



# The clinical benefit and cost-effectiveness of human papillomavirus vaccination for adult women in the Netherlands

Johannes A. Bogaards<sup>a,b,\*</sup>, Veerle M.H. Coupé<sup>a</sup>, Chris J.L.M. Meijer<sup>c</sup>, Johannes Berkhof<sup>a</sup>

<sup>a</sup> Department of Epidemiology and Biostatistics, VU University Medical Centre, P.O. Box 7057, 1007 MB Amsterdam, The Netherlands

<sup>b</sup> Centre for Infectious Disease Control, National Institute for Public Health and the Environment, P.O. Box 1, 3720 BA Bilthoven, The Netherlands

<sup>c</sup> Department of Pathology, VU University Medical Centre, P.O. Box 7057, 1007 MB Amsterdam, The Netherlands

## ARTICLE INFO

### Article history:

Received 24 June 2011

Received in revised form 1 September 2011

Accepted 13 September 2011

Available online 22 September 2011

### Keywords:

Cervical cancer  
Human papillomavirus  
Vaccination  
Cost-effectiveness  
Simulation model

## ABSTRACT

**Background:** The use of human papillomavirus (HPV) vaccines has been universally approved for women from age 12 to 25 years, but those older than 16 years receive no reimbursement for the cost of the vaccine in the Netherlands. Reductions in the vaccine price as well as new insights in the efficacy of HPV vaccines offer renewed arguments to consider HPV vaccination in adult women. We calculated the clinical benefit and cost-effectiveness of vaccinating women aged 17–25 years in 2010.

**Methods:** The calculations were based on an individual-based simulation model for cervical carcinogenesis, with HPV infection risks obtained from a type-specific HPV transmission model. The indirect protective effect from vaccinating 12 to 16 year-old girls was adjusted for. Cervical screening in the model was incorporated according Dutch screening guidelines, i.e. 7 cytology-based rounds at 5-year intervals from the age of 30. As base-case, we assumed the vaccine to offer full protection against HPV16/18 only if no prior exposure to that type had occurred before vaccination. In sensitivity analyses, we considered partial cross-protection against types 31/33/45/58 and efficacy against all future infections, irrespective of previous or current infection status.

**Results:** In base-case analyses, vaccinating 17 year-olds reduced their lifetime risk of treatment for precancerous lesions from 7.77% to 3.48% and their lifetime cervical cancer risk from 0.52% to 0.24%. These risks were 6.12% and 0.45%, respectively, for a 25 year-old vaccinee. The incremental cost-effectiveness ratio (ICER) for vaccinating 17–25 year-olds was €22,526 per quality-adjusted life-year (QALY) at a vaccine price of €65 per dose, a 50% reduction of the 2010 pharmacy price in the Netherlands. If cross-protection against types 31/33/45/58 was included, the ICER decreased to €14,734 per QALY. Results were robust to efficacy assumptions with respect to previous or current infection status.

**Conclusion:** The clinical benefit of HPV vaccination of women up to 25 years moderately depends on cross-protection to non-vaccine types. Refunding the cost of the vaccine to 17–25 year-old women in the Netherlands can be considered cost-effective at anticipated price reductions.

© 2011 Elsevier Ltd. All rights reserved.

## 1. Introduction

Cervical cancer is the second most common cancer among women worldwide [1]. Cytological screening has greatly reduced the burden of cervical disease in countries that have implemented wide-scale screening programmes [2]. In the Netherlands, the age-standardised incidence rate of cervical cancer has dropped from around 15 per 100,000 women in the 1960s to around 5 per 100,000 women since 2000 [3,4]. In 2008, 699 women were diagnosed with

invasive cervical cancer and 244 women died from cervical cancer according to the Dutch cancer registry [[www.ikcnet.nl](http://www.ikcnet.nl)]. Several analyses have suggested that the age-standardised incidence and mortality rate of cervical cancer will not be reduced further by cytological screening alone [5–7]. The availability of human papillomavirus (HPV) vaccines, however, offering protection against the two most prevalent HPV types in cervical cancer, is expected to contribute to a substantial decrease in the cervical cancer incidence in the next thirty years [8,9].

The use of HPV vaccines in women has been universally approved from age 12 up to 25 years (EMEA; FDA). So far, Australia has been the only country to publicly fund a vaccination programme for all women in this age group [10]. In other countries, inclusion into national HPV immunization programmes is restricted to (pre-)adolescent girls, mainly because HPV vaccine

\* Corresponding author at: Department of Epidemiology and Biostatistics, VU University Medical Centre, P.O. Box 7057, 1007 MB Amsterdam, The Netherlands. Tel.: +31 204444490; fax: +31 204444475.

E-mail address: [j.bogaards@vumc.nl](mailto:j.bogaards@vumc.nl) (J.A. Bogaards).

trials have demonstrated greatest immunogenicity and efficacy in preventing vaccine-type infections among women without evidence of (prior) type-specific infection at the time of vaccination [11,12]. As vaccine-type HPV is highly transmissible [13], the clinical benefit of vaccination after initiation of sexual activity is still uncertain.

