Scandinavian Journal of Public Health, 2012; 40: 406–411

ORIGINAL ARTICLE

Healthcare spending in the case of a HPV16/18 population-wide vaccination programme

GIEDRIUS VANAGAS & ZILVINAS PADAIGA

Academy of Medicine, Lithuanian University of Health Sciences, Kaunas, Lithuania

Abstract

Background: The policy of population-wide human papillomavirus (HPV) vaccination has been debated as the introduction of such a programme in a low-resource country faces the risk of insufficient cost-effectiveness. *Objectives:* To assess the potential healthcare spending changes after the introduction of a HPV16/18 population-wide vaccination programme in Lithuania. *Study design:* For a cost-effectiveness analysis, we used mathematical simulation and epidemiological data modelling based on a Lithuanian female population. We performed comparative analysis of an annual 12-year-old girls population-wide vaccination programme combined with cervical cancer screening programme compared to the screening programme strategy only. *Results:* HPV vaccination would gain an average of 35.6 life years per death avoided or up to 284.8 thousand life years would be gained over 90 years in total. The programme costs would be 2932.58 EUR per life year gained. All costs associated with the introduction of the vaccination programme could be recovered in 48 years. The HPV vaccination programme in Lithuania has the potential to generate up to 40.07 million EUR of economic returns annually compared with the current practice of the cervical screening alone. ***Conclusions:*** **In Lithuania the HPV16/18 vaccination programme would be economically effective only in the long term. The investment costs of HPV16/18 vaccination have the potential to be recovered.**

Key Words: *Cervical cancer, economic effectiveness, healthcare spending, Lithuania, vaccination*

Introduction

Lithuania is facing a high deficit in the healthcare budget, as most of the post-Soviet countries. This fact influences healthcare policy so that it is oriented to maintain the healthcare system with available resources. Therefore, new prevention programmes requiring high costs and showing their effectiveness only in the long term need to be justified in terms of possible economic return.

Cervical cancer is the most prevalent cancer in Eastern Europe [1]. In the Lithuanian female population, the highest rate, up to 31.5 per 100,000 population, was observed in 2004–2006 [2,3]. In Lithuania, the disease is quite often diagnosed in the late stage. Such a situation causes higher than average hospitalisation rates and treatment costs [4]. Lithuania introduced a national cervical cancer screening programme in 2004 and it has increased early diagnosis rates but the disease burden and morbidity rates are still high [2,3,5]: according to the latest data of the Lithuanian Cancer Registry, the morbidity from cervical cancer was 25.9 cases per 100,000 women in 2010, which demonstrates still-urgent needs for early prevention programmes such as HPV vaccination.

Recently, a number of clinical studies have demonstrated that the HPV16/18 vaccine can prevent HPV infection and disease caseness [6,7]. In particular, it is important to have information on the long-term epidemiological and economic consequences of the vaccination in different populations [8,9]. The results from long-term observational and experimental studies are not available until after the start of the initial vaccination programme. Due to this limitation, mathematical models are alternative information sources

Correspondence: Giedrius Vanagas, Preventive Medicine Department, Academy of Medicine, Lithuanian University of Health Sciences, Eiveniu 4-408, LT- 50161 Kaunas, Lithuania. E-mail: giedrius.vanagas@lsmuni.lt

(*Accepted 26 June 2012*)

DOI: 10.1177/1403494812455467

for decision making. With the help of the mathematical models, it is possible to forecast the long-term epidemiological and economic consequences of the vaccination programme. A number of different types of mathematical models has been developed to analyse the long-term benefits and costs of alternative HPV vaccination strategies [10,11]. These models differ both in their populations and by the complexity of covering costs and consequences. Most recent modelling publications have represented results on long-term HPV vaccination and cost-effectiveness in rich and well-developed countries, such as the USA. Due to differences in disease epidemiology, availability of diagnostic and treatment strategies, and differences in service costs, it is necessary to adopt the decision model according to the country specifics [12,13].

In Lithuania, the policy of a population-wide HPV vaccination programme has been debated: its implementation in low-resource setting would have relatively high costs and faces the risk of insufficient economic effectiveness. Currently, we have presented some evidence on how much a HPV vaccination programme would affect epidemiological changes in the Lithuanian population [14], but it is also important to understand when the possible investment to the prevention programme could generate cost savings and if the costs invested to the programme's implementation would be recovered and when.

Accordingly, our aim of this study was to assess the potential healthcare spending changes in the case of a human papillomavirus (HPV16/18) population-wide vaccination programme being implemented in Lithuania.

Materials and methods

Patient population

For modelling analysis, the average population (in 2004–2006) of the Lithuanian female population was taken. A comparative analysis strategy considered HPV16/18 vaccination of all 12-year-old girls. We compared a vaccination programme with the current practice of cervical screening alone. We used the annual vaccine strategy for only the selected adolescent age group.

Decision model

A mathematical decision model was developed using the Borland C++ Builder 6 software. The model integrated population-wide health-state transition to simulate the natural history of HPV infection. This model was based on 2004–2006 average cervical-cancer rates in the average Lithuanian women population (n=1,808,505).

The population in the model faces age-specific risks of acquiring cervical cancer, with all other health-related consequences or death. Accordingly, each year in the model, they face an age-specific risk of acquiring HPV infection that could either persist, progress (to ClN1 or ClN2–3), or resolve. The cases developing CIN1–3 could be detected by a screening programme and could have their disease persisting, regressing, or progressing. Also, they could either progress to the next stage or remain in the same stage according to the country-specific epidemiological transition data. Women with cancer stages I, II, III, or IV (FIGO) could have their disease detected and treated after passing a gynaecological examination, according to the current screening rate. We assumed that girls who were not vaccinated would receive the standard cervical cancer screening programme targeted to 25–60-year-old women every 3 years. Clinical health states in the model were defined for allocating women into three groups: women who had prior treatment for CIN, cancer survivors, and the rest who had died due to cervical cancer. The main model characteristics have been previously described in the literature [14].

Vaccination and vaccination strategy assumptions

Cervical cancer vaccines are likely to be limited to the female population. The target group for vaccination in Lithuania was females only because of available national regulatory approval. We made some initial assumptions regarding vaccination:

1. The HPV16/18 vaccine would be targeted against 77% of all oncogenic types [15,16].
2. Vaccine efficacy would range 90–100% over time, representing results from published HPV16/18 vaccine trials [17–20].
3. There would be no significant adverse effects due to vaccination.
4. The vaccination would be administered with a 3-series vaccine (at 0, 1, and 6 months).

Costs

We assumed that the HPV16/18 vaccine would be administered within current healthcare visits and it would not result in an increase of programme costs. All base-case direct medical cost estimates for screening and diagnoses were derived from National Sickness Fund healthcare claims registry SVEIDRA. All data were combined with Lithuanian Cancer Register data to address only cervical cancer-related healthcare costs. We included only direct medical costs to the cost analysis. Vaccine costs were based on the producers' declared vaccine price. All costs were expressed in 2007 Euro.

Economic analyses

We used a sensitivity analysis to estimate the cost-effectiveness and life expectancy changes associated to the selected vaccination strategies. We calculated incremental cost-effectiveness ratios in which the additional costs divided by the additional savings in life expectancy. We calculated the expected reductions in cancer incidence and prevalence, and/or mortality in different vaccine penetration levels for the key sensitivity analyses. We also adjusted future costs and outcomes to current values by discounting them at 3% annually.

Results

We tracked the whole Lithuanian women population for a 12-year-old girls vaccination strategy by annual 90% vaccine penetration at the age group over a 90-year period.

Base-case analysis

According to data from the 3-year period (2004–2006) without a vaccination programme, the incidence of cervical cancer in Lithuania reached an average of 530 new cases per year: prevalence, 3609 cases per year; and mortality, 221 cases per year. According to statistics, the age-specific incidence of cervical cancer peaked at an age of 42 years at a rate of 69.7 cases of cervical cancer per 100,000 women in Lithuania. The absolute lifetime risk of cervical cancer predicted by the model was 3.77% and with vaccination could be reduced up to 0.87%. The vaccination strategy, compared to the current epidemiological environment, would gain an average of 35.6 life years per death avoided.

Vaccine coverage changes using annual vaccine penetration strategy

Existing immunisation practices recommend vaccination for all females aged 11–12 years, and as young as 9 years. Catch-up vaccination is also recommended for all females aged 13–26 years who have not been previously vaccinated [21,22]. Our strategy developed in the model was in accordance to these recommendations. We tracked Lithuanian 12-year-old females with 90% annual vaccine penetration rate annually from the introduction of hypothetical vaccination programme. The programme started with a

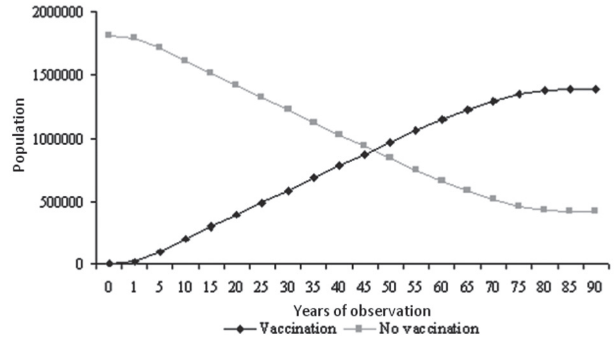

Figure 1. Vaccine coverage changes using an annual 90% HPV16/18 vaccine penetration rate in 12-year-olds over 90 years of observation.

