# Human Papillomavirus vaccination in general practice in France, three years after the implementation of a targeted vaccine recommendation based on age and sexual history

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**Running head**: Targeted HPV vaccine recommendation in France

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**Abstract**

**Introduction**

In France, vaccination against human papilloma virus (HPV) was recommended in 2007 for all 14-year-old girls as well as“catch-up” vaccination for girls between 15-23 years of ageeither before or within one year of becoming sexually active. We evaluated the vaccine coverage according to the eligibility for vaccination in a sample of young girls aged 14 to 23 years, who were seen in general practices.

**Patients and methods**

A survey was proposed to 706 general practitioners (GPs) and carried out fromJuly to September 2010. GPs, also called “family doctor”, are physicians whose practice is not restricted to a specific field of medicine but instead covers a variety of medical problems in patients of all ages. Each participating GP included, retrospectively, the last female patient aged 14-17 years and the last female patient aged 18-23 years whom he had seen. A questionnaire collected information regarding the GP and the patients’ characteristics. The vaccine coverage was determined according to the eligibility for vaccination,i.e. the coverage among younger women (14-17) and among those sexually active in the second age range (18-23). Sexual activity status was assessed by GP, according to information stated in the medical record.

**Results**

The 363 participating physicians (response rate 51.4%) included 712 patients (357 in the 14- to 17-year-old group and 355 in the 15- to 23-year-old group) in their responses. The rate of the vaccination coverage in the 14- to 17-year-old group was 55%. Among the girls in the 18- to 23-year-old group, 126 were eligible, and their vaccination coverage rate was 82%. The evaluation of the eligibility by the GPs was incorrect in 36% of the cases. Of the 712 patients, 6% of the girls had been vaccinated without a need for the vaccination, and 26% of the girls had not been vaccinated, although they needed to be vaccinated.

**Discussion**

Regarding the vaccine uptake, vaccination at the age of 14 was not as effective as vaccinating the older population for which vaccination was indicated as a catch-up program, based on sexual history. However, in more than one-third of the older population, difficulties remained regarding the determination of eligibility, according to the sexual history of the patient.

**INTRODUCTION**

In France, vaccination against HPV (human papilloma virus) was recommended in 2007 for all 14-year-old girls and as a "catch-up" vaccination for girls between 15 and 23 years of agebefore the first time they have sex or within one year of becoming sexually active.[1] This restriction regarding the sexual activity was specific to France. In most developed countries, vaccination is recommended for all girls with the target age varying between 9 and 14 years of age, occasionallywith a catch-up vaccination in older women.[2]

The rate of administration of the HPV vaccine in ambulatory medicalpractices in France is difficult to evaluate. The routine data that exist are only for girls between 14 and 17 years of age, independent of their sexual activity.Between 2008 and 2011 vaccination coverage has been estimated between 17 to 54%.[3-8]This vaccination is offered almost exclusively by private practitioners—mainly general practitioners (GPs) and gynecologists. Past studies have shown a very goodlevel of acceptance of the HPV vaccine by French GPs and their patients: nearly 90% of GPs had a favorable opinion,[9, 10] and more than 75% of young girls were favorable toward this vaccination.[3-6, 11]The main reluctance mentioned by young girls results from a lack of knowledge regarding the vaccination, the cost of the vaccine, the fear of adverse events and parental refusal.[3,4]The paradox between the good level of acceptance and the insufficient vaccination coverage shows that there are other barriers to this vaccination.It can be questioned whether the recommendation, based on not only age, but also on sexual activity, could impact vaccination coverage.In that context, we evaluated the vaccine coverage, according to eligibility for vaccination in a sample of girls who were seen in general practices in mainland France.

The French health care system is based on a universal "social security" system funded by the government, employers, and the working population. Social security health insurance covers the cost of general and specialized medical consultations, drugs prescription (including vaccines), laboratory analyses, and hospitalization. In the case of HPV vaccine, it provides reimbursement of 65% of its cost

(123.44 euros per dose) to those who are insured. Private health insurances may be subscribed to reimburse health related costs not covered by the social security. For the most disadvantaged, state-run programs provides universal health coverage. For them, reimbursement of HPV vaccine is at 100%.

**PATIENTS AND METHODS**

A national retrospective study was conducted in 2010 by the GPs of the Sentinelles network(http://www.sentiweb.fr). The retrospective nature of the study was essential to avoid any modification of the practices by the GP. The Sentinelles network is a computerized disease surveillance system that is located throughout mainland Franceand participates both in the surveillance of 10 health indicators and in epidemiological studies.[12, 13]A postal survey was proposed to 706 GPs (i.e., the GPs of the Sentinelles network who had accepted to participate at least once in previous epidemiological studies conducted in this network over the preceding five years).

