)	0.516
Source of vaccination information[a] (vs. no resp. information)				
Physician [%]	134 (83.2)	84 (87.5)	50 (76.9)	0.078
Parents [%]	104 (64.6)	60 (62.5)	44 (67.7)	0.499
School [%]	29 (18.0)	18 (18.8)	11 (16.9)	0.767
Friends [%]	24 (14.9)	15 (15.6)	9 (13.8)	0.756
Internet [%]	21 (13.0)	15 (15.6)	6 (9.2)	0.237
Newspapers and journals [%]	9 (5.6)	8 (8.3)	1 (1.5)	0.085
Other sources [%]	9 (5.6)	7 (7.3)	2 (3.1)	0.315
No specific source [%]	11 (6.8)	4 (4.2)	7 (10.8)	0.121

Notes: ⁺ Participants with at least one documented dose of HPV vaccine; #p-value was calculated: for variable "Age" using Kruskal-Wallis test, for variables school-levels, migration background and sources of Information using Chi-square and for all others using Fisher's exact test; [a] Respondents were free to select more than one source, thus column totals are greater than n = 161.

Knowledge on HPV and general vaccinations. Table 3 presents knowledge and attitudes of girls and boys regarding general vaccinations and HPV infection stratified (for girls only) by documented HPV vaccination status. Female students who had received at least one HPV vaccine dose had a statistically significant less negative attitude toward vaccinations in general than girls without HPV vaccine receipt (20.8% vs. 79.2%, p-value = 0.026). For attitude questions on general vaccinations boys reflect the same trend in answering as HPV-vaccinated girls (no statistical significant difference by gender).

For questions on HPV infection, boys showed the same trend in answering as HPV-unvaccinated girls. The statement "HPV infection occurs frequently" provoked a considerable high rate of neutral positions with about 50% among girls, regardless of their HPV vaccination status, and 60% among boys. Regarding the two knowledge questions on HPV, boys had considerable less knowledge when compared with vaccinated girls (for both questions, p-values < 0.001) but only slightly less knowledge than unvaccinated girls (p = 0.038 and p = 0.239) (**Table 2**).

In total 281/442 (63.6%) students specified HPV correctly as a sexually transmitted infection: 73.1% (174/238) among female and 52.5% (107/204) among male students (p ≤ 0.001). The correct answer was significantly more often given by second generation migrants when compared with students with no migration

Table 3. Knowledge about general vaccinations and HPV infection among boys and girls by actual HPV vaccination status (only children presenting their vaccination record included, n = 294), Berlin, 2010

	Girls (n = 161) %						Boys (n = 133) %		
	Received HPV vaccine+			No HPV vaccine receipt					
	Agree	Disagree	Neutral position	Agree	Disagree	Neutral position	Agree	Disagree	Neutral position
Vaccination in general									
Vaccinations prevent effectively from infectious diseases	89.6	3.1	7.3	93.9	3.0	3.1	90.2	4.5	5.3
Vaccinations often cause severe side effects	10.4	76.1	13.5	23.1*	64.6	12.3	8.3	78.8	12.9
Vaccinations weakens the immune system, therefore one shouldn't be vaccinated	1.0	82.3	16.7	9.2*	75.4	15.4	3.8	74.2	22.0
It is good to vaccinate as much persons as possible to protect also the unvaccinated	49.0	20.8	30.2	32.3	26.2	41.5	44.0	27.3	28.7
HPV infection									
HPV infection occurs frequently	31.3	19.8	49.0	23.1	26.1	50.8	13.6**	23.5	62.9
HPV infection can cause premalignant lesons and carcinosis of cervix and penis	64.6	15.6	19.8	50.8	6.2	43.0	43.9*	6.8	49.2

Notes: + Participants with at least one documented dose of HPV vaccine; * Statistical significant difference when compared with vaccinated girls, either by chi-square test or Fisher's exact test as appropriate; ** Statistical significant difference when compared with either vaccinated or unvaccinated girls.

background (67.6% vs. 47.7%, p = 0.027) and by students from high-level schools when compared with students from low-level schools (71.2% vs. 53.0%, p = 0.006). There was no difference in correct answers when comparing first generation migrants to students with no migration background (55.0% vs. 47.7%, p = 0.060). There was no statistical significant difference in knowledge about HPV-transmission in girls with or without at least one HPV vaccine shot (58.7% vs. 41.3%, p-value = 0.669).

