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Cost-effectiveness analysis of HPV vaccination alongside cervical cancer screening programme in Slovenia

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Background: The objective of the present study is to evaluate the cost-effectiveness of human papillomavirus (HPV) vaccination alongside cervical cancer screening programme in Slovenia. **Methods:** A previously published Markov model representing natural history of HPV infection was adapted to Slovenian context. The model followed a cohort of 12-year-old girls to 85-year-old women. Two strategies were compared: HPV vaccination alongside conventional cytological screening versus screening alone. Analysis was performed from the health care payer perspective. **Results:** Vaccination with screening compared with screening alone was associated with an incremental cost-effectiveness ratio (ICER) of 23 178 EUR per quality adjusted life-year (QALY) gained and 54 536 EUR per life-year gained (LYG) at the discounting rate of 5%. Sensitivity analyses demonstrated that the ICER was most sensitive to the need for booster dose and to different values of discount rates. In case the booster dose was assumed 10 years after initial vaccination, the ICER value was increased to 58 690 EUR per QALY. On the other hand, using lower values of discount rates than the base case 5% significantly reduced the ICER value. **Conclusion:** According to the cost-effectiveness thresholds of 30 000 EUR per QALY which was adopted by the Health Council in Slovenia, HPV vaccination alongside screening programme can be regarded as cost-effective. However, cost-effectiveness of HPV vaccination would become questionable in case a booster dose was needed to provide lifetime protection.

Keywords: cervical cancer screening, cost-effectiveness, human papillomavirus, natural history model, vaccine

Introduction

Worldwide, half a million new cases of cervical cancer are estimated to occur each year, resulting in a quarter of million deaths.[1] It has been found that human papillomavirus (HPV) is a necessary, although not sufficient cause of cervical cancer.[2] HPV is primarily spread through sexual contact and is associated with a wide range of diseases, including cervical, vulvar, vaginal, anal, penile, head and neck cancers as well as genital warts.[3] Although there are several high-risk HPV types, cervical cancer is most commonly a result of infection with HPV types 16 and 18. Namely, ~70% of cervical cancers are estimated to result from the infection with these two HPV types.[4]

In Slovenia, the age-standardized incidence rate of cervical cancer was ~15 per 100 000 women until 2003, which was significantly higher compared with countries in Western and Northern Europe where this rate was below 10 per 100 000 women.[5] In 2003, a national organized cervical cancer screening programme named ZORA was introduced.[6] Women from 20 to 64 years of age are recommended to be screened every 3 years. Since the introduction of organized screening, the incidence of cervical cancer has been steadily decreasing from 203 new cases in 2003 to 153 new cases in 2006.[7] Nevertheless, screening alone cannot prevent all cases of cervical cancer due to less than 100% sensitivity of diagnostic tests and limited coverage rate.

The approval of HPV vaccines that can prevent a substantial proportion of cervical cancers has received much of media attention. Two vaccines are currently available on the market. Namely, a bivalent vaccine (Cervarix®) prevents infection with oncogenic HPV types 16 and 18, while a quadrivalent vaccine (Gardasil®) also prevents an infection with HPV types 6 and 11 which are the main cause of genital warts.[8] Both vaccines were proven to be safe, immunogenic and highly effective against type-specific persistent infection.[9,10] Nevertheless, a relatively high cost of vaccination, combined with the time lag between vaccination costs and benefits occurring in a distant future presents a significant barrier to its widespread use.

Therefore, the objective of the present study was to evaluate the cost-effectiveness of HPV vaccination of 12-year-old girls alongside the current cervical cancer screening programme from the perspective of the health care payer in Slovenia.

Methods

A previously published and validated state transition Markov model[11] used for simulating natural history of HPV infection and cervical cancer in the United States was recently adapted to the European context.[12,13] Compared with the original model, this model was revised to separate high-grade squamous intraepithelial lesions into CIN 2 and CIN 3 dysplasia. This revised model was also adapted to reflect the national screening and treatment pathways in Slovenia.