Each participating GP was asked to retrospectively include thelast two female patientsseen for a consultation: the last 14-to 17-year-old (all of whom turned 14 years old between 2007 and 2010) and the last 18- to 23-year-old.

The participating GPs responded to a postal questionnaire on each included patient. Information regarding the attitudes toward the HPV vaccine, eligibility, and vaccination status of the included patient was collected. Each questionnaire was completed from the medical record.

All girls in the 14- to 17-year-old groupwere or at least had beeneligible because they all turned 14 years old between 2007 and 2010. Among the 18- to 23-year-old group, girls were eligible if sexual activity had not begun or had existed for less than 1 year and ifthey were 15 years or older in 2007. For the patients who were already vaccinated, the eligibility was retrospectively verified at the time of vaccination. For the non-vaccinated patients, the eligibility was defined, according to their age and

sexual history on the day of the survey. The sexual history was evaluated, according to the information reported by the GPs, based on their medical records.

The GPs were asked to mention which of the non-vaccinated patients in the 18- to 23-year-old group they thoughtbelonged to the population for which the vaccination was recommended, based on the information that they had available for each patient. This information was qualified as “eligibility according to the GPs”, whichreflectsthe understanding and knowledge of the vaccination against HPV recommendations. The concordance between the “eligibility” of the patient for the HPV vaccine, according to the French guidelines and the eligibility according to the GP was estimated by a kappa test, which was interpreted according to the Landis and Koch ranking.[14]

The patients were considered vaccinated against HPV if they had received at least one injection of the vaccine. The patients for whom the vaccination status was unknown by the GP were considered not vaccinated for the data analysis.

The transmitted data were anonymized and entered into the EPIDATA software. The data quality was checked, and every meaningless value was corrected. If necessary, the GPs were called to complete the missing data. The analysis of the data was conducted using the STATA software.

**RESULTS**

Of the 706 GPs whom we approached, 363 (51.4%) participated. Their average age was 53.5 years, and 80% were male. Among these GPs, 344 declared that they felt very comfortable or rather comfortable in providing care for teenagers (95%);302 declared that the HPV vaccine was useful or very useful (83%)and 349 were reported to be slightly worried or not worried regarding side effects of the HPV vaccine (96%).Characteristics of GPs and included girls are presented in Tables 1 and 2.

The participating GPs included 712 patients in their care as follows: 357 (50.1%) in the 14- to 17-year-old group and 355 (49.9%) in the 18- to 23-year-old group.

All girls in the 14- to 17-year-old groupwere or had beeneligible at the time of the study. Among the 18- to 23-year-old group, girls were eligible according to their sexual activity as reported by the GP.

In the 18- to 23-year-old group, 126 patients (35%) were eligible for the HPV vaccine, 137 (49%) were not eligible (sexual activity for more than one year) and for 92 patients (26%), the eligibility could not be determined because thesexual activity was unknown. The vaccination status of patients, according to their eligibility, is represented in Figure 1.

Of the 341 vaccinated patients (Table 3), 196 were between 14 and 17 years old, and 145 were between 18 and 23 years old. Among the 196 subjects vaccinated in the 14- to 17-year-old group, they were all eligible for the HPV vaccine. Among the 145 subjects vaccinated against HPV in the 18- to 23-year-old group, 103 were eligible for the HPV vaccine on the day of the vaccination (71%), 30 were not eligible (21%), and the eligibility was undetermined for 12 girls (8%). Thus, among the 341 total vaccinated subjects, 299 (88%) were eligible, 30 (9%) were not eligible, and the eligibility was undetermined for 12 (3%).

Of the 371 unvaccinated patients (Table 3), 161 were between 14 and 17 years old, and 210 were between 18 and 23 years old. Among the 161 patients who were not vaccinated against HPV in the 14- to 17-year-old group, all were (or had been) eligible for the HPV vaccine. Among the 210 subjects who were not vaccinated against HPV in the 18- to 23-year-old group, 23 were eligible for the HPV vaccine on the day of the study (11%), 125 were not eligible (59%) and the eligibility was undetermined for 62 (30%). Among the 371 total unvaccinated subjects, 184 (49%) were eligible, 125 (34%) were not eligible, and the eligibility was undetermined for 62 (17%).