Reasons for declining and future intentions of HPV vaccination. Unvaccinated females were asked to provide reasons for lacking HPV vaccination (multiple answers possible). Primary barriers for vaccine receipt were dissuasion by parents (25/65, 38.5%), concerns about side-effects or bad experience with vaccines in general (20/65, 30.8%), and physicians advising against the vaccine (12/65; 18.5%) (**Table 4**). Of interest, there were also concerns specifically about HPV vaccine safety (9/65, 13.8%) and the opinion that the HPV vaccine is rather new and more research on its safety and benefits is needed (6/65, 9.2%). **Table 4** also lists proportions of future intention for HPV vaccination of unvaccinated participants. Two-thirds (9/12) of individuals, who received a physician's advice against HPV vaccination indicated that they will definitely or probably still decide for a HPV-vaccination in the future. In contrast, two-thirds (6/8) of students, who reported that the vaccination is too time consuming, were also definitely or probably not willing to receive the vaccination in future. For all other reasons of refusal there were equal proportions of individuals who intended to receive the vaccination in the future or not.

Table 5 lists the variables tested in univariable analysis for their association with the outcome "receipt of at least 1 HPV vaccine dose." In the multivariable analysis, the odds of being vaccinated increased with increasing age (Odds Ratio (OR) 2.19 per year of age; 95% confidence interval (CI) 1.16, 4.15). In contrast, a general negative attitude toward vaccination significantly decreased the odds of being HPV-vaccinated by two thirds (OR 0.33; 95% CI 0.13, 0.84).

Discussion

In Germany, despite having adopted HPV vaccination in the national immunization schedule in 2007, there is no comprehensive program in place to promote or to monitor vaccine uptake on a national level. In our setting we found that only 41% of interviewed girls had received the recommended 3 doses of HPV-vaccines even though the recommendation was in place for already three years; a considerable proportion had an incomplete vaccination series with more than 12 mo between interview and last vaccine shot. A negative attitude toward vaccinations in general was significantly associated with HPV vaccination status, and there was a significant lack of knowledge related to HPV-infection among girls. Our results highlight the need for more public education on HPV and HPV-vaccines targeting all stakeholders: Parents, students, and healthcare providers.

To the best of our knowledge, this is the first study that assessed knowledge, attitude and practise related to HPV and HPV vaccination among school students in Germany. In several industrialized countries with HPV vaccination recommendation, similar studies have been conducted,[16-20] but country-specific data are required to design and implement tailored programs. In our study setting, vaccination coverage was low among young females corroborating data from previous regional surveys in Germany with 42% of female 10th grade students in the city of Essen and 32.8% of school girls in the federal state of Brandenburg.[3,4] Therefore, we assume that the identified barriers

Table 4. Reasons for non-vaccination and future intentions of HPV vaccination of unvaccinated girls (n = 65), Berlin, 2010

Reasons for refusal of HPV vaccination	Unvaccinated girls indicating reasons for refusal n = 56(%)	Future intention for HPV vaccination despite initial decline	
		Yes (definitely or probably) n = 29 (%)	No (definitely not or probably not) n = 30 (%)
Parents had advised against HPV vaccination	25 (38.5)	10 (40)	15 (60)
Concerns about side-effects or bad experiences with vaccines in general	20 (30.8)	9 (45)	11 (55)
Physician had advised against HPV vaccination	12 (18.5)	9 (75)	3 (25)
Concerns specifically about HPV vaccine safety	9 (13.8)	1 (11)	8(89)
Too time-consuming	8 (12.3)	2 (25)	6 (75)
Concerns that HPV vaccine is new and further research is needed on safety and efficacy	6 (9.2)	1 (17)	5 (83)
No interest in HPV vaccinations	6 (9.2)	2 (33.3)	4 (66.7)
I pay attention not to get infected with HPV	4 (6.2)	2 (50)	2 (50)
Other reasons*	29 (44.6)	14 (48.3)	15 (51.7)

Notes: * "Other reasons" included multiple responses, for example: "There is need for more research concerning this vaccination; it is too new on the market," "I´m already sexual active."

to HPV vaccine uptake might be generalizable to other settings in Germany, where uptake of other vaccines e.g., against tetanus and measles is usually not a major problem as also indicated in our study.

The German Health Interview and Examination Survey for Children and Adolescents (KiGGS) from 2007 showed a significant difference in vaccination coverage for basic immunization such as tetanus, diphtheria and poliomyelitis among students with and without migration background.[12] There was, however, no association of HPV vaccination with migration background in our study population, which might be also due to the small number of participating girls with migration background. In a study investigating the effect of social inequalities on the uptake of HPV vaccine in the UK, the authors found that HPV vaccine uptake was significantly lower in more deprived areas and in ethnic minority girls.[21] It will be important in future studies in Germany to record ethnicity on vaccine uptake monitoring activities to complete the panel of possible predictors for HPV vaccination.