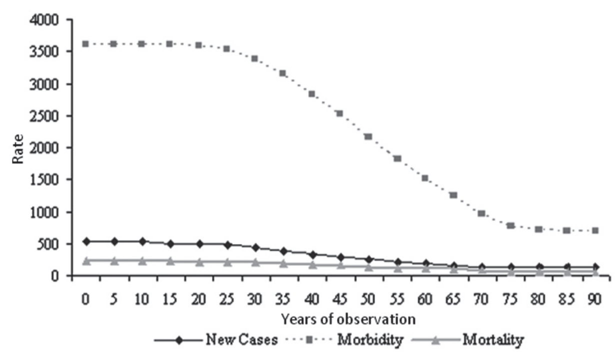

Figure 2. Reduction in incidence, morbidity, and mortality rates with an annual 90% HPV16/18 vaccine penetration rate in 12-year-olds over 90 years of observation.

target of 19,698 12-year-old girls to be vaccinated during the first year. Therefore, hypothetically, in 46.7 years we vaccinated 50% of Lithuanian female population against HPV16/18 virus types. During our selected observation period of 90 years, vaccine penetration would reach up 77% of the whole Lithuanian female population (Figure 1).

Epidemiological changes due to the vaccination programme

According to our 12-year-old age group vaccination strategy, current epidemiological situation, and available epidemiological data, the changes in incidence and prevalence of cervical cancers would appear 10 years after implementation. The mortality reduction would be evident only 16 years after implementation (Figure 2).

Cost-effectiveness and healthcare spending changes

According to the expected epidemiological changes caused by the implementation of HPV16/18

Table I. Cost-effectiveness changes over 90 years of observation for population-wide vaccination programme with annual vaccine penetration in 12-year-old girls.

Year of observation	Accumulated period costs (EUR)	LYG	Cost per LYG (EUR)
1	9,322,686.37	0	0
10	97,538,037.44	0	0
20	186,249,644.54	306.79	607,095.40
30	278,393,919.49	4788.36	58,139.77
40	365,389,192.66	21,806.14	16,756.26
50	445,629,799.54	51,140.71	8713.80
60	520,394,169.06	89,715.25	5800.51
70	590,725,513.05	138,122.64	4276.82
80	657,594,609.31	189,606.90	3468.20
90	723,848,254.59	246,830.14	2932.58

LYG, life years gained.

vaccination programme, there was average of 35.6 life years gained (LYG) per death to be avoided. According to our study, during the first 15 years after implementation, a LYG gain is impossible. The mortality reduction could be expected only when vaccinated girls would reach specific age groups. The investments only should be considered during this period (Table I).

During the first year, the maximum amount of required investment (including vaccination and regular treatment costs) would reach about 9.32 million EUR per year. Afterwards, in the following years (according to the epidemiological changes in disease incidence, prevalence, and mortality), the standard treatment costs could be reduced by up to 6.62 million EUR per year. During the 90 years of observation, it would be possible to generate up to 284.8 thousand life years gain. Cost-effectiveness of the HPV16/18 vaccination programme in 30–40 years would reach the economically acceptable range. The economic effectiveness (as cost per LYG) would be most significant in the longest possible period of observation (Table I).

Expected economic return of investments

According to our calculations, the first 15 years would require investments and no economic return would be gained. After this period, it is expected that the vaccination programme would generate the economic return associated with reduced cervical cancer costs in different sectors. According to our model, all costs associated with investment would be covered in 48 years. Annually, a HPV16/18 vaccination programme in Lithuania has the potential to generate up to 40.07 million EUR of economic return per year compared with the status quo (Figure 3).

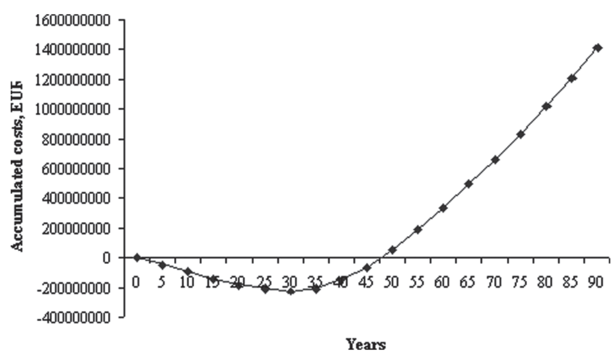

Figure 3. Expected economic return of investment from an annual 90% HPV16/18 vaccine penetration rate in 12-year-olds over 90 years of observation.