In the Netherlands, vaccinating girls older than 16 years was not considered feasible from an economic viewpoint – given that the two available HPV vaccines (Gardasil® and Cervarix®) were rather expensive following licensure – and from a clinical point of view, since HPV DNA was detected in cervical smears and HPV16/18 antibodies were found in blood from 16 years off; indicating that these women were not always HPV naïve [14]. New insights in HPV transmission, in the efficacy of HPV vaccines, and reductions in the vaccine price offer renewed arguments to consider HPV vaccination in adult women. In this study, we evaluate the clinical benefit and cost-effectiveness of vaccinating women from age 17 to 25 years compared to no vaccination in these age groups. In all analyses, we include vaccination of 12–16 year-old girls and screening from 30 to 60 years of age – i.e. the current HPV vaccination and cervical screening programmes in the Netherlands. The presented estimates are obtained from a simulation model for cervical carcinogenesis that is linked to a dynamic HPV transmission model [9]. An earlier version of this model has been used for assessing the cost-effectiveness of vaccinating 12 year-old girls in the Netherlands [15].

## 2. Methods

### 2.1. Simulation model

Calculations are based on an individual-based simulation model in which the natural history of cervical cancer is described as a consequence of a persistent infection with any of 14 oncogenic HPV types [9]. The main data source for the model is a population-based screening trial, where genotyping has been performed on all high-risk HPV (hrHPV) positive samples [16,17]. The model simulates health trajectories of birth cohorts of women aged 17–25 years in 2010, until they are deceased. All cohorts have the same background mortality rate, taken from Statistics Netherlands [www.cbs.nl]. The birth cohorts differ with regard to the proportion of women previously infected with hrHPV types at baseline, i.e. at the age of vaccination. They also differ with regard to the age-specific forces of infection for each of the 14 hrHPV types considered in the model. For instance, girls aged 17 years at baseline experience a stronger reduction in infection hazards than girls aged 25 years at baseline. The baseline infection risks and the anticipated impact of herd immunity were informed by a type-specific HPV transmission model [13].

Regarding the sexual contact structure of the HPV transmission model, we assumed equal adjustment of reported rates of partner change by men and women. We also assumed an age-specific preference for partners and random mixing with respect to sexual activity. The contact structure was estimated from two Dutch surveys on sexual behaviour [18,19], and the transmission parameters were estimated by fitting the model to population-based data on hrHPV prevalence prior to introduction of the vaccine in the Netherlands [20]. Model fitting procedures and best-fitting parameters are given in the supplementary annexes of previous publications [9,13].

### 2.2. Screening and vaccination characteristics

We consider the clinical benefit and cost-effectiveness of HPV vaccination for Dutch women from the age of 17 to 25 years in

2010, i.e. those born over the period 1984–1992. The rationale for the age range is that girls born from 1993 onward have been offered free vaccination and the vaccine was not licensed for women born before 1984. All analyses are under the assumption that women from 30 to 60 years of age are invited to participate in the cytological screening programme at 5-year intervals. Five-year coverage rates in the screening programme are between 70% and 80% in the Netherlands [21]. To account for heterogeneity in screening attendance, we assumed that 10% of the women will never attend screening and that the compliance among the remaining women is 80% per round [22]. The accuracy of cytology was estimated from a population-based screening trial and from histopathological registry data (Table 1).

The clinical benefit and cost-effectiveness of HPV vaccination above 16 years is evaluated under the assumption that a woman will complete the full vaccination course, consisting of 3 doses of 0.5 ml injections over 6 months. The immunization coverage among 12–16 year-old girls was set at 50%. As of 2010, 57% of girls born between 1993 and 1997 had received  $\geq 1$  dose of Cervarix but a small fraction did not complete the 3-dose schedule or may have been infected at the time of vaccination [23]. The herd immunity effects resulting from vaccinating 12 to 16 year-olds are included in all analyses, but we did not consider the herd immunity effects from vaccinating 17 to 25 year-olds. Thus, the actual vaccine uptake in this age group does not influence the health gain per woman in our individual-based simulation model. A full vaccination course is assumed to offer 100% protection against incident infections by HPV16 and HPV18 in women naïve to those types at the time of vaccination. In the base-case, we ignored cross-protection against non-vaccine types, i.e. we set vaccine efficacy against HPV types other than 16/18 at zero.

### 2.3. Costs and health utilities

We performed a cost-effectiveness analysis from a societal perspective. The costs per unit of healthcare resource utilization (index year 2010) have been described in previous publications [24,25]. Utilities for the different health states were also taken from the literature [26,27]. In addition, we considered three pricing levels for the HPV vaccine: €125 per dose (based on the pharmacy price in the Netherlands as of 2010); €65 per dose; and €35 per dose. These dose prices were assumed to include overhead costs of administration and delivery.

### 2.4. Health effects and cost-effectiveness calculations

For each of the 1984–1992 cohorts, we estimated the number of detected cervical intraepithelial neoplasia grade 2 or 3 (CIN2/3) lesions, the number of cervical cancer cases and associated deaths, and per capita costs in the settings with and without vaccination. In both settings, we assumed that free vaccination has been offered to women born from 1993 onward and cervical screening will be offered from 30 to 60 years of age at 5 year intervals. Estimates were obtained by simulating 100 times the health trajectories of 100,000 women, the approximate size of each of the 1984–1992 cohorts. We calculated the gain in quality-adjusted life-years (QALY) by comparing settings with and without vaccination, for each cohort separately and for all cohorts combined. The cost-effectiveness of vaccination is measured by the incremental cost-effectiveness ratio (ICER), which is the ratio of extra costs resulting from vaccination divided by the gain in QALYs. Following Dutch guidelines, we used discounting rates of 4% per year for costs and 1.5% per year for health gains [28]. Discounting started at the age of vaccination.

متن کامل مقاله

دریافت فوری ←

**ISI**Articles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات