INSTITUTE
OF ECONOMIC STUDIES
Faculty of Social Sciences
Charles University

COST-EFFECTIVENESS OF WOMEN'S VACCINATION AGAINST HPV: RESULTS FOR THE CZECH REPUBLIC

Martina Luskova
Kseniya Bortnikova

IES Working Paper 16/2024

Institute of Economic Studies,
Faculty of Social Sciences,
Charles University in Prague

[UK FSV – IES]

Opletalova 26
CZ-110 00, Prague
E-mail : ies@fsv.cuni.cz
http://ies.fsv.cuni.cz

Institut ekonomických studií
Fakulta sociálních věd
Univerzita Karlova v Praze

Opletalova 26
110 00 Praha 1

E-mail : ies@fsv.cuni.cz
http://ies.fsv.cuni.cz

Bibliographic information:
Luškova M., Bortnikova K. (2023): " Cost-Effectiveness of Women's Vaccination Against HPV: Results for the Czech Republic " IES Working Papers 16/2024. IES FSV. Charles University.

Cost-Effectiveness of Women's Vaccination Against HPV: Results for the Czech Republic

Martina Lušková
Kseniya Bortnikova

Institute of Economic Studies, Charles University, Prague, Czech Republic
Email: martina.luskova@fsv.cuni.cz, kseniya.bortnikova@fsv.cuni.cz

April 2024

Abstract:
This paper evaluates the cost-effectiveness of vaccinating women against human papillomaviruses (HPV) in the Czech Republic, where HPV is the main cause of most cervical carcinomas. It examines the cost-effectiveness of the current reimbursement policy for HPV vaccination compared to the suggested change. Using a homogeneous multistate Markov model, we approximate transitions among states that represent the progression stages of cervical carcinoma, utilizing healthcare reimbursement data from public health insurance. The analysis reveals that increasing immunization coverage from 65.8% to 80% is cost-effective, given the threshold of 1.2 million CZK per quality-adjusted life year. Similarly, expanding the eligible age for vaccination reimbursement from 13 to include ages 13 through 15 years, while also increasing coverage, results in comparable cost-effectiveness. Despite certain limitations, our findings suggest that enhancing the immunization coverage of HPV vaccination for women is economically justified. Consequently, we advocate for the implementation of the proposed policy modifications.

JEL: I11, I13, I18, C61
Keywords: Cost-effectiveness, Markov model, HPV, vaccination, cervical carcinoma, women, Czech Republic

1 Introduction

Cervical carcinoma is one of the most commonly diagnosed cancer diseases in women worldwide (Ferlay *et al.*, 2021). In the Czech Republic, approximately eight hundred women are diagnosed with the disease annually, and about three hundred women die from it each year (Hejduk *et al.*, 2018). The majority of diagnosed cervical cancers are attributed to the Human Papillomavirus (HPV) (Mohan, 2018; Serrano *et al.*, 2015). Epidemiological data from the Global Cancer Observatory indicate that vaccination against HPV types typically associated with cervical carcinoma reduces its incidence and mortality (Ferlay *et al.*, 2021; Majek *et al.*, 2021b). According to Act No. 48/1997 Coll., on Public Health Insurance, the costs of voluntary vaccination against HPV for thirteen-year-olds are fully reimbursed for both girls and boys. However, immunisation coverage in the Czech Republic is only at 65.8%, indicating that a significant portion of eligible individuals have not been vaccinated, even though their vaccination would have been reimbursed (Hejduk *et al.*, 2018). Additionally, the average cost of treating female genital cancer is approximately 30,000 CZK per patient per year (General Health Insurance Company of the Czech Republic (VZP), 2020).

This study evaluates the cost-effectiveness of vaccinating women against human papillomavirus (HPV) in the Czech Republic. It compares the cost-effectiveness of the current reimbursement policy for HPV vaccination to a proposed policy change. We suggests two strategies to enhance vaccination coverage in the country. The first strategy involves increasing vaccination coverage through a promotional campaign under the 2021 reimbursement conditions. The second strategy extends reimbursement for vaccination to the age group of thirteen to fifteen-year-old females, concurrently aiming to boost vaccination coverage. To analyze these strategies, we developed a multi-state Markov model that simulates transitions over time among states that represent the progression of the disease. The outcomes from this model are used to calculate the incremental cost-effectiveness ratio (ICER), evaluating the cost-effectiveness of each intervention relative to the existing policy. Given that both assessed strategies demonstrate cost-effectiveness within the established threshold of 1.2 million CZK per quality-adjusted life year (QALY), this study contributes valuable insights to the body of literature on HPV vaccination programs, with a specific focus on the Czech Republic. The findings corroborate the existing literature, highlighting the significance and efficacy of such interventions in preventing cervical cancer.