The model follows a cohort of women through different health states corresponding to the natural history of HPV infection, from the age of 12 until the age of 85 years. Movement through the health states of the model over time is based on annual transition probabilities derived from the literature. Women who are infected with HPV can have their infection clear, progress or persist. For those women whose infections persist, the majority is assumed to develop CIN 1 but a minority is assumed to develop CIN 2 directly; these rates are age-dependant. Women who develop CIN 1, CIN 2 or CIN 3 can have their disease progress, regress or persist.

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Women with cancer can have their cancer detected during screening or by a physician after becoming symptomatic. Women who do not have their disease detected can remain in the same stage or progress to the next stage. A proportion of women with cancer die each year, depending on the cancer stage. Those women who are treated for cancer and survive 5 years are considered as cancer survivors. Each year, women also face an age-specific risk of dying from other causes. The model scheme is presented in Supplementary Figure S1.

The model was empirically calibrated to reflect the age-specific cervical cancer incidence rate, the prevalence of FIGO cervical cancer stages, and cervical cancer mortality rate in Slovenia. The model was fitted to the actual cervical cancer incidence rate by adjusting the incidence and regression rates of HPV infection and the probability of progression from CIN 3 to cancer stage FIGO I. Furthermore, the model fit to the prevalence of FIGO cervical cancer stages and cervical cancer mortality rate was achieved by adjusting the probability of cancer detection, cancer progression, and survival rate in each FIGO cervical cancer stage. A similar calibration was performed in other studies.[12,14,15] Local age-specific mortality rate from all causes in the general female population was used in the model.[16] Women who undergo benign hysterectomy would not develop cervical cancer and were controlled for in the model. Age-specific hysterectomy rates were obtained from the Institute of Public Health of the Republic of Slovenia.[16] Annual transition probabilities used in the model that were derived from Canfell *et al.*[13] and Myers *et al.*[11] or were adjusted to Slovenian context are presented in Supplementary Tables S1 and S2.

Screening programme and management of precancerous lesions in Slovenia

In Slovenia, a national programme of cervical cancer screening was introduced in 2003.[6] Women between 20 and 64 years are invited to participate in the screening programme every 3 years. Additionally to the active screening programme, some women who are either younger than 20 years or older than 64 years also undergo screening. Data on the cervical cancer screening coverage rate from 2004 to 2007 were used in the model.[7] Sensitivity and specificity of diagnostic tests were obtained from the literature.[12,17,18] Screening characteristics are presented in table 1.

Detection and management of precancerous lesions were based on guidelines and general patterns of clinical practice in Slovenia.[19,20] Primary screening was performed by Pap smear. In case the result of Pap smear was a pathological abnormality of a high grade, a woman was directly referred to colposcopy. However, if the result of Pap smear was a pathological abnormality of a low grade, additional Pap test was performed after 3–4 months. In case the second Pap smear was again abnormal, a woman was referred to a colposcopic examination. The proportion of high grade pathological abnormalities was estimated from the correlation between histological diagnosis and the Pap smear that was obtained at maximum 6 months before the histological diagnosis was made, and amounted to 20.2, 52.7 and 80.3% of women who had already developed CIN 1, CIN 2 and CIN 3 lesions, respectively.[7]

In case a colposcopic examination was positive, targeted biopsy was performed to confirm the colposcopic diagnosis and to determine the stage of precancerous lesions (CIN 1, CIN 2 or CIN 3). If the biopsy was negative, abrasion of cervical canal was performed. This procedure was also performed if the colposcopic examination was negative.

According to Lomšek *et al.*,[21] 65.8% of CIN 1 lesions during 1996–2000 were treated, mostly by laser vaporization. On the other hand, all CIN 2 and CIN 3 lesions were treated. Treatment success was above 90% regardless of the procedure used. Unsuccessfully treated patients were again treated by conventional conisation. The model assumed that

Table 1 Screening, vaccine and cost parameters

Parameters	Base case	Range[a]
Screening characteristics		
Coverage rate for age groups[7]		
15–19	16%	
20–24	80%	
25–29	78%	
30–34	78%	
35–39	76%	
40–44	75%	
45–49	72%	
50–54	63%	
55–59	57%	
60–64	48%	
above 65	16%	
Pap smear[12,18]		
Sensitivity for CIN 1	61%	51–80%
Sensitivity for CIN 2/3 and cancer	65%	65–90%
Specificity	95.7%	90–99%
Colposcopy[12,17]		
Sensitivity	90%	88–100%
Specificity	100%	65–100%
Vaccine characteristics		
Efficacy for HPV types 16 and 18[9,19]	98%	86–100%
Duration of efficacy	lifetime	from 10 years to lifetime
Vaccine coverage	80%	50–100%
Booster coverage	50%	–
Costs[b] (EUR)[20]		
Pap smear	25.76	20.61–30.91
Colposcopy	65.76	52.61–78.91
Biopsy, abrasion of cervical canal	584.63	467.70–701.56
Precancerous lesions (CIN 1, CIN 2, CIN 3)	660	528–792
Invasive cancer	5662	4530–6794
Vaccine cost/dose	100	80–120
Administration cost/dose	16.28	13.02–19.54
Utilities[12,14,15]		
Routine screening Pap smear (duration 1 month)	0.9764	annual disutility varied for 20%
ASCUS diagnosis from Pap smear (duration 2 months)	0.9404	annual disutility varied for 20%
LSIL/HSIL diagnosis from Pap smear (duration 2 months)	0.9062	annual disutility varied for 20%
CIN 1 (duration 2 months with 10 months follow-up)	0.9333	annual disutility varied for 20%
CIN 2/3 (duration 2 months)	0.8658	annual disutility varied for 20%
FIGO I (duration 5 years)	0.7598	0.6078–0.9118
FIGO II–IV (duration 5 years)	0.6693	0.5354–0.8032
Discount rate		
Costs	5%	0–5%
Benefits	5%	0–5%

ASCUS: atypical squamous cells of undetermined significance; LSIL: low-grade squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion; CIN: cervical intraepithelial neoplasia; FIGO: cervical cancer stage

a: In case of probabilistic sensitivity analysis triangular distribution was used. Min and max parameters of the distribution were defined by the range. Most likely value of the distribution was defined by the base case value

b: A. Možina, Personal communication

treatment of CIN lesions was 100% effective. An extra cost of conventional conisation was added to 5% women treated. It was assumed that HPV infection remained in 23% of cases.[13]

Women who have been treated for precancerous lesions are monitored on a yearly basis.[6] Approximately one-half (57%) of these women regularly attend gynaecological examinations every year, while others only every 3 years or at times.[22] For the latter, we presumed the same screening coverage as for women who had not yet been treated for precancerous lesions.

HPV vaccination

Phase 3 trials showed that the bivalent vaccine was 100% [95% confidential interval (CI) 47–100%, $N = 1113$] effective against HPV types 16 and 18, and quadrivalent vaccine 98% (95% CI 86–100%, $N = 10\,565$).[9,23] In the base case, we assumed that HPV vaccine was 98% effective against infection with HPV types 16 and 18. Vaccine efficacy was varied from 86 to 100% in sensitivity analysis. The lower value of 95% CI of quadrivalent vaccine (86%) was considered, as this vaccine was tested in a larger sample compared with bivalent vaccine, and hence provides a more reliable result. Based on the proportion of CIN lesions and invasive cancer that is attributable to HPV types 16 and 18 (36% in CIN 1, 52% in CIN 2/3 and 67% in invasive cancer)[24,25] vaccination was assumed to reduce approximately 35% of CIN 1 lesions, 51% of CIN 2 and CIN 3 lesions, and 66% of invasive cancer.