GPs had to answer for each girl if HPV vaccine was recommended or not. This was considered “eligibility accorting to the GPs”. “Real eligibility” was assessed by researchers,according to information of age and sexual activity reported by (i.e. available to) the GP. The evaluation of

eligibility by GPs was wrong in 36% of the cases. The concordance between the real eligibility and the eligibility according to the GPs was low (kappa was 0.36).

Of the 483 patients eligible for the HPV vaccine, 299 were vaccinated (67%) as follows: 55% in the 14- to 17-year-old group and 82% in the 18- to 23-year-old group.

**DISCUSSION**

Three years after the implementation of a targeted HPV vaccination recommendation, based on age and sexual history, vaccination coverage of eligible patients was 67%. The vaccination rate was higher in the catch-up age group. GPs correctly evaluated the eligibility for vaccination in two-thirds of the patients; however, they lacked data on the sexual activity and, thus, on the eligibility for vaccination in 26% of the cases,predominantlyin the catch-up age group.

The vaccination coverage was 67% for all of the eligible patients (every age group), 55% for the 14- to 17-year-old girls who were (or had been) eligible, and82% in the catch-up age group (eligible girls who were 18-23 years old). In 2009, the vaccination coverage was 25% among a sample of adolescents (a mean age of 16 years old).[4] According to another studyconducted in 2009, the vaccination coverage was estimated at 33% among 14-year-old and 54% among 17-year-old adolescents, which is quite close to our results.[5] Based on the refunding data and regarding the vaccines by the French Social Security System, the vaccination coverage among the 14-to23-year-old girls in Paris was 17% in 2009.[6]The results are close to those obtainedfor the 14- to 17-year-old girls; however, they were different for the 18- to 23-year-old eligible patients. That the older age group had higher vaccination coverage than the younger group might suggest that GPs are more comfortable discussing a vaccination linked to sexual activity with older patients.[11] The concordance between the real eligibility of the patient and the eligibility according to the GP was low. It was not possible to establish the eligibility of 26% of the patients in the 18- to 23-year-old group. These data

showthat for the catch-up vaccination, establishing eligibility based on the current recommendations is not always easy in practice.

The implementation of the HPV vaccine had varied in different countries. The vaccination coverage rates of ≥1 dose of any HPV vaccine in the USA, Germany, and Sicilia were 57.3%, 47.6%, and 43.1%, respectively.[14-16] Access to the HPV vaccine is shaped by decisions at different levels of the socio-ecological model, including the policy context, social norms and values, views and actions of healthcare professionals, and parental consent [17]An important facilitator of HPV vaccination appears to be the decision ofa healthcare professional to recommend vaccination.[17]The simpler the recommendations are,the better is the adherence.[18] In our study, the analysis of the determinants of the HPV vaccination was carried separately for the two groups of patients (14- to 17-years-old and 18- to 23-years-old).None of the examined characteristics were associated with HPV vaccination status(data not shown). HPV vaccine is strongly related to sexuality and raises issues that interest young teenagers, their parents, and society.

Several studies about the optimal age for HPV vaccine have been published with heterogeneous results. Having to address sexuality has an impact on acceptability of vaccination for young teenagers, their parents and their doctor, and thereby, on the most acceptable age for vaccination. Studies have showed different perceptions, according to the countries where they were conducted, or even within the same country where several studies were conducted. For example, according to the majority of participants, the ideal age for vaccination was before 13 years in California.[19] Another study conducted in the United States discovered those surveyed favoured “during adolescence and not pre-adolescence”. [20]In other countries, preferred ages are between 15 and 17 years in Sweden,[21] between 12 and 16 years in Belgium,[22, 23] and at the age of 13 or beyond in New Zealand.[24] Overall, opinions are divided between supporters of vaccination at a later age who go along with the provision of information on sexuality and STDs and supporters of early vaccination who avoid addressing this issue. A recommendation with a wider range of ages allows more flexibility, leaving

the physician, the patient and her parent(s) to decide to offer vaccination at the age that seems most appropriate to each situation.