It is essential to recognize that our analysis utilizes data collected before the most recent policy amendments. As such, it offers insights into the cost-effectiveness landscape under the previous vaccination reimbursement scheme. Until January 1, 2024, HPV vaccination coverage in the Czech Republic was restricted to individuals aged 13; however, a notable policy adjust-

ment has since expanded this coverage to include those aged 11 to 15. This significant change in vaccination policy is indicative of evolving strategies designed to improve public health outcomes. Crucially, the extended age range for vaccination is consistent with the policy modifications suggested by our findings, demonstrating the strategic alignment of our analysis with public health objectives. The insights provided by this analysis are vital for comprehending the effectiveness of vaccination strategies and could be invaluable for countries with similar vaccination frameworks and disease profiles.

The paper is structured as follows. Section 2 addresses the vaccination against HPV, including a description of the current state of vaccination in the Czech Republic, the status of vaccination in other countries, and a literature review of conducted cost-effectiveness analyses of HPV vaccination. Section 3 defines the methodology of Markov chains used in the survival analysis and introduces the approach for assessing cost-effectiveness. In Section 3, we present the input data. Section 5 describes the modelling process, proposed strategies, and results. Finally, Section 6 summarises the study.

2 Literature review

Vaccination against human papillomavirus has been a pivotal prevention program over the past decade (Albright & Ondrus, 2021a). Complete vaccination not only prevents cancers but also pre-cancerous changes. The vaccines, containing non-infectious viral proteins, stimulate the immune system to produce antibodies. Consequently, if exposed to the virus later, the immune system is better equipped to suppress the infection. The greatest efficacy is achieved by vaccinating both girls and boys before the onset of sexual activity, thereby reducing the likelihood of HPV exposure. However, receiving the vaccine after becoming sexually active still lowers the risk of developing HPV-related conditions (Markowitz, 2007; Majek *et al.*, 2021a,b).

In the Czech Republic, a comprehensive vaccination program against HPV has been in place. Since April 1, 2012, health insurance companies cover the cost of voluntary vaccination for girls beginning at the age of thirteen. The reimbursement applies from the time a girl turns thirteen until she reaches fourteen. Further, an amendment in Act no. 290/2017, effective August 2017, expanded this coverage to include boys, funded by public health insurance (Hejduk *et al.*, 2018). In 2017, the immunization coverage rate — the ratio of vaccinated female patients to the total population eligible — for those initiating vaccination at the age of thirteen was 65.8% across the Czech Republic. Nevertheless, this rate varied by region, ranging from 51.5% to 82.7%. These percentages reflect only those women who met the age criteria for vaccination reimbursement under public health insurance (Hejduk *et al.*, 2018).

Three medical products were utilized for HPV vaccination in 2021, with their protective scope determined by the number of HPV types they guard against (Albright & Ondrus, 2021b). Table 1 provides a detailed overview of the vaccines available in 2021. As outlined in Table 1, the maximum reimbursement from public health insurance covers the cost of the least expensive medical product. The prices and surcharges listed in Table 1 correspond to one dose of the vaccine only. The required number of doses for complete immunization varies with the age at which vaccination commences. CERVARIX may be administered according to a two-dose regimen if the first dose is given between the ages of nine and fourteen. For those first vaccinated at the age of fifteen or older, a three-dose schedule is necessary (State Institute for Drug Control (SUKL), 2021).