In the base case model, lifetime duration of vaccine efficacy was considered. Use of a booster dose to achieve lifetime duration of efficacy was tested in a sensitivity analysis. A booster dose was assumed to be administered 10 years after the initial vaccine, i.e. at age 22.

HPV vaccine was assumed to be administered to girls of age 12 through a school-based programme, with two additional GP visits. As HPV vaccination shall be available in Slovenia as part of the nonobligatory program, the base case model assumed 80% vaccination coverage rate. In case of need for a booster dose, vaccination coverage at age 22 was assumed to be 50%. Women who would not be vaccinated again at age 22 years were conservatively assumed to acquire no benefit from vaccination.

Costs

Only direct costs were included in the analysis, assuming a health care payer perspective. Cost of a gynaecologist visit, Pap test, colposcopy, biopsy and abrasion were obtained from the latest list of average prices of health services obtained from the Health Insurance Institute of Slovenia.[26] Cost of treating a precancerous lesion was calculated from the Disease Related Groups (DRG) weights. Due to the lack of comprehensive data on the cost of cervical cancer treatment in Slovenia, estimates provided by an expert panel were used in the analysis (A. Možina, Personal communication). In the base case analysis, we assumed that a dose of HPV vaccine would cost 100 EUR, whereby three doses are needed. An additional cost of two GP visits was considered, based on the proposed administration scheme.[27] Costs are presented in table 1.

Utilities

Utilities for calculating quality-adjusted life expectancy were obtained from previously published cost-effectiveness studies of HPV vaccination and are presented in table 1.[12,14,15] Utility for those surviving cancer was set at 1.0. The model also took into account the disutility associated with having a routine Pap smear and the effect of the diagnosis as a result of the smear.

Analysis

Health outcomes and costs were discounted at 5% annual rate. Results are presented as average costs, life-years gained (LYG) and quality adjusted life-years (QALYs) gained for each comparison intervention as well as incremental cost-effectiveness ratios (ICERs) for vaccination along with screening versus screening alone. The number of detected precancerous lesions, cervical cancer cases and cervical cancer deaths avoided by vaccination are also provided. Univariate sensitivity analysis was performed to test the effect of different vaccine efficacy, the need for a booster dose, sensitivity and specificity of diagnostic tests, utility scores, cervical cancer mortality rate, an additional effect of the national screening program on the cervical cancer incidence rate, costs and discount rates. Moreover, probabilistic sensitivity analysis was performed considering wide parameter ranges as defined in table 1, using a base case discount rate as a non-stochastic parameter. Modelling was performed in TreeAge Pro software (TreeAge software Inc., Williamstown, MA, USA).

Results

Validation of the model

The model was calibrated to fit the observed age-specific incidence of cervical cancer,[28] observed distribution of FIGO stages[29] and observed cervical cancer mortality rate.[7] Predicted age-specific incidence of cervical cancer is presented in Figure 1, and is highly comparable to the average age-specific incidence from 2005 to 2007. Predicted and observed distribution of FIGO stages from 2005 to 2006 are presented in Figure 2. Predicted cervical cancer mortality rate amounted to 5.7 per 100 000 women, and the actual cervical cancer mortality rate ranges from 5 to 6.5 per 100 000 women.[7]

Base case analysis

The predicted cervical cancer incidence rate for no screening was 78.6 and for screening 17.1 per 100 000 women. HPV vaccination would further reduce this rate to 5.8 per 100 000 women if all girls were vaccinated or to 8.1 per 100 000 women if the vaccination coverage rate was 80%. The effect of HPV vaccination on cervical cancer incidence rate is shown in Figure 1. The model predicted a lifetime cervical cancer risk of 1.25% and a lifetime cancer mortality risk of 0.4% for women undergoing cervical cancer screening in Slovenia. By vaccinating 80% of the 12-year-old girls, the predicted lifetime cervical cancer risk was reduced to 0.59% and the lifetime cancer mortality risk to 0.22%.