During our survey in 2010, the vast majority of participating girls were 15 y old or even older, meaning a period of three years within they could have initiated HPV vaccination before our interviews. Of these, altogether only 59.6% started HPV vaccination so far despite eligibility for vaccination and costs covered by their health insurance. The fact that almost half of them received their first vaccine dose in 2007, the year when the STIKO recommendation for HPV vaccination was endorsed, suggests some positive effects of advertising and advocating in the first year after market launch. Due to the cross-sectional nature of our study, it remains unclear whether the decline in the following years was due to a public debate on HPV vaccine effectiveness and safety that took place in Germany or due to catch-up effects in the first year. Nevertheless, when focusing on the almost 50% of eligible girls that did not initiate HPV vaccination after endorsement of the STIKO recommendation, this may reflect some capability for comprehensive public health campaign focusing on HPV vaccine safety and benefits.

Overall, female students appeared to be more knowledgeable in terms of transmission of HPV than male students. The fact that information campaigns about HPV and the vaccination are targeted only to females so far and HPV vaccination is not recommended and offered to boys may explain this observed gender differences. Vaccinated female students were also more likely to know about the frequency of HPV infection and relationship between cancer and HPV. Being immunized against HPV may lead to an increased awareness and knowledge of the disease (probably through the information material given to female students and parents prior to vaccination). However, given that still one-third of female students were unaware that HPV is sexually transmissible, our results indicate that young females lack fundamental knowledge about this widespread sexually transmitted infection and the vaccination that protects from it. As health beliefs are shown to influence health behaviors,[22,23] lack of knowledge regarding HPV infection and vaccination may hinder efforts for prevention.

The vast majority of respondents reported that their preferred source of information on vaccination are first the physician and second the parents, regardless of actual HPV vaccination status. Furthermore, given the fact that the second and third most frequent reason for HPV vaccine refusal was dissuasion by parents and physicians, this underlines the influence of these two peergroups on adolescent vaccination decision. Our findings are in agreement with published literature that have shown adolescents' acceptance of a vaccine is associated with their parents' attitude toward the vaccine, and their perception that parents felt the vaccine is efficient and safe.[24,25] In addition, a primary predictor

Table 5. Univariable and multivariable analysis of variables potentially associated with having received at least one HPV-vaccine dose (n = 161 girls), Berlin, 2010

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	2.30	1.29–4.08	0.005	2.19	1.16–4.15	0.02
School level (high vs. low)	0.98	0.50–1.90	0.945	NS		
Birth place of student	0.20	0.00–1.62	0.144	NS		
Migration background						
No migration background	Ref					
"First generation migrant"	1.73	0.72–4.42	0.234	NS		
"Second generation migrant"	1.13	0.56–2.27	0.731	NS		
Knowledge, HPV is a sexually transmissible virus	0.81	0.37–1.80	0.607	NS		
Negative attitude toward vaccination in general	0.37	0.14–0.99	0043	0.33	0.13–0.84	0.02
Documented vaccinations against						
Measles	0.58	0.11–3.07	0.520	NS		
Mumps	0.88	0.20–3.82	0.865			
Rubella	0.88	0.20–3.82	0.865			
Tetanus	0	0.00–2.84	0.242	NS		
Major source of vaccination information						
Newspapers and Journals	5.82	0.74–262.08	0.085	NS		
Physician	2.10	0.84–5.32	0.089	NS		
Others	2.48	0.50–12.32	0.268	NS		

NS, not significant.

of parental acceptance of a vaccine is recommendation by their child's healthcare provider.[26] Healthcare providers, in particular pediatricians, gynecologists and general practitioners are likely to be influential in educating patients and their parents about HPV infection and the vaccine. Several studies report that parents and general practitioners express general apprehension toward the safety of the vaccine itself and to discuss its usefulness with adolescent girls, often due to its sexual transmission route.[27,28] Therefore continuing education for providers who see preadolescent girls in conjunction with a parent or who treat women of school age may be a worthwhile endeavor.

The intention to be vaccinated depends on several factors including individual perceptions and concerns on vaccination, especially HPV vaccine decision. Demographic characteristics such as age, ethnicity, and access to health care may influence initiation of HPV vaccination,[29] but also other factors have to be considered. Besides dissuasion by physicians or parents, a frequently reported reason for HPV vaccine declination in our study was concerns about vaccine safety and efficacy. This finding is in line with results of previous studies. Especially the degree of protection against cervical cancer, protection duration, and risk of serious side-effects influence girls HPV vaccination preferences.[30] Uptake of HPV vaccines may change considerably if girls are supplied with evidence-based information about these important issues. High levels of vaccine acceptance can be observed if the specific vaccine is recommended by health professionals and supported by the government.[27] Therefore, safety and efficacy should be a priority when informing adolescents on vaccines.