Table 1: Overview of vaccines available in the Czech Republic

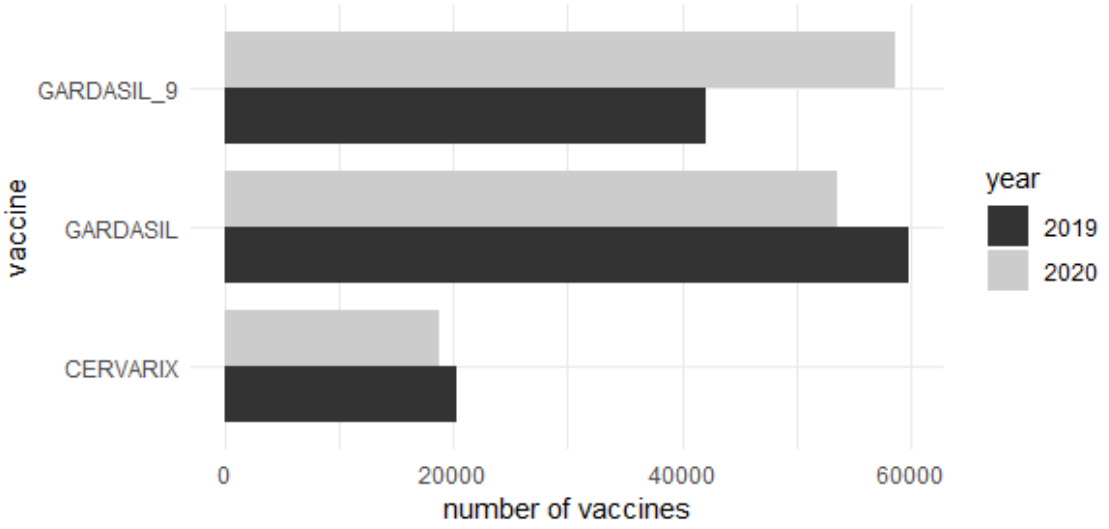
Vaccine	HPV types protection	selling price [CZK]	reimbursement [CZK]	patient surcharge [CZK]
CERVARIX	16, 18	1,765.79	1,765.79	0.00
GARDASIL	6, 11, 16, 18	3,138.54	1,765.79	1,372.75
GARDASIL 9	6, 11, 16, 18, 31, 33, 45, 52, 58	4,032.63	1,765.79	2,266.84

Note: The table displays an overview of vaccines available in the Czech Republic, their characteristics, prices, and reimbursement. Data source: State Institute for Drug Control (SUKL) (2021), HPV = human papillomavirus.

Regarding GARDASIL and GARDASIL 9, a two-dose schedule is adequate for individuals receiving their first dose between nine and thirteen years of age. If vaccination begins at the age of fourteen or later, three doses are required (State Institute for Drug Control (SUKL), 2021).

Patients in the Czech Republic have the option to select the vaccine type for their immunization. The State Institute for Drug Control (SÚKL) compiles and publishes summary information on the availability of medicinal products, derived from the monthly reports of entities authorized to distribute medicinal products in the Czech Republic, as stipulated by Article 23 of the Act on Medicinal Products. Figure 1 shows the distribution of HPV vaccines provided to medical doctors and pharmacies, which are the primary avenues through which patients access these vaccines. The data on supplies to distribution centers are not included. In 2019, GARDASIL was the most commonly chosen vaccine; however, GARDASIL 9 became the most supplied in 2020. Across both years, the fully reimbursed vaccine, CERVARIX, accounted for approximately 15% of the total (SÚKL, 2020a, 2021a). In addition to the previously mentioned vaccination program, nearly all health insurance funds in the Czech Republic provide supplementary vaccination programs and offer financial contributions to support their patients (Table 2).

Figure 1: The number of vaccines supplied to medical doctors and pharmacies



Note: The figure shows the number of vaccines supplied to medical doctors and pharmacies in the year 2019 and 2020. The supplied medical products are used to vaccinate both female and male patients, source of the data: State Institute for Drug Control (SUKL) (2019, 2020a)

Table 2: HPV vaccination programmes and financial contributions insurance funds

Insurance fund	children	adults
Ministry of the Interior Health Insurance Fund (ZPMV) (2021)	1500	1000
Coalfield Brotherhood Cash Office, a health insurance compan (RBP) (2021)	4000	4000
Czech Industry Health Insurance Fund (CPZP) (2021)	1500	1000
Occupational Health Insurance Company for Employees of the Banking, Insurance and Building Industry (OZP) (2021)	1000	1000
Skoda Employees Health Insurance Fund (ZPS) (2021)	4000	800
General Health Insurance Company of the Czech Republic (VZP) (2021)	-	-
Military Health Insurance Company of the Czech Republic (VoZP) (2021)	-	-

Note: The table displays HPV vaccination programmes and financial contributions in the maximum possible amounts of Czech insurance funds in 2021.

According to European Centre for Disease Prevention and Control (ECDC) (2021), the majority of countries within the European Union and the European Economic Area have implemented HPV vaccination programs that are recommended but not mandatory. This study discusses the vaccination strategies, including catch-up programs, in selected European countries. Catch-up vaccination is defined as the administration of vaccine doses to individuals who missed receiving them at the recommended age (National Cancer Institute (NCI), 2021).