Considering a cohort of 10 000 girls, which is an approximate number of 12-year-old girls in Slovenia, the model predicted that with screening alone the following number of outcomes would be detected over lifetime: 125 cervical cancer cases, 40 cervical cancer deaths, 2363 CIN 1, 679 CIN 2 and 604 CIN 3 cases. If 80% of the same cohort was vaccinated, 65 cervical cancer cases, 18 cervical cancer deaths, and 664 CIN 1, 279 CIN 2 and 249 CIN 3 cases would be avoided.

From the health care payer perspective, introducing vaccination alongside current cervical cancer screening programme in Slovenia would result in additional 42.7 LYG, 100.6 QALYs gained, and 2.33 mio EUR per 10 000 vaccinated girls. The incremental cost-effectiveness ratio amounted to 54 536 EUR per LYG and 23 178 EUR per QALY gained.

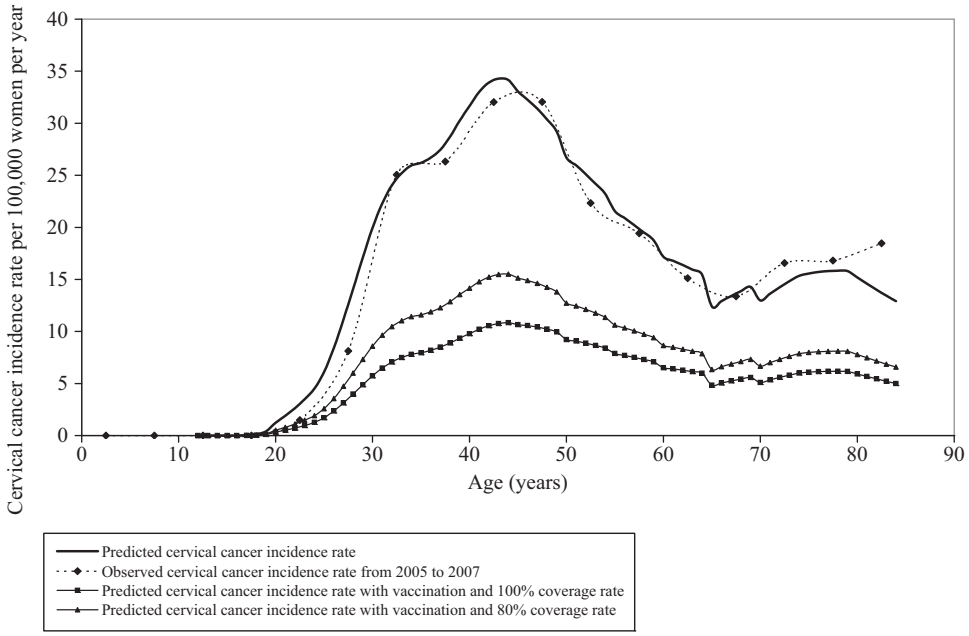

Figure 1 Predicted and observed age-specific cervical cancer incidence rate from 2005 to 2007[29], and predicted reduction of cervical cancer incidence rate by HPV vaccination, assuming 80 and 100% vaccination coverage rate