Both HPV 16/18 vaccines are expected to protect against approximately 70% of high risk HPV types in most regions worldwide.[31] A high efficacy in preventing both HPV 16 and 18 infections and associated precancerous lesions was demonstrated in clinical trials.[1,2,32,33] Still, the long-term protective value of HPV vaccination is unknown to date. Post-licensure safety monitoring of the quadrivalent HPV vaccine utilized a large population-based cohort. There was no statistically significant increased risk for any severe event following vaccination such as the development of Guillain-Barré Syndrome (GBS).[34] In addition to HPV vaccination, the need for an organized and continuing cervical screening is vitally important. For example, in the UK a comprehensive cervical screening program showed to have reduced HPV-related mortality by up to 80%.[35] Despite the major success of cervical screening programs important limitations have to be recognized. Recent studies showed poor sensitivity of cervical cytology,[36] poor predictive value for adenocarcinoma,[37] and poor uptake by some communities.[38,39]

Our study's results should be interpreted with some limitations. First, our sample is not representative for the student population in Berlin. In preparation of the study we used a purposeful selection process of school classes based on school type. Due to lack of participation of selected classes and schools after several selection rounds to reach the calculated sample size, we decided on a convenience sample of schools neglecting sampling weights in the statistical analyses. In consequence we had a smaller sample size, especially for girls with valid data on the vaccination status and therefore loss of statistical power. Second, the responses and vaccination coverage results may be biased by differential

non-response. It can be assumed that students presenting their vaccination card are more likely to be vaccinated than students without the document. Social desirability may also bias in survey research, particularly if respondents lacked privacy during the paper-questioning in the class-room. Third, in the study population students from non-German speaking background are under-represented. Parents' consent and students' questionnaire were all written in German. Equally under-represented are students with religious or cultural backgrounds, where research on sexual health is considered inappropriate. Fourth, due to restrictions on the questionnaire design by the senate department for education, science and research in Berlin, we were asked not to enquire on information related to religion and sexual experiences of the students. These factors may play an important role when interpreting the results. Finally, we limited our study to public schools. Results from private schools may be different even though the majority of students in Germany visit public schools.[40] Nonetheless, we believe that these results provide important information, and identified barriers should be taken even more seriously when there is a chance of differential non-response.

In conclusion, the observed HPV vaccination coverage was low, and knowledge about HPV and the vaccine was poor, both, in male and female students participating in our study. Besides concerns about vaccine safety, another reason for non-vaccination was that the process of receiving the vaccine is too time-consuming. Schools can be an important resource of informing adolescent students about vaccine related health issues.[41] Therefore, with more targeted information on one hand and low-barrier access to vaccination on the other hand, e.g., by offering information and vaccinations at school, HPV-vaccine uptake could be increased. The sole availability of HPV vaccines will not change the burden of cervical cancer in a population, unless there is both widespread demand for and access to those vaccines. Demand requires recognition of the need for protection against HPV infection and knowledge of the fact that HPV vaccines are safe and efficacious. Further efforts are needed to promote the understanding of HPV infection and of the benefits and harms of HPV vaccines among adolescents, family members, and healthcare providers likewise.

Methods

Study population and design. This cross-sectional study composed of a self-administered questionnaire and review of vaccination cards. The study population consisted of 10th grade students from a sample of participating schools in Berlin. Schools were selected from a statistical report of the school year 2009/2010 issued by the senate department for education, science and research in Berlin and were contacted to participate in the study between September 2010 and November 2010. The statistical report summarized data on general-education schools in Berlin including district, school identification number, school name and type, number of 10th grade classes per school as well as number of male and female students.

The German school system is hierarchically tiered. Basic primary school (classes 1–4) is followed by a secondary school education for an additional 6 to 9 y. Depending on the school performance during the first 4 classes, a student is advised to continue education on one of the following school types. "General schools" cover classes 5 to 10 (ground level). "Intermediate level schools" provides extended general education and qualify for attendance of specialized grammar schools (level 1). "Comprehensive schools" combine the different types of secondary schools in various organizational and curricular forms (level 2). We summarized secondary general, intermediate, and comprehensive schools as "low-level schools." Finally, "grammar schools" are secondary schools which cover classes 5–13 and qualify for studies at universities (level 3). This school type defined our "high-level school." Both high- and low-level school types were included. We targeted a sample size of 700 students to allow for statistical significant comparisons between those girls who had received HPV-vaccination and those who hadn't. Schools from each district and each school type were randomly contacted by telephone. They were asked for their willingness to participate as well as preferred date for ideally two visits of the investigation team at 10th grade school classes. Detailed information on the study procedures and information documents for the teachers was sent to all participating schools before visiting them.