In Austria, a non-mandatory vaccination is offered to both girls and boys aged ten to twelve. Additionally, a catch-up program is available for individuals aged thirteen to thirty, although national health system funding for the vaccination only extends up to the age of fifteen (European

Centre for Disease Prevention and Control (ECDC), 2021). Vaccination coverage rates in Austria are reported at 60% for girls and 40% for boys (Boiron *et al.*, 2016). In 2018, the age-standardised incidence rate of new cervical cancer cases in Austria was 5.5 per 100,000 women, compared to 9.9 in the Czech Republic. Moreover, the cervical cancer mortality rate in Austria was 1.7 deaths per 100,000 women, lower than the 4.0 in the Czech Republic (Bruni *et al.*, 2019), indicating that the number of deaths due to cervical cancer is almost 2.4 times higher in the Czech Republic. It is noteworthy that the immunization programs in both the Czech Republic and Austria were initiated relatively recently, in 2012 and 2014, respectively. A significant difference between the two countries is the implementation of national screening programs: Austria implemented its screening program in 1974, whereas the Czech Republic did so in 2009 (Duskova *et al.*, 2014; Austrian Institute for Health Technology Assessment, 2018).

In Germany, a gender-neutral immunisation program is available for individuals aged nine to fourteen years, complemented by a catch-up program for females up to seventeen years of age. Estimates from 2018 indicate that the incidence of newly diagnosed cases per 100,000 women stands at 7.5, with the age-standardised mortality rate at 2.2 per 100,000. Vaccination coverage among the youth is reported to be 50%, according to Damm *et al.* (2017). In contrast, Latvia has implemented a compulsory vaccination program for females at the age of twelve (European Centre for Disease Prevention and Control (ECDC), 2021), likely in response to a cervical cancer incidence rate of 25.0 cases per 100,000 women (Bruni *et al.*, 2019). It is important to note that vaccination strategies and catch-up programs are subject to annual revisions. The true impact of these immunisation programs will become clearer once the vaccinated population reaches the age at which cervical carcinoma is typically diagnosed.

Selected literature on the cost-effectiveness of HPV vaccination and cervical cancer prevention in Europe is examined. Westra *et al.* (2011) focused on the vaccination of women in the Netherlands, analyzing both health-economic and clinical impacts for women aged twelve to fifty across one-year age cohorts. A Markov transition model was employed to analyze transitions among stages, including HPV susceptibility, HPV infection, pre-cancer, cancer, and cancer mortality. Findings indicate that vaccinating women against HPV is highly cost-effective for those aged twelve to sixteen. Notably, as the age of vaccine recipients increases to twenty-five years, the cost-effectiveness decreases only gradually, suggesting significant health benefits at reasonable costs. However, the cost-effectiveness of vaccinating women older than twenty-five diminishes rapidly. It is concluded that vaccination remains cost-effective for women even after the initiation of sexual activity.

The study by Demarteau *et al.* (2013) analyzed the incremental cost-effectiveness of admin-

istering the HPV vaccine to Belgian women both before and after the onset of sexual activity. This analysis utilized a previously published, multiple-stage Markov model designed to simulate the lifetime trajectory of a cohort of women. This model accounts for the natural progression of HPV infection, the impact of regular screening, and the benefits of HPV vaccination (Debicki *et al.*, 2008). The primary scenario considered in this study involves the vaccination of twelve-year-old girls, supplemented by a catch-up program. Findings from the study indicate that the use of the bivalent HPV-16/18 vaccine, in conjunction with screening, significantly reduces the incidence of cervical cancer in Belgium when provided to women post-sexual debut. The research concludes that the bivalent HPV-16/18 vaccine remains a cost-effective intervention for women aged up to 33 to 40 years.

In the research conducted by Favato *et al.* (2012), a health economic evaluation of strategies for preventing HPV-related diseases in Italy is presented, employing a Bayesian multi-cohort Markov model. This model makes use of probability distributions derived from either observed data or the expert opinions regarding uncertain parameters. The findings indicate that the primary scenario, which involves vaccinating cohorts of women aged twelve and sixteen, as well as an expanded multi-cohort scenario that additionally encompasses age groups of eighteen and twenty-five, are deemed cost-effective. It is noteworthy that more recent studies focusing on vaccinating older women and employing Markov chain methodology have been primarily conducted in Asian countries.

