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The current state of introduction of HPV vaccination into national immunisation schedules in Europe: Results of the VENICE 2008 survey ☆

D. Lévy-Bruhl^{a,*}, V. Bousquet^a, L.A. King^a, D. O'Flanagan^b, S. Bacci^c, P.L. Lopalco^d, S. Salmaso^c, the country specific VENICE gate keepers and contact points^e

^aInstitut de Veille Sanitaire, Saint-Maurice, France

^bHealth Protection Surveillance Centre, Dublin, Ireland

^cIstituto Superiore di Sanita, Rome, Italy

^dEuropean Centre for Disease Prevention and Control, Stockholm, Sweden

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ABSTRACT

Three surveys have been undertaken in European Union (EU) member states since January 2007, within the European Commission funded Vaccine European New Integrated Collaboration Effort (VENICE) project, to monitor the decision status regarding the introduction of human papillomavirus (HPV) vaccination into national immunisation schedules. A web-based questionnaire was developed and completed online by the 28 countries participating in VENICE. According to the last update (31st December 2008), 15 countries have decided to introduce HPV vaccination into their national immunisation schedule, while another six have started the decision-making process with a recommendation favouring introduction. Varying target populations have been selected by the countries which have introduced vaccination. The number of countries which have made a decision or recommendation has increased from 12 to 21 between October 2007 and December 2008. This survey demonstrates the rapidly evolving nature of HPV vaccine introduction in Europe. A further update should be available in the second half of 2009.

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1. Introduction

Two vaccines protecting against human papillomavirus (HPV) infections have recently been licensed in the European Union (EU): a quadrivalent vaccine (Gardasil[®]), in September 2006, and a bivalent vaccine (Cervarix[®]), in September 2007. Both vaccines have a prophylactic indication and aim to prevent pre-cancer lesions (CIN II+) and cancers due to persistent infection with HPVs 16 and 18 in women who have not been previously infected with these HPV types. HPV 16 and 18 have been

estimated to cause 73–76% of cases of cervical cancer in Europe.^{1,2} The quadrivalent vaccine also prevents infection with HPV 6 and 11, viruses responsible for 80–90% of genital warts.³

Despite the high efficacy of these two vaccines, the decision to introduce HPV vaccination into a national immunisation schedule is complex and requires thorough epidemiological and economical analyses. Many factors must be considered, for example, the high vaccine cost and the added benefit of vaccination over an effective cervical cancer screening programme.⁴

☆ Vaccine European New Integrated Collaboration Effort.

* Corresponding author: Tel.: +33 141796874; fax: +33 141796872.

E-mail address: d.levybruhl@invs.sante.fr (D. Lévy-Bruhl).

^e See list at <http://venice.cineca.org>.

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No mechanism allowing the monitoring of decisions taken by each individual country exists in Europe and the vaccine industry represented, up to now, the almost exclusive source of information regarding the status of a newly licensed vaccine in various countries. Within the framework of the VENICE project, we set up a mechanism to gather such information for both the rotavirus and HPV vaccines. Venice was a 3-years European Commission (DG SANCO) sponsored project launched in January 2006 to which 28 European countries participate, 26 EU member states (MS) (all except Malta) and two European Economic Area/European Free Trade Association countries (Iceland and Norway). It aimed to create an EU vaccination network capable of collecting and collating information on MS vaccination programmes and to encourage a rational approach to vaccination policy decision-making.⁵ Three surveys were conducted during the project in all Venice participating countries regarding the status of the decision regarding HPV introduction in national immunisation schedules, in early and late 2007^{6,7} and in late 2008. For this last round, a shorter version of the questionnaire was developed, aiming at allowing bi-annual updating of the situation, based on a questionnaire of acceptable length. We present the results collected in November and December 2008 through this revised version of the questionnaire. We have tried in the analysis to correlate the decision status regarding HPV vaccination introduction with the data presented in this current issue of the *European Journal of Cancer* regarding national screening policies and coverage as well as cervical cancer mortality data.

2. Materials and methods

2.1. Questionnaire

A web-based questionnaire to explore the decision-making process for the introduction of HPV vaccination was posted on the VENICE website in November 2008. The questionnaire was filled in by the national VENICE project gatekeeper, or a designated contact point, in each participating country, using the dedicated web-based VENICE platform and stored on a secure domain of the website. The questionnaire focused on the current status of the decision regarding HPV vaccination integration into national (or if applicable regional) immunisation schedules and on the undertaking and current status of supporting studies for the introduction decision (disease burden studies, mathematical modelling, economic analysis). Only the results regarding the integration of the vaccination into the immunisation programmes are presented here.

