

## Actions improving HPV vaccination uptake – Results from a national survey in Italy

Cristina Giambi<sup>a</sup>, Martina Del Manso<sup>a</sup>, Fortunato D’Ancona<sup>a</sup>, Barbara De Mei<sup>b</sup>, Ilaria Giovannelli<sup>b</sup>, Chiara Cattaneo<sup>b</sup>, Valentina Possenti<sup>b</sup>, Silvia Declich<sup>a</sup>, Local representatives for VALORE<sup>1</sup>

<sup>a</sup>Communicable Disease Epidemiology Unit, National Centre for Epidemiology, Surveillance and Health Promotion, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy

<sup>b</sup>Unit of Training and Communication, National Centre for Epidemiology, Surveillance and Health Promotion, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome

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### Abstract

**Background.** In Italy, HPV vaccination is offered to 11-year-old girls since 2007. In 2012 coverage was 69%. Strategies for offering and promoting HPV vaccination and coverage rates (26–85%) vary among Regions and Local Health Authorities (LHAs). We conducted a national study to identify strategies to improve HPV vaccination uptake. **Methods:** In 2011–2012 we invited the 178 LHAs to fill a web-questionnaire, inquiring implementation of HPV vaccination campaigns (immunization practices, logistics of vaccine delivery, training, activities to promote vaccination, barriers, local context). We described type of offer and vaccination promotion in each LHA and studied the association of these factors with vaccination coverage rates. **Results:** We analyzed 133 questionnaires. The communication tools more frequently used to promote vaccination were: brochures/leaflets (92% of LHAs), fliers/posters (72%). Television (24%) and radio (15%) were less used. Using  $\geq 3$  communication channels was associated to a coverage  $\geq 70\%$  ( $OR_{adj} = 5.9$ , 95%CI 2.0–17.4). The probability to reach a coverage  $\geq 70\%$  was higher if the invitation letter indicated a pre-assigned date for HPV vaccination ( $OR_{adj} = 7.0$ , 95%CI 1.2–39.8) and  $>1$  recall for non-respondents was planned ( $OR_{adj} = 4.1$ , 95%CI 1.8–9.3). Immunization services and paediatricians were involved in informative and training activities in most LHAs (80–90%), instead general practitioners, women and family’s healthcare services and public gynaecologists in 60–70%, cervical cancer screening services and private gynaecologists in 20–40%. The main factors that negatively affected vaccination uptake were: poor participation to training events of professional profiles different from personnel of immunization services (reported by 58% LHAs), their mistrust towards HPV vaccination (55%) and insufficient resources (56%). **Conclusion:** The synergy of multiple interventions is necessary for a successful vaccination programme. Practices such as pre-assigning vaccination date and repeatedly recalling non-respondents could improve vaccination uptake. Efforts are required to strengthen the training of different professional profiles and services and encourage their collaboration.

### Background

Following recommendations from the World Health Organization (WHO) [1], in 2007 the Italian Ministry of Health (MoH) introduced routine human papillomavirus (HPV) vaccination in the National Immunization Program (NIP) in order to reduce cases and deaths due to cervical cancer (CC) in Italy (5.3 incident cases and 2.4 deaths per 100,000 in 2012) [2]. In Italy the National Health Service has been decentralized since 2001 [3]. This endows all the 21 Italian Regional Health Authorities (RHAs), including the 19 Italian regions and two autonomous provinces, with the responsibility of organizing, delivering and allocating budget for all health services, with the