3 Methodology

3.1 Survival analysis - Markov chains

Markov models are extensively utilized in health economic modeling to evaluate the cost-effectiveness of healthcare strategies and guide public policy decisions (Russell, 1996). They are particularly effective for analyzing processes with inherent uncertainties over time. These models are well-suited for scenarios where the timing and recurrence of events are critical, making them ideal for assessing strategies that are sequential or repetitive in nature (Gray *et al.*, 2011).

A Markov model employs a Markov process to simulate transitions between different states. A stochastic process, denoted as $X(t), t \in T$, is identified as a first-order Markov process if, for any sequence $t_0 < t_1 < \cdots < t_n$, the conditional probability distribution of $X(t_n)$, given the values of $X(t_0), X(t_1), \ldots, X(t_{n-1})$, relies solely on $X(t_{n-1})$. This principle, articulated in the equation below, suggests that the future state depends only on the current state and not on the

sequence of events that preceded it.

$$\begin{aligned} P[X(t_n) \leq X_n \mid X(t_{n-1}) = x_{n-1}, X(t_{n-2}) = x_{n-2}, ..., X(t_0) = x_0] \\ = P[X(t_n) \leq x_n \mid X(t_{n-1}) = x_{n-1}] \end{aligned} \tag{1}$$

Markov chains are employed to model transitions over time among states that represent different health statuses. The discrete-time process denoted by $X_k, k = 0, 1, 2, \ldots$ qualifies as a homogeneous Markov chain if, for any indices i, j and any time step $k \geq 0$, the following condition is satisfied:

$$P[X_k = j \mid X_{k-1} = i, X_{k-2} = n, \ldots, X_0 = m] = P[X_k = j \mid X_{k-1} = i] = p_{ij} \tag{2}$$

The quantity p_{ij} represents the state transition probability in a Markov process, which is notable for its time independence. This implies that the probability p_{ij} for transitioning from state i at time $k-1$ to state j at time k remains constant, irrespective of time. Therefore, the future state of the Markov process, given its current state, does not depend on its past history. This characteristic is known as the Markov property (Filipovic-Pierucci *et al.*, 2017; Ibe, 2013).

The state transition probability p_{ij} in a homogeneous Markov chain exhibits two primary properties:

1. The probability p_{ij} is confined to the interval between zero and one, expressed as:

$$0 \leq p_{ij} \leq 1$$

2. The sum of the probabilities of transitioning from state i to all other possible states j equals one, as each state i must transition to some state j in the next time step. This is represented by:

$$\sum_j p_{ij}, i = 1, 2, \ldots n$$

These principles, derived from the conditions that states are mutually exclusive and collectively exhaustive, underscore the foundational logic of Markov chain models in analyzing transitions over time.

The state transition probabilities between different states can be succinctly represented by a state transition probability matrix, denoted as P. This matrix P consists of n rows and n columns, where each entry p_{ij}, located at the intersection of the i-th row and j-th column, signifies the probability of transitioning from state i to state j. The requirement that the sum

of all entries in any given row must equal one reflects the stochastic nature of the matrix P, indicating that the total probability of moving from any state to all possible subsequent states is certain, as formalized below.

$$\begin{bmatrix} p_{11} & p_{12} & \cdots & p_{1n} \\ p_{21} & p_{22} & \cdots & p_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ p_{n1} & p_{n2} & \cdots & p_{nn} \end{bmatrix} \tag{3}$$

Assuming a finite Markov chain, the state transition probability at the n-th step, denoted as $p_{ij}(n)$, represents the probability of the system transitioning to state j after n steps, given that it is currently in state i. This probability, $p_{ij}(n)$, is determined according to the specific dynamics of the Markov process and is defined in the equation presented below.