At first visit of the investigation team, students were informed of the study procedures, and consent forms and information leaflets for parents were handed out. They were requested to bring the signed informed consent together with their vaccination card at date of second visit of the investigation team. Schools that preferred to have only one site visit were sent the documents to hand them out to students via class teachers ahead of the visit. At a follow-up school visit, students with signed parental consent received a paper questionnaire to fill in at the class room. While filling out the questionnaires, available vaccination cards were reviewed for vaccination status by the investigation team. The study protocol was approved by the Ethics Committee of the Charité, University Medicine Berlin (approval number: EA2/024/10).

Data collection. A structured questionnaire consisted of 20 questions collecting information from male and female students on socio-demographic factors, sources of information about vaccines as well as knowledge and attitudes toward vaccines and HPV. Knowledge about HPV was assessed by providing multiple options to answer the question "What do you know about HPV?." Respondents were asked to select only one answer that applies: ("It is…"): "a sexually transmissible virus," "a virus transmitted by a mosquito," "don't know" and "no statement." Especially for the attitude items (**Table 3**) we used a 5-point likert-type response frame. Their response options included "I don't agree at all," "I rather do not agree," "no opinion," "I rather agree," and "I fully agree."

Besides age and sex, socio-demographic information included also country of birth of the student, of the mother, and of the father to identify a migration background. This allowed a multidimensional view by categorizing the students into first and second generation migrants.[42] First generation migrants were students either with both parents born in another country than Germany and/or a nationality other than German, or the student has immigrated to Germany and at least one parent was born in a foreign country. Second generation migrants (binational)

were students born in Germany and one parent immigrated to Germany and/or had a foreign nationality.

Respondents were asked to report if they were vaccinated against measles, mumps, rubella, and tetanus. On a separate sheet handed out only to female students we asked for receipt of HPV vaccination. Among those with self-reported refusal of HPV vaccination we asked why this was the case, allowing respondents to indicate multiple reasons of denial. In addition, we asked for their future intention for HPV vaccination.

During questionnaire design all questions were discussed in the team for usefulness and importance. Partially, the questions used in KiGGS served as well-proven examples for appropriate wording and structure for our target population. Our questionnaire was tested and validated during a pilot study in a 10th grade high school class in Berlin before data collection.

From available vaccination cards we recorded data on age, sex as well as number, type and date (month and year) of documented HPV vaccine doses. A girl was regarded to be incompletely vaccinated if she had received only one or two HPV-vaccine doses. In addition, we abstracted the number of documented doses of measles, mumps, rubella, and tetanus vaccines from the vaccination card.

Statistical analyses. Descriptive statistics were used to characterize the study population and to detect differences in sociodemographic characteristics as well as in knowledge and vaccination status. Information on knowledge obtained from the questionnaire was combined with documented vaccination status from reviewed vaccination cards. Bivariate associations between HPV vaccine receipt and sociodemographic as well as vaccine knowledge and sources of vaccine information were explored. The Kruskal-Wallis test was used to compare medians of continuous measures, while either the Chi-Square test or Fisher's exact test was used to compare distributions of categorical measures among the group of HPV vaccinated and unvaccinated girls. Age was analyzed as a continuous variable. Likert-scaled answers were dichotomized reflecting agreement or disagreement. A negative attitude toward vaccinations was defined by combining agreement to statements "Vaccinations often cause severe side effects" and "Vaccinations weakens the immune systems, therefore one shouldn't be vaccinated."

Timeliness of vaccination was calculated on basis of vaccination schedules given in the respective German SPC for Gardasil® and Cervarix®. A girl was vaccinated in a timely manner when receiving all three vaccine doses within the recommended six months.

Multivariable logistic regression was conducted to examine independent predictors of HPV-vaccine receipt. HPV-vaccine receipt was defined as receiving at least one dose of the recommended three-shot HPV vaccine series according to documentation in vaccination cards. Variables which were found in univariable analysis being associated with the dependent variable with a p-value < 0.2 were considered in the multivariable model by using a forward selection approach. A p-value < 0.05 was considered as statistically significant. Missing data were treated as such and not imputed. Analyses were performed using STATA®, version 12.0 (STATA Corporation, College Station, TX 2010).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed. The first draft of the manuscript was written by P. Stöcker. No honorarium or other form of payment was given to the authors.

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