This study has some limitations. First, the vaccination coverage of the catch-up group might be overestimated because the patients for whom the eligibility could not be determined (predominantly because the GP did not know the sexual history of the patients) were not considered when calculating the vaccination coverage. It is likely that the GPs with better knowledge of the eligibility of a patient were more prone to give her the vaccine. Second, girlswith unknown vaccination status were considered non-vaccinated, which might underestimate vaccination coverage. Nevertheless, it is important to note that two French studies reported that the majority of HPV vaccine were done by GPs (82.84 to 92% of cases),[25,26]Third is the questionable ascertainment of eligibility for vaccination. Indeed, we compared eligibility estimated by the physician and eligibility based on the information about sexual activity found in the routine records of the medical doctors.It is not clear what the true situation is. The problem could go in both directions - doctors not being aware of sexual activity status or patients reporting false information about activity.However, our study was a “real life” ascertainment and represented the way that the vaccination recommendation was implemented “in the field”: the physician reported his or her understanding of eligibility, and the true eligibility was determined, according to information that was indeed available to the physician. Thus, we considered that this ascertained eligibility was representative of the understanding and implementation of vaccine recommendation by the GPs in real life, which was the scope of the study. Fourth, eligibility based on information stated in the medical record could have an impact on the estimation of the vaccine coverage because registration of sexual initiation may be heterogeneous;but it could over or underestimate the results. Fifth, this studywasconducted in a population of girls who consulted a GP and not in a group of girls from the general population. It is likely that these young girls have,on average, a more regular medical follow-up than do young girls without follow-up by a GP. Sixth, it is possible that girls who do not consult a GP have different sexual behaviours. Seventh, the participating GPs were part of a health-monitoring network:the GPs who

participated in this study might be more concerned regarding vaccination and HPV infection than non-responders, and their practices mightdiffer. The demographic characteristics of and the number of patients seen daily by Sentinelles GPs are consistent with those of all French GPs.[27]However, among the participating physicians here, male GPs were over represented (80%, versus 69% in all French GPs in 2010 [28]). We could hypothesize that female and male practices are different regarding HPV vaccination, but in our study there was no association between HPV vaccination status of patients andGP's gender.

To our knowledge, this study is the firstto estimate vaccination coverage according to eligibility in the context of targeted vaccination based on age and sexual history. It showed that the vaccine uptake in the older population for which the vaccination was indicated as a catch-up program, was higher than in the targeted 14-year old patients. Even if difficulties remained for the GPs to establish eligibility according to sexual history, they were more successful in convincing girls reaching the age of sexual activity than younger adolescents to be vaccinated. The French recommendations for vaccination against HPV changed in 2013[29]as follows:vaccination is now recommended for girls aged 11 to 14 yearsand as a "catch-up" vaccination for girls aged 15 and 20 yearswithout anylimitation by sexual activity. Vaccination from 11 years of age allows initiation of the HPV vaccination at the same time as other vaccinationsthat are typically provided at this age. It is hoped that this new vaccination strategy will increase the coverage of girls less than 17 years of age, which is currently very low.

Table 1: Characteristics and attitudes of general practitioners

| Characteristics | n (%) |
|---|---|
| Demographic characteristics, N = 354* | |
| Sex : Male versus Female | 262 (80) vs 72 (20) |
| Age, median (years) | 55 |
| Attitudes towards Human papillomavirus (HPV) vaccine and gynecology consultation, N=363 | |
| Documentation about HPV vaccine in thewaiting room | |
| Yes | 200 (55) |
| Pap smear practice: (missing data =1) | |
| Never | 77 (21) |
| Rarely | 35 (10) |
| Occasionally | 111 (31) |
| Often | 139 (38) |
| Contraceptive Initiation | |
| Never | 3 (1) |
| Rarely | 23 (6) |
| Occasionally | 133 (37) |
| Often | 204 (56) |
| **Opinionstowards HPV vaccine, N=363** | |
| Facility in the care of adolescents: (missing data =2) | |
| Not at all comfortable | 0 (0) |
| Not very comfortable | 17 (5) |
| Somewhat comfortable | 250 (69) |
| Very comfortable | 94 (26) |
| Age appropriate to talk about sexuality : | |
| 12-14 years | 51 (14) |
| 14-17 years | 220 (61) |
| More than 17 years | 32 (9) |
| Never approach the subject itself | 19 (5) |
| Do not know | 41 (11) |
| Felt the usefulness of anti- HPV vaccine | |
| Not at all useful | 8 (2) |
| Moderately useful | 53 (15) |
| Helpful | 128 (35) |
| Very useful | 174 (48) |
| Anxiety-related side effects of HPV vaccine: (missing data =1) | |
| Not at all worried | 240 (66) |
| A bit worried | 109 (30) |
| Worried | 10 (3) |
| Very worried | 3 (1) |