$$p_{ij}(n) = P[X_{m+n} = j \mid X_m = i] \tag{4}$$

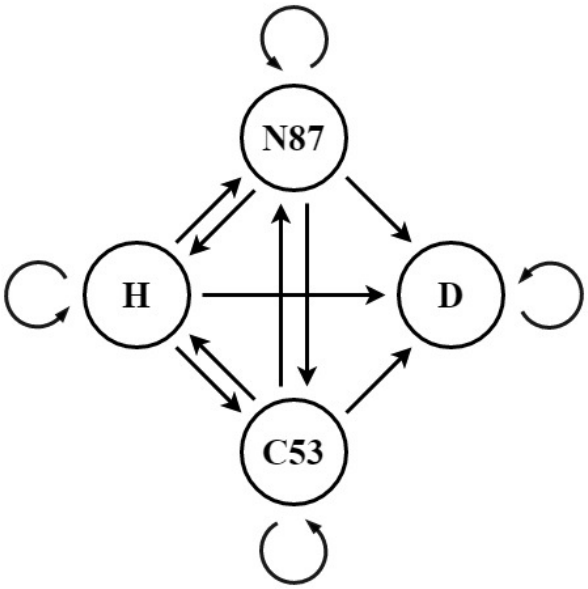
Additionally, the probability $p_{ij}(n)$ can be determined for all possible combinations of i and j. Through this approach, it is feasible to construct an N-state Markov chain matrix P^n, which encompasses all probabilities $p_{ij}(n)$. Each entry $p_{ij}(n)$, located at the intersection of the i-th row and j-th column within the matrix P^n, represents the probability of transitioning from state i to state j after n steps. The matrix P^n is derived by raising the initial transition matrix P to the n-th power, effectively multiplying P by itself n times.

$$\begin{bmatrix} p_{11}(n) & p_{12}(n) & \cdots & p_{1N}(n) \\ p_{21}(n) & p_{22}(n) & \cdots & p_{2N}(n) \\ \vdots & \vdots & \ddots & \vdots \\ p_{N1}(n) & p_{N2}(n) & \cdots & p_{NN}(n) \end{bmatrix} \tag{5}$$

A Markov chain is characterized by various types of states. A state j is considered accessible or reachable from state i if there exists some $n > 0$ such that the transition probability $p_{ij}(n) > 0$. Accessibility implies the potential of eventually transitioning into the state. When two states are mutually accessible, they are described as communicating with each other. A Markov chain is irreducible if every state in the model can communicate with every other state. A state i is recognized as an absorbing or trapping state if, once reached, the process cannot transition to any other state j, which means $p_{ij} = 0$ for every $j \neq i$. Consequently, for an absorbing state, the probability of remaining in state i, $p_{ii} = 1$. A Markov chain that contains at least one absorbing state, and from every other state there exists a nonzero probability of transitioning

to this absorbing state, is termed an absorbing Markov chain (Ibe, 2013).

Figure 2: Graphical representation of Markov model



Note: The figure shows the graphical representation of the Markov model for transition analysis. H = healthy state, N87 = cervical neoplasia, precancerous state, C53 = cervical carcinoma, cancerous state, D = dead

Figure 2 presents a graphical illustration of the developed model, featuring four mutually exclusive and collectively exhaustive states: H (Healthy), N87 (Cervical Dysplasia), C53 (Cervical Carcinoma), and D (Death). These states are delineated based on the diagnoses reported for the corresponding year, utilizing the International Classification of Diseases and Related Health Problems (ICD-10). This classification system organizes and codifies human diseases, disorders, health issues, and various symptoms, situations, or conditions (Institute of Health Information and Statistics of the Czech Republic (UZIS), 2021). Specifically, the diagnoses considered are N87, representing cervical dysplasia (a precancerous stage), and C53, indicating cervical carcinoma (a cancerous stage). The state termed "Healthy" signifies the absence of these diagnoses.The model developed for this study categorizes the health status of women into four distinct states, each representing a specific condition within the cycle of observation:

- H (Healthy) denotes the state of women who, in a given cycle, were not diagnosed with either N87 (cervical neoplasia) or C53 (cervical carcinoma) and were not deceased. The designation "H" facilitates clearer identification of this state, implying that a woman classified under "H" may still have conditions other than N87 and C53.

- N87 (Cervical Neoplasia, Precancerous State) identifies women diagnosed with cervical dysplasia, coded as N87, during a specific cycle. This state represents the precancerous stage of cervical disease.
- C53 (Cervical Carcinoma, Cancerous State) refers to women whose medical condition was identified as cervical carcinoma, coded as C53, within a particular cycle, indicating the cancerous stage of the disease.
- D (Dead) encompasses women who have passed away in a certain cycle. By definition, deceased individuals are not categorized within any of the model's "alive" states for that cycle.