2.2. Data analysis

Data were analysed using Microsoft Excel[®] and Stata v8[®].

3. Results

Completed questionnaires were received from all 28 participating countries. The analysis performed was validated by the participants in January 2009.

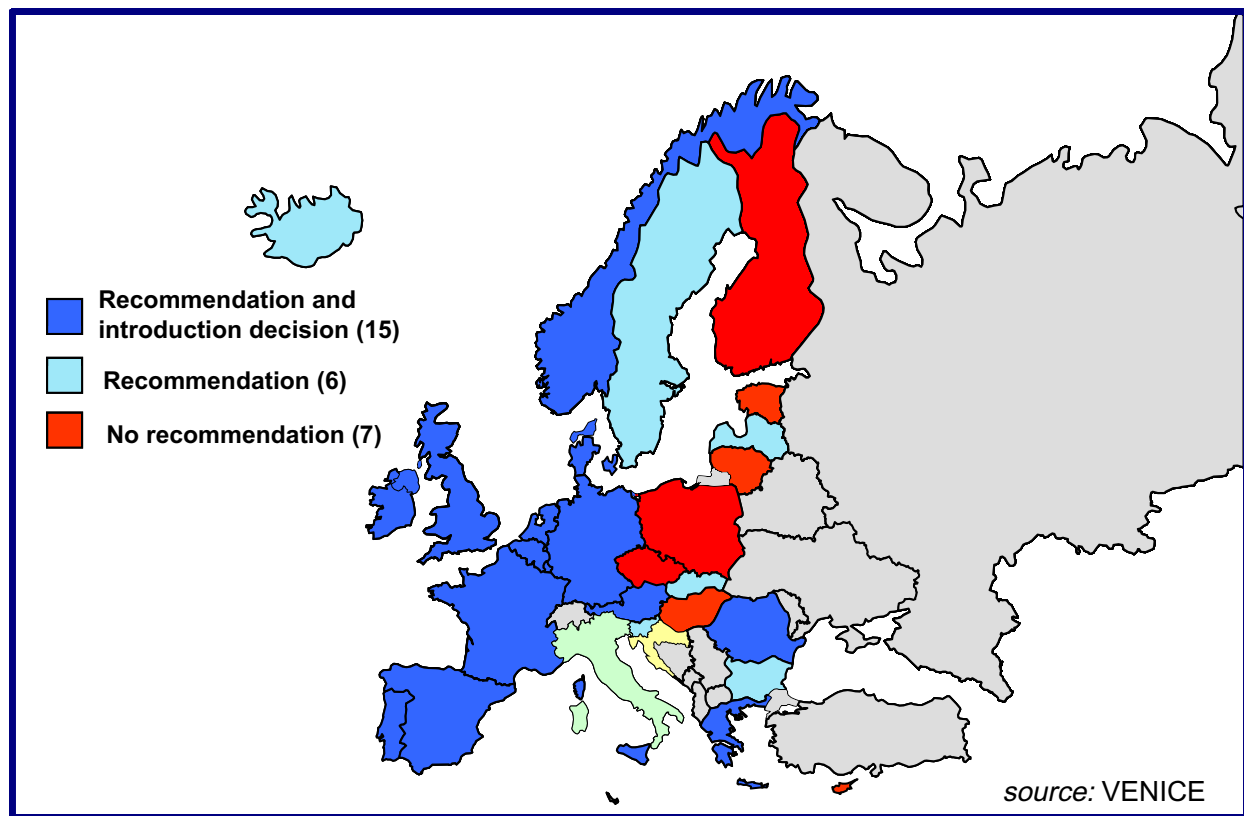
3.1. Status of countries concerning the introduction of HPV vaccination (Fig. 1)

The process of introducing a new vaccine into the national immunisation schedule in European countries occurs in two steps: firstly, a recommendation is made by a national vaccine advisory body; secondly, an official decision is taken by the national health authorities. As of the end of December 2008, the advisory bodies in 21 countries (75%) had made a recommendation (in all cases positive) regarding the introduction of HPV vaccination into their national immunisation schedules. The national health authorities in 15 of these countries (54% of the 28 participating countries) subsequently took the decision to introduce HPV vaccination into their national immunisation schedule (Austria, Belgium, Denmark, France, Germany, Greece, Italy, Ireland, Luxembourg, Norway, Portugal, Romania, Spain, The Netherlands and the United Kingdom). These countries are, in the majority, located in the Western part of Europe. No recommendation has been made so far in the remaining seven countries. There was no distinction made in the questionnaire regarding the nature of the HPV vaccine (bivalent or quadrivalent) to be used in the national immunisation schedule.