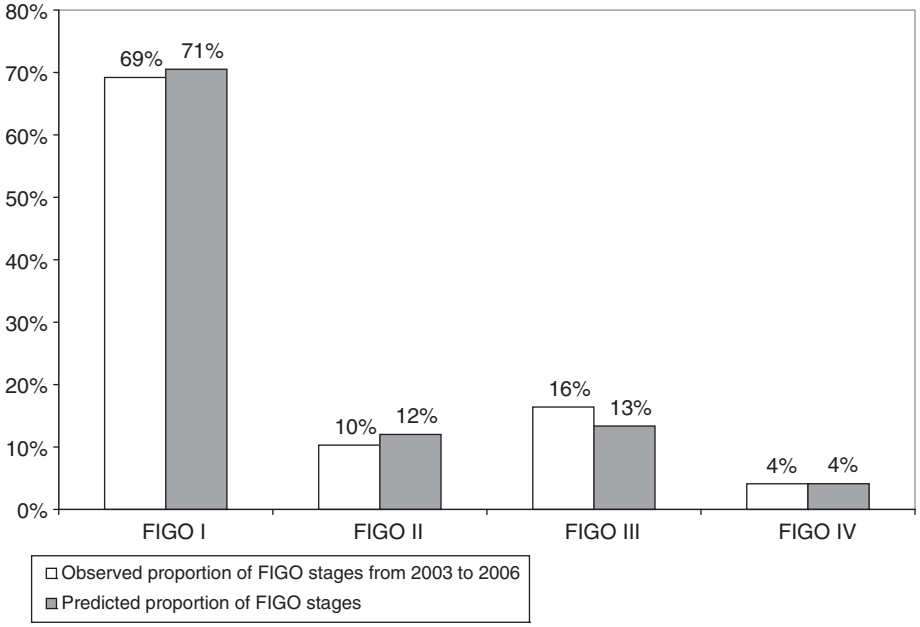

Figure 2 Predicted and observed distribution of FIGO stages in women with newly detected cervical cancer from 2003 to 2006.[30]

Sensitivity analyses

The impact of changing various parameters on the incremental cost-effectiveness ratio is shown in table 2. Results were most sensitive to the assumption that a booster dose after 10 years was needed. The incremental cost-effectiveness ratio for this strategy amounted to 58 690 EUR per QALY, whereby 50% revaccination coverage rate was assumed. Under the assumption that all vaccinated girls at the age of 12 would be re-vaccinated at the age of 22, the ICER value decreased to 39 419 EUR per QALY. Lowering discount rates from 5 to 3% or 0% significantly decreased ICER value. Varying the sensitivity and specificity of diagnostic tests, utility scores, vaccine costs and assuming an additional effect of screening on cervical cancer incidence had a moderate impact on the cost-effectiveness ratio, as shown in table 2.

Probabilistic sensitivity analysis showed there was 75% probability that vaccination was cost-effective at the cost-effectiveness threshold of 30 thousand EUR per QALY gained, whereby considering 5% discount rate for costs LYG and benefit and no need for a booster dose. In case a booster dose was needed, there was 0% probability that vaccination was cost-effective at the same cost-effectiveness threshold.

Discussion

According to the cost-effectiveness threshold value of 30 000 EUR per QALY which was recently accepted by the Health

Table 2 The impact of varying parameter values on the incremental cost-effectiveness ratio of vaccination plus screening versus screening alone