3.2 Cost-effectiveness analysis

Cost-effectiveness analysis is a critical method employed for economic evaluation in healthcare. It involves comparing a new intervention with an existing treatment program, considering the incremental costs and effects of both the new and the existing treatments (Olsen, 2009). To facilitate this comparison, the Incremental Cost-Effectiveness Ratio (ICER) is utilized:

$$ICER = \frac{C_A - C_B}{E_A - E_B} = \frac{\Delta C}{\Delta E} \tag{6}$$

In this context, C_A and E_A denote the costs and effects of intervention A, respectively, while C_B and E_B correspond to the costs and effects of the existing treatment (Gray *et al.*, 2011). The effectiveness of an intervention is assessed using the metric of quality-adjusted life years (QALYs), which integrates both the length and quality of life. The QALY metric is calculated by multiplying the duration of life, expressed in years, by a health-related quality of life (HRQoL) score associated with those years:

$$QUALY = T * HRQoL \tag{7}$$

HRQoL is quantified on a utility scale ranging from zero to one, where zero signifies the utility value of the "dead" state, and one represents the utility of living in "perfect health." This metric is derived from patient surveys, such as the EQ-5D, which evaluate various dimensions including mobility, pain, mental health, among others (Prieto & Sacristan, 2003; Whitehead & Ali, 2010; Komorowski & Raffa, 2016).

To determine the cost-effectiveness of an intervention, a cost-effectiveness threshold is required. In line with the decision-making practices of SÚKL, a threshold of 1.2 million CZK

per QALY is generally considered acceptable for assessing cost-effectiveness (State Institute for Drug Control (SUKL), 2020b).

4 Data

4.1 Data for survival analysis

To assess survival duration, a data request was submitted to the National Health Information System (NZIS). This dataset comprises the number of women categorized into three health states (healthy, precancerous, and cancerous) in 2018, along with their health status in the following year. A total of 5,446,053 women are included, each precisely classified into one of the defined health states. These data facilitate the calculation of transition probabilities between states, encompassing the probability of mortality. Further details about the requested data are available in Appendix A.

The data provider, ÚZIS, highlighted limitations due to the reliance on patient identification from health care reimbursement reports within the public health insurance system. This dataset is not derived from a clinical database, and it excludes cases not covered by public health insurance. When comparing the provided data with official statistics on the incidence, prevalence, and mortality rates of cervical carcinoma in the Czech Republic, discrepancies were noted. These differences are primarily attributed to the distinction between clinical registries and reimbursement data. Other potential sources of inaccuracy include errors in the reporting of diagnoses, the omission of patients who missed their check-ups during the observation period (thus not appearing in the reimbursement data), and the possibility of multiple diagnoses for a single patient. Despite these challenges, the focus of this study is on evaluating the costs and financial implications of the current situation versus the proposed change. Therefore, the data on actual reimbursed costs are deemed representative for this purpose. Table 3 and Table 4 present the derived transition matrices for unvaccinated and vaccinated women, respectively.

4.2 Health-related quality of life

Health-related quality of life (HRQoL) is assigned to each health state within the Markov model, with values ranging from zero to one. HRQoL values for the precancerous and cancerous stages are derived from literature. The state N87, representing the precancerous stage, has HRQoL values ranging from 0.87 to 0.91, depending on the progression of precancerous conditions. State C53, indicative of cervical carcinoma, sees HRQoL values vary from 0.48 to 0.76 based on the

Table 3: Transition matrix for unvaccinated

	H	N87	C53	D
H	0.9740	0.0150	0.0010	0.0100
N87	0.5510	0.4450	0.0020	0.0020
C53	0.2620	0.0270	0.6550	0.0560
D	0.0000	0.0000	0.0000	1.0000

Note: The table shows the transition matrix for unvaccinated women. H = healthy state, N87 = cervical neoplasia, precancerous state, C53 = cervical carcinoma, cancerous state, D = dead

Table 4: Transition matrix for vaccinated

	H	N87	C53	D
H	0.9884	0.0015	0.0001	0.0100
N87	0.5510	0.4450	0.0020	0.0020
C53	0.2620	0.0270	0.6550	0.0560
D	0.0000	0.0000	0.0000	1.0000

Note: The table shows the transition matrix for vaccinated women. H = healthy state, N87 = cervical neoplasia, precancerous state, C53 = cervical carcinoma, cancerous state, D = dead

stage of carcinoma (local, regional, distant) (Elbasha *et al.*, 2007; Boiron *et al.*, 2016). For this analysis, HRQoL for N87 and C53 has been standardized to 0.89 and 0.6, respectively. The HRQoL for state D, representing death, is set to zero. Although state H, denoting healthiness, is assigned an HRQoL of one, it is important to clarify that this does not equate to "perfect health." The rationale behind this assignment is that the average HRQoL for the general population without conditions would likely be lower than that for state N87 (Elbasha *et al.*, 2007), suggesting an incongruity where being in a precancerous state would seemingly be preferred over being free from C53 or N87 in terms of quality of life. This is a simplification for modeling purposes.