*****Nine doctors do not identify themselves on the form, so their demographic data could not be determined.

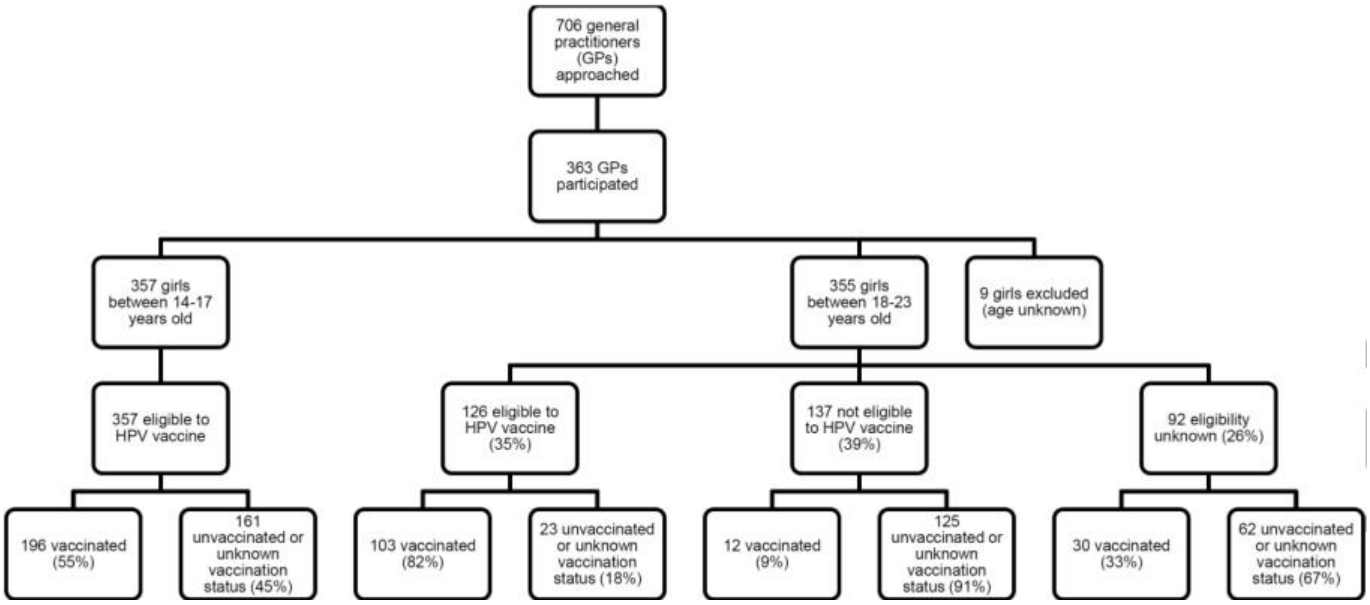
Table 2: Characteristics of included girls

| Characteristics | 14-17 group n(%) N = 357 | 18-23 group n(%) N = 355 |
|---|---|---|
| Parent's socio -professionalcategory | | |
| Farmers | 20 (6) | 20 (6) |
| Artisans, merchants , entrepreneurs | 37 (10) | 29 (8) |
| Higher managerial and professional occupations | 74 (21) | 67 (19) |
| Intermediate occupations (clerical, sales, service) | 53 (15) | 44 (12) |
| Small employers and own account workers | 86 (24) | 91 (26) |
| Lower supervisory and technical occupations | 39 (11) | 37 (10) |
| Retirees | 3 (1) | 3 (1) |
| Never worked and long-term unemployed | 27 (7) | 28 (8) |
| Do not know | 18 (5) | 36 (10) |
| Living place: (missing data for 18-23 group = 15) | | |
| Alone | 2 (1) | 46 (14) |
| With her parent | 348 (97) | 203 (60) |
| In a couple | 1 (0) | 84 (25) |
| Other | 6 (2) | 7 (2) |

Table 3: Eligibility to HPV vaccine according to vaccination status.

| | Eligible | | | Not eligible | Unknown eligibility | Total |
|---|---|---|---|---|---|---|
| Age Group (years) | 14-17 | 18-23 | All | 18-23 | 18-23 | 14-23 |
| Vaccinated | 196 (55%) | 103 (82%) | 299 (62%) | 12 (9%) | 30 (33%) | 341 (48%) |
| Unvaccinated or unknown vaccination status | 161 (45%) | 23 (18%) | 184 (38%) | 125 (91%) | 62 (67%) | 371 (52%) |

Figure 1:Flow chart and vaccination status according to eligibility and age (HPV: human papilloma virus)



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