strategic support of the MoH. A third level is represented by the Local Health Authorities (LHAs) that are committed to providing healthcare services to the population, including vaccinations that are delivered in public immunization services. A NIP provides national recommendations and lists the vaccines to be provided by law free-of-charge across Italy in order to guarantee equity of access to all population; RHAs autonomously plan the strategies for offering and promoting immunization programmes and manage the services delivered by their LHAs [4]. Modalities of calling target population and delivering vaccinations may vary among RHAs and LHAs. In December 2007 the Italian State-Region Committee approved the nationwide free-of-charge offer of HPV vaccination to 11-year-old girls [5]. Some RHAs extended the offer to older girls, with target age groups varying among regions. In spring 2007 the MoH started a nationwide information campaign; additional communication campaigns were conducted in most regions in order to disseminate clear and understandable information on HPV vaccination and maximize adherence to vaccination. The NIP 2012–2014 has fixed the target coverage at a minimum of 70% for 2012; it should increase to 95% within a 3-year time frame [6]. However, five years after the introduction of HPV vaccination the national coverage of the first cohorts called for vaccination (birth cohorts 1997–1999) was stable at 70%, with a regional variability from 26% to more than 80% [7]. Vaccination coverage also varied among LHAs of the same region. Therefore, we surveyed the local coordinators to describe the modalities for offering and promoting HPV vaccination that were adopted by each LHA during the first immunization campaign, in order to identify actions improving HPV vaccination uptake.2.

### *Methods*2.1. *Data collection*

The study, performed in the period August 2011–March 2012, was coordinated by the National Institute of Public Health (Istituto Superiore di Sanità, ISS) and funded by the MoH. All the 178 LHAs of the 21 Italian regions were invited to participate in the study. The local coordinators of HPV immunization campaigns were asked to fill an electronic questionnaire. It was developed using “SurveyMonkey”, a software for the creation of online surveys. Questions, mainly closed, inquired about strategies and activities carried out during the immunization campaign involving the first two birth cohorts invited for HPV vaccination (1997 and 1998) in each LHA. In particular, the following aspects were explored: (1) immunization practices, including modalities for calling the target population and recalling the non-respondents, structured procedures for counselling of target population and catch up of untraceable girls; (2) logistics of vaccine delivery, including opening time of vaccination centres; (3) activities carried out to inform and train health care workers (HCW); (4) activities to promote HPV vaccination and communication strategies, such as tools and channels used for communication; (5) social local context, including the presence of anti-vaccine groups, religious minorities and hard-to-reach groups. Finally, the local coordinators were asked to indicate how much some listed factors negatively affected HPV vaccination uptake on a 4-point scale (A lot/sufficiently/a little/not at all). We piloted the questionnaire with five LHAs and modified accordingly. We also collected HPV vaccination (three doses) coverage data of the birth cohort 1998, by region and LHA.

### 2.2. Statistical analysis

We performed: (a) descriptive analysis of strategies and activities to promote and offer HPV vaccination; (b) univariate and multivariate analysis to test the association between LHA vaccination coverage and variables regarding immunization practices, logistics and communication strategies. We summarized categorical variables using frequencies and proportions and used Chi-square test, Fisher’s exact test and Chi-square for trend to compare proportions. We defined statistical significance as a 2-tailed p-value of <0.05. For the purpose of the univariate and multivariable analysis, we used as outcome a LHA vaccination coverage  $\geq 70\%$ , representing the

“short-term” target coverage rate fixed by the NIP 2012–2014 [6]. We used a forward-stepwise logistic regression model to identify significant determinants of a vaccination coverage  $\geq 70\%$ ; we calculated Odds Ratio (OR) and 95% Confidence Intervals (95%CI). We used the statistical package STATA 11.2 to analyze data (Stata Corporation, College Station, Texas, USA).<sup>3</sup> Results<sup>3.1</sup>. Study participation and coverage data. The questionnaire was filled by 133 LHAs of 17/21 regions. LHAs were distributed across the country: 40% were located in the North, 32% in the South and 28% in the Centre of Italy. Forty percent had a population size of resident 11-years-old girls  $>1350$  units (mean: 2598), 30% between 750 and 1350 (mean: 1039) and 30%  $<750$  (mean: 539). HPV immunization coverage data was collected for all LHAs, mostly updated at 31/12/2011. Coverage largely varied among LHAs of the same region (Fig. 1)