3.2. Vaccination strategy in countries where HPV vaccination was introduced

The available information is detailed in Tables 1a and 1b. Countries have been grouped according to their decision regarding the implementation or not of an initial catch-up vaccination strategy. In each of the two groups, they have been ranked according to the date of the decision of introduction. The most striking feature is the heterogeneity of the target populations chosen by the different countries for the routine vaccination. Almost half of the countries (7/15) have chosen to target a single year of age, ranging between 12 and 14 years. In the other eight countries in which a multi-cohort age range has been identified as the target for routine vaccination, the lower bound varies between 10 and 12 years of age and the age range involved between 2 and 5 years. Only one country has included in the recommendation the vaccination of boys/young males (Austria). The population targeted by the initial catch-up vaccination activities also varies within the six countries having decided such a strategy at the national level. The lower bound is dependant on the target age for routine vaccination. The upper bound does not, in all countries except one (France), exceed 18 years of age. Only Italy anticipated different catch-up policies across the country, and as such a decision is taken at the regional level.

Regarding who bears the cost of the vaccine, 12 countries have answered that the HPV vaccine was offered free of charge or reimbursed for the target population (Belgium, Denmark, France, Germany, Greece, Italy, Luxembourg, Norway, Portugal, Spain, The Netherlands and the UK). Romania has answered that the vaccine was offered free of charge from the National Cancer Programme and Austria that it was partly paid for by some federal counties. In Sweden, the vaccine will be offered free as of 2010, but is already reimbursed to 12- to 18-years-old adolescent girls through insurance. In Ireland,



N=28 (26 EU + 2 EEA countries), for Ireland implementation not funded

Fig. 1 – Status of HPV introduction decision making process in Europe – Data as of the end of 2008.

Table 1a – Details of HPV vaccination introduction to immunisation schedules (countries with catch-up vaccination).

Countries	Date of decision	Target group for routine vaccination		Catch-up
		Gender	Age	
France	March 2007	Female	14 y	15–23 y (or having started sexual life < 1y ago)
United Kingdom	October 2007	Female	12–13 y	13–18 y
Portugal	November 2007	Female	13 y	17 y (2009–2011)
Italy	December 2007	Female	11 y	According to regions
Denmark	January 2008	Female	12–14 y	F born in 1993–1995 (13–15 y in 2008) October 2008/end 2010
Luxembourg	March 2008	Female	12 y	13–18 y
Netherlands	November	Female	12 y	13–16 y

the actual implementation of the programme has been postponed as, in the context of the financial crisis, the government has not been able to fund it in 2009.

4. Discussion

This study is the first documentation of the status of European countries regarding HPV vaccination. The very high participation rate in this study indicates the high level of interest in this issue among European countries and the effectiveness of the VENICE network as a means of collecting and sharing vaccination information at a European level.

In a little more than 2 years (up to the end of 2008) after the European licensing of the first HPV vaccine, Gardasil®, the national health authorities of 15 MS decided to introduce HPV vaccination into their national immunisation schedules, while another six countries have started the decision-making process with a recommendation favouring introduction. It is noteworthy that all advisory bodies that made a recommendation advised the introduction of the HPV vaccine and all national health authorities that made a decision opted for the integration of the HPV vaccination into their national immunisation programmes. These results represent very significant increases as compared with those of the previous

Table 1b – Details of HPV vaccination introduction to immunisation schedules (countries without catch-up vaccination).