Discussion

Typically, the progression from persistent infection to cervical cancer is very slow, often requiring a period of 20 years or longer [23]. This is associated with a low economic benefit of a HPV vaccination programme in the short term and therefore urges the need for economic assessment in the long term. According to our previous research [14], in the long term, the proportion of cervical cancer cases prevented would be higher if early adolescent groups are targeted. Current guidelines recommend HPV vaccination at 11–12 years [21,22]. According to these recommendations, we simulated and followed population epidemiological dynamics in the case of annual 12-year-old girls vaccination together with the current existing cervical cancer screening programme. Our results were compared with the results of the screening programme as a base-case.

The cost-effectiveness of HPV16/18 vaccination would reach the economically acceptable range in 30–40 years. Also, according to our modelling results, the recommended vaccination strategy would require up to 15 years of investment before the first economic returns. All costs associated with investment for the programme would be recovered in 48 years. A HPV16/18 vaccination programme in Lithuania has the potential to generate up to 40.07 million EUR of economic returns per year comparing to the status quo of a screening programme only.

The structure of our model differs from Markov cohort and dynamic models previously used in a number of studies [24]. Our population is changing over time at all ages. Individuals constantly enter the model as they are born and exit as they die from cervical cancer or from all other causes. At every point of analysis, individuals enter and exit according to real population dynamics over selected period of observation. Hence, our model does not have a natural stopping point, as in the majority of Markov cohort models [10]. Additionally, our model takes into account the duration of vaccine protection, prevalence, incidence, progression rates, and death probabilities between disease states; it also depends on the specific age group selected for the simulation.

For economic cost analyses, we used age- and cancer stage-specific healthcare cost data from national healthcare claims registry SVEIDRA (owned by National Sickness Fund). According to other studies, it is acceptable to use claims data for evaluation of healthcare costs and outcomes in non-experimental settings and to apply the results to a whole population [25]. Claims data is a relatively inexpensive way to obtain useful information about patient demographics, as well as healthcare resources used for specific medical conditions and procedures from large numbers of patients over extended periods of time. With claims and registry data, we are able to identify patients who meet specific medical or sociodemographic criteria; also we can estimate their costs, define episodes of medical care, and assess cost outcomes for the whole population [26,27].

Conclusion

A HPV16/18 vaccination programme in Lithuania would be economically effective in the long term. The invested costs of such a programme in Lithuania have the potential to be recovered in long term.

Funding

This study was partially supported by a research grant from Kaunas University of Medicine and JSC GlaxoSmithKline Lietuva (grant no.V-444).