### 3.2. Immunization practices and logistics.

All the participating LHAs sent a personal letter to invite the primary target (girls of the birth cohorts 1997 and 1998) to immunization services for HPV vaccination. In most LHAs the invitation letter included: a proposal of date for HPV vaccination (86%), informative material (79%) and a telephone number to get informed on HPV vaccination (81%). At least one recall for non-respondents was planned in 88% of LHAs; at least two recalls in 38%. In most cases the non-respondents were re-called by letter. Systematic procedures for tracking down the untraceable girls were not available in 26% of LHAs (Table 1). The date for the first dose of HPV vaccine was pre-assigned by the immunization service in most LHAs (89%). The date for the second or third dose was fixed during the previous vaccination session in 70% of LHAs; it was fixed during the previous vaccination session and reminded by telephone/letter in 16% (Table 1). The immunization service was open one or two days a week in 60% of LHAs and also in the afternoon in 85%. No pre-immunization counselling was planned in 26% of LHAs and no phone line for vaccination was available in 20% (Table 1).

### 3.3. Activities to inform and train health professionals

In most LHAs, procedures, official documents, informative letters on HPV vaccination were transmitted to HCWs working in the immunization services (98%) and family paediatricians (85%); these documents were transmitted to general practitioners (GPs), HCWs working in women and family's healthcare services, public gynaecologists in about 70% of LHAs (Table 2). In most LHAs, training courses and events were addressed to HCWs working in the immunization services (95%) and family paediatricians (78%); women and family's healthcare services, public gynaecologists and GPs were involved in 60–70% of LHAs. Health professionals working in CC screening services and private gynaecologists were marginally involved in these activities (approximately in 40% and less than 20% of LHAs, respectively) (Table 2). Bulletins or reports providing data on vaccination, HPV and CC (or related activities) were mainly disseminated to the immunization services (83% of LHAs) and family paediatricians (58%); the other professional profiles were involved in few LHAs (Table 2).

### 3.4. Activities to promote HPV vaccination and communication strategies

All LHAs except seven (94%) carried out a communication campaign to promote HPV vaccination. In most LHAs (68%) the campaign was organized in collaboration with RHAs; the organization was mainly regional in 16%, while it was mainly coordinated at local level in the remaining 30%. In most LHAs the campaign was carried out only once, in 40 LHAs (30%) it was repeated over time. Most LHAs (82%) addressed communication activities both to general population and HCWs; 11%

to general population only and 7% to HCWs only. Communication activities targeted paediatricians (in 83% of LHAs), parents (72%), adolescents and pre-adolescents (72%), general practitioners (65%), gynaecologists (64%), general population (32%). The communication tools more frequently used to promote HPV vaccination were: brochures/leaflets (used in 92% of LHAs) and fliers/posters (72%). Television and radio channels were used in few LHAs (24% and 15% respectively) (Fig. 2). Most LHAs used more than one communication tool to promote vaccination; in particular 41% used 3–6 tools among those reported in Fig. 2 and 59% less than 3. Seventeen LHAs (13%) translated the informative material into other languages. The sites where the communication material was more frequently distributed were: vaccination services (in 100% of LHAs), paediatricians' practices (75%) and women and family's health care services (74%). Other sites were: GPs' practices (56%), schools (36%), gynaecologists' practices (31%), and pharmacies (15%). Forty-five LHAs (34%) organized meetings with adolescents and their families to inform on HPV vaccination, mainly at school (32 LHAs) and immunization service (16 LHAs). Junior high schools were involved in the campaign to promote HPV vaccination in 64 LHAs (48%). Among them, communication material was distributed at school in 48 LHAs; informative meetings with adolescents and parents were organized in 39 LHAs; a letter to adolescents and their family to inform or invite to vaccination was delivered at school in 36 LHAs; HPV vaccination days were organized in 10 LHAs.