Countries	Date of decision	Target group for routine vaccination	
		Gender	Age
Austria	November 2006	Both	Females before sexually actives; boys, young males
Germany	March 2007	Female	12–17 y
Spain	October 2007	Female	1 Cohort between 11 and 14 y differing according to region
Belgium	November 2007	Female	10–13 y
Greece	January 2008	Female	12–15 y
Ireland	August 2008	Female	12–13 y
Norway	December 2008	Female	12 y
Romania	2008	Female	10–11 y

survey conducted in Autumn 2007. At that time, the advisory bodies in 12 countries (44%) had made a recommendation regarding the introduction of HPV vaccination into their national immunisation schedules and the national health authorities in five of these countries (Austria, Germany, France, Italy and the UK) had subsequently taken the decision to introduce HPV vaccination into their national immunisation schedules. This suggests a high public health priority given to HPV vaccination which probably reflects the high expected gain from a vaccine that can prevent cancer.

This contrasts with the situation regarding the rotavirus vaccination. Although the two rotavirus vaccines were licensed a few months before Gardasil®, a similar survey to the one described here for HPV vaccination has shown that out of the 23 countries who provided information at the end of 2008, only nine have made a recommendation regarding the inclusion or not of this vaccination in their immunisation schedules.

The survey results show that the countries which decided to introduce HPV vaccination adopted varying vaccination policies. This is particularly evident in terms of target ages and catch-up campaigns. Such a result is not unexpected considering the variety in national immunisation programme delivery services and diversity of health service infrastructures in European countries. Our short version of the questionnaire did not allow us to further document the anticipated or current modalities of delivery of the vaccine. Regardless of the vaccination policy adopted, all but two countries out of the 15 countries with an effective integration into national immunisation schedules have chosen to offer the vaccine free or to reimburse it. The data collected in the survey do not allow us to be sure that in all countries with a reimbursement policy, the cost of the vaccine will be fully reimbursed.

Our data suggests that there may be two different profiles within the 13 countries which have not, at least as of early 2009, introduced HPV vaccination. The first category would include countries with a very effective control of cervical cancer through a high coverage of the screening programme, making routine HPV vaccination cost-effectiveness questionable. This category includes three countries, located in the Northern part of Europe, Finland, Sweden and Iceland. All three have a nationwide screening policy with coverage of at least 70% of the target population.^{8,9} Their standardised incidence rates of cervical cancer were below 10 for 100,000 women-years and their mortality rates below 1 for 100,000

women-years in 2004.¹⁰ The second category would include countries which have, for the vast majority, a lower performance of the screening programme. In the remaining 10 countries which have not yet integrated HPV vaccination into their national immunisation schedules, all situated in the Eastern part of Europe, only three (Estonia, Slovenia and Hungary) have a nationwide screening policy.⁸ Within the nine countries for which cervical cancer incidence data are available (all but Bulgaria), they all have an incidence above 10 per 100,000 women-years and seven have an incidence of 18 per 100,000 women-years or above.¹⁰ The nine countries for which cervical cancer mortality rates are presented in this current issue of the *European Journal of Cancer* (all but Cyprus) show values above 4 per 100,000 women-years and, even more strikingly, they rank second to tenth when countries are graded by decreasing mortality rates.¹¹ This situation may at least partly reflect the insufficient financial resources to fund a comprehensive screening programme in those countries, a situation which may also hamper the inclusion of the expensive HPV vaccine into their routine immunisation schedules. The comparison of the national per capita gross domestic product (GDP) of the 21 countries where a recommendation of introduction has been made (20,600 €) with one of the seven countries with no recommendation so far (13,140 €) could indeed reflect a financial barrier to the decision, although these two groups of countries may differ for other reasons that also contribute to the decision making process. It therefore appears from this analysis that, at least as of early 2009, the countries which have not yet introduced the vaccine into their national immunisation schedules are, in the vast majority, those where the impact of the vaccination is expected to be the highest due to the high epidemiological burden of cervical cancer and the insufficient implementation of screening activities. The postponing of the implementation of the vaccination programme in Ireland for financial reasons is a source of concern for the sustainability of HPV vaccination programmes in the EU.

A new update will be launched in the second half of 2009. It should allow the assessment of the changes that have occurred in 2009. It will be carried out within the VENICE 2 project, funded by the European Centre for Disease Prevention and Control, which took over VENICE in early 2009. It will encompass additional aspects of HPV vaccination programmes such as vaccination delivery strategies and monitoring activities which were not covered in the 2008 survey. Thanks to VENICE 2, this first experience of close monitoring

of the vaccination decision making process and of regular exchanges of information between member states regarding decisions taken will be maintained and extended to HPV vaccination implementation and evaluation strategies and to other vaccines.

Conflict of interest statement

None declared.

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