Parameters	ICER (EUR/LYG)	ICER (EUR/QALY)
Booster dose after 10 years	137.250	58.690
Vaccine efficacy		
86%	68 958	29 113
100%	53 074	22 560
Cervical cancer mortality		
5.0/100 000 women	49 161	22 392
6.4/100 000 women	61 527	24 056
Cervical cancer incidence		
current incidence rate reduced for 25%	73 884	29 639
Sensitivity and specificity of Pap smear		
minimum values	52 869	23 280
maximum values	99 391	31 662
Sensitivity and specificity of colposcopy		
minimum values	54 433	23 136
maximum values	55 087	23 412
Utilities		
−20% (for utility scores for FIGO states only)	54.536	18 605
+20% (for utility scores for FIGO states only)	54.536	30 733
Costs of diagnostic procedures (Pap smear, colposcopy, abrasion)		
−20%	54 727	23 259
+20%	54 346	23 097
Costs of treating precancerous lesions and cervical cancer		
−20%	55 768	23 702
+20%	53 304	22 654
Vaccine cost/dose		
80 EUR	43 306	18 405
120 EUR	65 766	27 951
Discount rate for costs/benefits		
0%/0%	3079	1708
3%/0%	4291	2381
5%/0%	4662	2587
3%/3%	19 913	9606
Parameters		
Booster dose after 10 years	137.250	58.690
Vaccine efficacy		
86%	68,958	29,113
100%	53,074	22,560
Cervical cancer mortality		
5.0/100 000 women	49,161	22,392
6.4/100 000 women	61,527	24,056
Cervical cancer incidence		
10.2/100 000 women (CIN3 to FIGO = 1,4)	93,553	35,538
Sensitivity and specificity of Pap smear		
minimum values	52,869	23,280
maximum values	99,391	31,662
Sensitivity and specificity of colposcopy		
minimum values	54,433	23,136
maximum values	55,087	23,412
Utilities		
−20% (for utility scores for FIGO states only)	54.536	18,605
+20% (for utility scores for FIGO states only)	54.536	30,733
Costs of diagnostic procedures (Pap smear, colposcopy, abrasion)		
−20%	54,727	23,259
+20%	54,346	23,097
Costs of treating precancerous lesions and cervical cancer		
–20%	55,768	23,702
+20%	53,304	22,654
Vaccine cost/dose		
80 EUR	43,306	18,405
120 EUR	65,766	27,951
Discount rate for costs/benefits		
0%/0%	3,079	1,708
3%/0%	4,291	2,381
5%/0%	4,662	2,587
3%/3%	19,913	9,606

Council (Health Council is the supreme counseling body to the Ministry of Health of the Republic Slovenia. Reimbursement decision-making procedure used by Health Council is available in Slovenian language at: URL: http://www.mz.gov.si/) in Slovenia, introducing HPV vaccination alongside current screening programme can be regarded as cost-effective. However, in case a booster was needed to provide lifetime effectiveness, HPV vaccination would no longer be cost-effective.

Discounting has a high effect on cost-effectiveness of preventive interventions, as cost-savings and health benefits occur in the future. In the base case, a conservative approach was considered by applying a 5% discount rate on both costs and benefits, as is common practice in several countries. Nevertheless, some authors have argued that applying lower discount rate for benefits compared with costs is theoretically more appropriate.[30] In such cases, the ICER value for HPV vaccination was significantly lower compared with equal discounting of costs and benefits. Also, discounting at the lower values than the base case 5% had a high impact on ICER, regardless of using equal or lower discount rate for benefits compared with costs. This is the case for all vaccination strategies where benefits are accrued far in the future. In addition, based on the one-way sensitivity analysis, which keeps all variables at the base case value except for the variable that is varied, the ICER value was relatively insensitive to changes in the cost of cervical cancer. Likewise, the ICER value was moderately sensitive to changes in the utility scores and characteristics of diagnostic tests used in the model for which no local data were available. Moreover, vaccination coverage rate had no effect on ICER as both costs and benefits changed proportionally to the coverage rate.

The model was calibrated to reflect the observed incidence of cervical cancer in Slovenia. Since the introduction of the national screening programme in 2003, the incidence rate of cervical cancer has been continuously decreasing. Average incidence rate for the last 3 years for which the data was available was used in the analysis. However, a full impact of implementing a national screening programme is yet unknown. In case the incidence rate of cervical cancer further declines to a significant extent, the benefits of vaccination would, in such cases, be smaller than the estimated benefits obtained from the presently available data. For example, if the current cervical cancer incidence rate further declined by 25%, i.e. to the approximate level of cervical cancer incidence rate in the Western Europe,[5] the ICER value would increase to 29 639 EUR per QALY.

No distinction was made between bivalent (Cervarix®) and quadrivalent vaccine (Gardasil®) regarding their effectiveness in preventing infections with HPV 16 and 18 genotypes, as no data from head-to-head trial are yet available. The effect of quadrivalent HPV vaccine on prevention of genital warts, and other potential benefits that HPV vaccination might bring, such as reduced incidence of anal, vulval, vaginal or head and neck cancer were not included in the analysis. Furthermore, vaccination also has other benefits, which are relevant from the societal perspective, such as lowering of indirect costs due to productivity loss.