### 3.5. Critical aspects of HPV vaccination campaigns.

A percentage of local coordinators were not able to report on the presence of large ethnic communities, anti-vaccination movements and groups of individuals objecting to vaccines for religious or ideological reasons in the catchment area of their LHA (8%, 18% and 24% respectively). Among those who replied, the presence of ethnic communities, anti-vaccine groups and objectors for religious or ideological reasons was referred by 45%, 40% and 40% respectively. Fig. 3 reports the proportion of LHAs that declared that each of the listed factors negatively affected "a lot/sufficiently" HPV vaccination uptake in their catchment area. The main factors that negatively affected vaccination uptake were: the poor participation to training events of professional profiles different from personnel working in the immunization services (reported by 58% of LHA); insufficient staff resources (56%); mistrust towards HPV vaccination from professional profiles different from personnel working in the immunization services (55%) (Fig. 3).

### 3.6. Determinants of HPV vaccine uptake

According to the univariate analysis (Table 3) the probability to achieve a vaccination coverage  $\geq 70\%$  was higher if: the date for HPV vaccination was pre-assigned by the immunization service; the invitation letter reported a phone number to get information; it contained informative material; at least two recalls were planned for non-respondents (for which a dose dependent effect was observed,  $p < 0.001$ ); communication material was distributed in the gynaecological practices; magazines or local tele-vision channels were used to promote vaccination; more than three communication tools were used. At the multivariate analysis, the factors that remained associated to the probability to achieve a coverage  $\geq 70\%$  were: pre-assigned date for HPV vaccination, more than one recall for non-respondents, more than three communication channels used to promote vaccination (Table 3).

## 4. Discussion

To our knowledge it is the first study to investigate barriers and facilitators to HPV vaccination in Italy, evaluating the aspects of implementation of the campaigns. In our survey, the probability of achieving a better coverage was higher if the date for HPV vaccination was pre-assigned. It is likely that receiving an invitation for a prearranged immunization session has a positive impact

on acceptance: on one side it could be interpreted as a more relevant need, instead the opportunity of accessing to the immunization service at any day could encourage parents to delay or drop the access; on the other side dismissing the parents with the task of contacting the immunization service to take the date might be beneficial. Also recalling non-respondent girls more than once was associated with a better coverage. Twenty-six percent of LHAs did not have systematic procedures for trace back the adolescents that were not reached by the invitation letter. The development of a computerized immunization registry is included among the objectives of the current and previous national immunization plan [6,9]; however it is not implemented in all RHAs and LHAs yet [10]. An interactive connection between the immunization registry and the population lists, currently available in 67% of LHAs, could allow the automatic update of the addresses of the immunization archives and reduce the number of untraceable families. These findings comply with the Community Preventive Services Task Force Recommendations [8] that identified a series of actions of proved efficacy to increase vaccination coverage on the basis of a systematic literature review. Besides the free-of-charge offer, the active call to vaccination (by phone call or letter) and the reminder to non-responders are included among the actions that are strongly recommended to improve acceptance. The Community Preventive Services Task Force includes the vaccination campaigns at school among the recommended interventions to improve vaccination coverage [8]; also experiences in America, Australia and Scotland showed that offering HPV vaccination at school had a positive impact on the acceptance of vaccination [11–14]. We found no association between the involvement of schools and a higher vaccination coverage; however the type of interventions and the territorial coverage highly varied among LHAs, so it was difficult to analyze this information. Initiatives to promote HPV vaccination involved the schools in less than 50% of LHAs (mainly for delivering the invitation to vaccination or distributing printed material). Vaccination days at schools were organized only in 10 LHAs; it could be an efficacious strategy but it entails a rearrangement of resources and procedures that could not be feasible in all LHAs, taking into account that in Italy vaccinations (except for influenza vaccination in elderly) are routinely provided in public immunization services. A crucial finding is that the poor participation of health professionals not routinely working with vaccination to training and informative events and their mistrust towards HPV vaccination presented the main factors (together with poor resources) that, according to local coordinators, negatively affected HPV vaccination uptake. This survey clearly highlighted the marginal role of health professionals that are not routinely involved in the field of vaccination. Professionals working in the immunization services and paediatricians were generally involved in the initiatives carried out at local level to sensitize, train and inform the health professionals; general practitioners and public gynaecologists were moderately involved; instead private specialists (gynaecologists and paediatricians) and professionals working in the cervical cancer screening programme participated marginally. Again, informative material for promoting HPV vaccination was distributed in the family doctors only in 56% of LHAs and gynaecologists' practices in 31%. At this age, paediatrician represents the most commonly consulted source of information on vaccination [15]. However, taking advantage of the gynaecologist's role might be beneficial. Mothers (who are fully involved in the decisional process regarding vaccination of their 11-years-old daughters) could rely on their gynaecologist as a trusted source for information and advice on HPV vaccination. Moreover in many RHAs the active free-of-charge offer is extended to older girls, routinely consulting a gynaecologist for preventive and non-preventive care visits. In Italy, most women consult private gynaecologists who, according to our results, are rarely involved in the activities regarding HPV vaccination. The added value of involving gynaecologists is supported by a study conducted in the Netherlands [16]; it suggested that communicating with gynaecologists and organizing information meetings at schools might be advantageous. It was the only European study that we retrieved, that