References

[1] Parkin DM and Bray F. Chapter 2: The burden of HPV-related cancers. Vaccine 2006;24 Suppl 3:S11−S25.
[2] Arbyn M, Antoine J, Magi M, Smailyte G, Stengrevics A, Suteu O, et al. Trends in cervical cancer incidence and mortality in the Baltic countries, Bulgaria and Romania. Int J Cancer 2011;128(8):1899−907.
[3] Jariene K, Vaitkiene D, Bartusevicius A, Tvarijonaviciene E, Minkauskiene M, Nadisauskiene R, et al. Prevalence of human papillomavirus types 16, 18, and 45 in women with cervical intraepithelial changes: associations with colposcopic and histological findings. Medicina (Kaunas) 2012;48(1):22−30.
[4] Arbyn M, Raifu AO, Autier P and Ferlay J. Burden of cervical cancer in Europe: estimates for 2004. Ann Oncol 2007;18(10):1708−15.
[5] Arbyn M, Antoine J, Valerianova Z, Magi M, Stengrevics A, Smailyte G, et al. Trends in cervical cancer incidence and mortality in Bulgaria, Estonia, Latvia, Lithuania and Romania. Tumori 2010;96(4):517−23.
[6] Goldie SJ, O'Shea M and Kim JJ. Finding consensus on cervical cancer prevention. Am J Public Health 2012;102(6):1050–1051.
[7] Mao C, Koutsky LA, Ault KA, Wheeler CM, Brown DR, Wiley DJ, et al. Efficacy of human papillomavirus-16 vaccine to prevent cervical intraepithelial neoplasia: a randomized controlled trial. Obstet Gynecol 2006; 107(1):18−27.
[8] Ault KA. Long-term efficacy of human papillomavirus vaccination. Gynecol Oncol 2007;107(2 Suppl):S27−S30.
[9] Termrungruanglert W, Havanond P, Khemapech N, Lertmaharit S, Pongpanich S, Khorprasert C, et al. Cost and effectiveness evaluation of prophylactic HPV vaccine in developing countries. Value Health 2012;15(1 Suppl):S29−S34.
[10] Dasbach EJ, Elbasha EH and Insinga RP. Mathematical models for predicting the epidemiologic and economic impact of vaccination against human papillomavirus infection and disease. Epidemiol Rev 2006;28:88−100.
[11] Elbasha EH, Dasbach EJ and Insinga RP. Model for assessing human papillomavirus vaccination strategies. Emerg Infect Dis 2007;13(1):28−41.
[12] Coupe VM, van Ginkel J, de Melker HE, Snijders PJ, Meijer CJ and Berkhof J. HPV16/18 vaccination to prevent cervical cancer in The Netherlands: model-based cost-effectiveness. Int J Cancer 2009;124(4):970−8.
[13] Goldie SJ, O'Shea M, Diaz M and Kim SY. Benefits, cost requirements and cost-effectiveness of the HPV16,18 vaccine for cervical cancer prevention in developing countries: policy implications. Reprod Health Matters 2008;16(32):86−96.
[14] Vanagas G, Padaiga Z, Kurtinaitis J and Logminiene Z. Cost-effectiveness of 12- and 15-year-old girls' human papillomavirus 16/18 population-based vaccination programmes in Lithuania. Scand J Public Health 2010;38(6):639−47.
[15] Clifford G, Franceschi S, Diaz M, Munoz N and Villa LL. Chapter 3: HPV type-distribution in women with and without cervical neoplastic diseases. Vaccine 2006;24 Suppl 3:S26−S34.
[16] Saranath D, Khan Z, Tandle AT, Dedhia P, Sharma B, Contractor R, et al. HPV16/18 prevalence in cervical lesions/ cancers and p53 genotypes in cervical cancer patients from India. Gynecol Oncol 2002;86(2):157−62.
[17] Hughes JP, Garnett GP and Koutsky L. The theoretical population-level impact of a prophylactic human papilloma virus vaccine. Epidemiology 2002;13(6):631−9.
[18] Stanley M. Prophylactic HPV vaccines: prospects for eliminating ano-genital cancer. Br J Cancer 2007;96(9):1320−3.

[19] Harper DM, Franco EL, Wheeler CM, Moscicki AB, Romanowski B, Roteli-Martins CM, et al. Sustained efficacy up to 4.5 years of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18: follow-up from a randomised control trial. Lancet 2006;367(9518):1247–55.
[20] Paavonen J, Jenkins D, Bosch FX, Naud P, Salmeron J, Wheeler CM, et al. Efficacy of a prophylactic adjuvanted bivalent L1 virus-like-particle vaccine against infection with human papillomavirus types 16 and 18 in young women: an interim analysis of a phase III double-blind, randomised controlled trial. Lancet 2007;369(9580):2161–70.
[21] HPV vaccination recommended for 9- to 26-year-old male patients. AIDS Patient Care STDS 2010;24(8):531.
[22] Committee opinion no. 467: human papillomavirus vaccination. Obstet Gynecol 2010;116(3):800–3.
[23] Insinga RP, Dasbach EJ, Elbasha EH, Liaw KL and Barr E. Incidence and duration of cervical human papillomavirus 6, 11, 16, and 18 infections in young women: an evaluation from multiple analytic perspectives. Cancer Epidemiol Biomarkers Prev 2007;16(4):709–15.
[24] Holmes J, Hemmett L and Garfield S. The cost-effectiveness of human papillomavirus screening for cervical cancer. A review of recent modelling studies. Eur J Health Econ 2005;6(1):30–7.
[25] Lewsey JD, Leyland AH, Murray GD and Boddy FA. Using routine data to complement and enhance the results of randomised controlled trials. Health Technol Assess 2000;4(22):1–55.
[26] Birnbaum HG, Cremieux PY, Greenberg PE, LeLorier J, Ostrander JA and Venditti L. Using healthcare claims data for outcomes research and pharmacoeconomic analyses. Pharmacoeconomics 1999;16(1):1–8.
[27] Von Euler-Chelpin M, Lynge E and Rebolj M. Register-based studies of cancer screening effects. Scand J Public Health 2011;39(7 Suppl):158–64.