The present study assumed long-term safety of the HPV vaccine. This is in agreement with the most recently published data on adverse events following immunizations (AEFI) that come from the US Vaccine Adverse Event Reporting System (VAERS). Based on the passive surveillance data from more than 23 million doses of the quadrivalent HPV vaccine distributed in the United States, a total of 12 424 AEFI were reported from 1 June 2006 to 31 December 2008.[31] The vast majority (93%) of the adverse events reports has been non-serious, and included fainting, pain and swelling at the

injection site, headache, nausea and fever. Experts have not found a common medical pattern to the reports of serious adverse events that would suggest that they were caused by the HPV vaccine. Nevertheless, the significance of these findings must be tempered with the limitations of a passive reporting system, such as possible underreporting and non-systematic validation of reported events.

The model used in the present analysis is a cohort model. This type of model follows a single cohort throughout the period of the analysis. Although cohort models are one of the most frequently used models for estimating cost-effectiveness of health care interventions, their use in the field of infectious diseases has a key limitation that they cannot capture the effect of 'herd immunity' that is achieved if a sufficient proportion of the population is vaccinated, and changes in the population over time.[32] These effects can be evaluated by using a transmission dynamic model. Nevertheless, these models require more data, such as data on sexual contacts, which can represent significant uncertainty if the data are not available. Moreover, studies that have accounted for herd immunity obtained slightly lower ICER values for vaccination interventions than studies that have not.[33]

Nevertheless, to maximize the benefits of vaccination, several factors should be taken into account. First, the vaccination should start before the onset of sexual activity. Most of the high-income countries recommend vaccination of girls up to the age of 14 years.[34] A 'catch-up' vaccination programme may also be appropriate for older adolescent girls who have not been exposed to HPV. Secondly, the present analysis showed that the need for a booster dose was a major factor influencing cost-effectiveness of vaccination. At present, there is evidence of at least 5 years of sustained efficacy of vaccination.[35,36] Continued monitoring of efficacy will be essential to determine the need for booster doses. Moreover, the registry of vaccinated girls would be necessary to maximize vaccination coverage rate if the booster dose was needed. Thirdly, awareness is important that screening coverage could decline if the public developed a misbelief that HPV vaccination removes the need for screening. Therefore, a vaccination programme needs to be supported by public education to reinforce the continued role of screening. Finally, introduction of HPV vaccination could lead to modification of cervical cancer screening interval.[37]

Conclusion

The present analysis evaluated potential costs and benefits of introducing HPV vaccine alongside current screening programme in Slovenia from the health care payer perspective. According to the cost-effectiveness threshold of 30 000 EUR per QALY which was adopted by the Health Council in Slovenia, HPV vaccination alongside screening programme can be regarded as cost-effective. However, cost-effectiveness of HPV vaccination would become questionable in case a booster dose was needed to provide lifetime protection.

Supplementary data

Supplementary data are available at *EURPUB* online.

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Conflicts of interest: None declared.

Key points

- Cost of HPV vaccine presents a significant burden for its widespread use. Several previously published studies have investigated the cost-effectiveness of introducing HPV vaccination alongside screening programme to a specific country.
- No data exists about the cost-effectiveness of introducing HPV vaccine to Slovenia, where the incidence of cervical cancer is higher, but costs of health services are lower compared with countries from Western and Northern Europe.
- Incremental cost-effectiveness ratio of HPV vaccination alongside screening versus screening alone was below 30 000 EUR per QALY under most assumptions.
- Results indicate that introducing HPV vaccination alongside current cervical cancer screening programme in Slovenia is cost-effective. However, cost-effectiveness of HPV vaccination would become questionable in case a booster dose was needed to provide lifetime protection.

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