investigated determinants for HPV vaccine uptake taking into account the aspects of implementation of the campaign. Training and integration of different professional profiles are crucial for HPV vaccination, whose target is represented by adolescents and that involves two highly sensitive topics: sexual transmission and cancer. Additionally, to make an informed decision regarding vaccination women need to be provided with quite complex information (link between viral infection and cancer, vaccine preventing only certain oncogenic types, high efficacy only in women who are naïve for vaccine-related types, current offer only to females, adhesion to CC screening programmes also for vaccinated women). Therefore it is necessary that information and attitudes on HPV vaccination is shared among HCWs. A recent national survey showed that in Italy, beside the fear of adverse events, discordant information received from health professionals represented the main barrier to HPV vaccination as reported by the parents of unvaccinated girls [15]. According to the univariate analysis, using local television and newspapers to promote HPV vaccination and using more than three different channels facilitate immunization uptake. The multivariate analysis confirmed the use of more than three different channels as a determinant of high vaccination coverage, proving that an intervention with multiple components is needed to achieve high errates and facilitate a successful vaccination campaign. However printed material was used in most LHAs; while mass media, as tele-vision, radio, web and newspaper, were used in less than 50% of LHAs. Economical constrains can explain the limited use of these promotion tools. Some limitations have to be discussed. Firstly, strategies and activities broadly vary among LHAs, thus it was difficult to test the association of a specific action with vaccination coverage. Secondly, the questionnaire collected detailed information on the activities carried out at local level, but it was not possible to quantify neither their frequency (e.g. how many events were launched), their quality nor the response to those activities (e.g. how many health professionals participated to training activities or number of schools involved inside each LHA). Furthermore, the survey is based on the perception of the respondents.

## 5. Conclusions

The synergy of multiple strategies and interventions, targeting both population and health professionals, is necessary to guarantee the success of a vaccination programme. Some actions improving HPV vaccination uptake, such as pre-assigning the date for vaccination and repeatedly recalling non-respondents, could be easily adopted. More efforts are required to strengthen the training of different professional profiles (family doctors, paediatricians, gynaecologists) and services (vaccination clinics, women and family's healthcare services, cervical cancer screening services) and encourage their collaboration; dissemination of clear and homogenous information and advice towards HPV vaccination is crucial for improving acceptance. Economical resources are needed to pro-mote the vaccination programmes at local and national level.

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and critically revised the manuscript. BD,IG, CC and VP revised the material used for the study and critically revised the manuscript. SD coordinated and monitored the study activities and critically revised the manuscript. Local representatives for VALORE collected data and critically revised the manuscript. All authors read and approved the final manuscript.

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