4.3 Costs of vaccination and vaccine efficacy

For this analysis, the vaccination costs encompass solely the direct health-care-related expenses, including the costs of medical products and their administration. These costs vary depending on the age at which vaccination is initiated. The total vaccination costs are calculated by summing the costs of the medical products and the administrative expenses. The price of the medical product is based on the least expensive option available. Administrative costs for the vaccine account for both the vaccine's application and a general examination conducted by a medical

doctor. These costs are determined in accordance with Regulation No. 269/2019 Coll., which amends Regulation No. 134/1998 Coll. This regulation issues a list of medical services with associated point values, as further amended by Regulation No. 428/2020 Coll. This latter regulation specifies the point values, payment amounts for reimbursed services, and regulatory limits for the year 2021. Table 5 outlines the total vaccination costs for both two- and three-dose schedules.

Table 5: Costs associated with vaccination

Price per one dose of vaccine	1,765.79 CZK
Price of application and examination per one dose	263.32 CZK
Total costs of administration per one dose	2,029.11 CZK
Total costs of administration of two doses	4,058.22 CZK
Total costs of administration of three doses	6,087.33 CZK

Note: The table displays the decomposition of costs associated with vaccination. Data source: Ministry of Health, CR (2019, 2020); State Institute for Drug Control (SUKL) (2021). Point values of application of the vaccine and general examination are 138 and 89 points respectively. The value of a point is 1.16 CZK (Ministry of Health, CR, 2019, 2020).

Vaccine efficacy against the precancerous stage is derived from the summary of product characteristics for each vaccine, as published by State Institute for Drug Control (SUKL) (2021). The reported efficacy of vaccines against precancerous stages varies between 78% and 100%, encompassing data from all three vaccines. Due to the extended period required for the development of cervical carcinoma, efficacy data against the cancerous stage are not yet available. Based on information from European Medicines Agency (2007, 2008, 2015), CERVARIX was approved for use in 2007, GARDASIL in 2006, and GARDASIL 9 in 2015. For the purposes of this analysis, we have assumed a vaccine efficacy of 90%. Additionally, a sensitivity analysis is conducted using an efficacy rate of 80% to assess potential variations in outcomes.

4.4 Costs assigned to the specific states

The costs associated with specific health states are derived from the 2019 Yearbook of VZP, which covered nearly 6 million insured individuals in 2019, accounting for about 60% of the insured population (General Health Insurance Company of the Czech Republic (VZP), 2020). Therefore, the VZP insured cohort serves as a representative sample of the Czech Republic's population.

For the H (healthy) state, costs are determined based on the median of the average total annual healthcare expenses for five-year age groups, ranging from ten to fourteen years to eighty

to eighty-four years, amounting to 22,270 CZK. The costs for the D (dead) state are assumed to be zero, reflecting no ongoing healthcare costs after death. The costs for the N87 state (precancerous condition) are calculated by adding the average costs for diagnoses N80 – N98, as reported in the 2019 Yearbook, to the costs for the H state, resulting in a total of 22,270 CZK + 1,621.34 CZK = 23,891.34 CZK. Similarly, the costs for the C53 state (cervical carcinoma) are derived by adding the average costs for diagnoses C51 – C58 to the costs for the H state, yielding a total of 22,270 CZK + 30,113.38 CZK = 52,383.38 CZK (General Health Insurance Company of the Czech Republic (VZP), 2020). Table 6 provides a summary of the average total annual costs for each state, the potential transitions among states, and the health-related quality of life (HRQoL) values assigned to each.

Table 6: Average total annual costs assigned to each state

State	In	Out	HRQoL	Costs
H	H, N87, C53	H, N87, C53, D	1.00	22,270.00 CZK
N87	H, N87, C53	H, N87, C53, D	0.89	23,891.34 CZK
C53	H, N87, C53	H, N87, C53, D	0.67	52,383.38 CZK
D	H, N87, C53, D	D	0.00	0.00 CZK

Note: The table displays the states, possible transitions among them, assigned Health-related quality of life, and average total annual costs. The costs are per cycle and person. Data source: General Health Insurance Company of the Czech Republic (VZP) (2020); Elbasha *et al.* (2007); Boiron *et al.* (2016), H = healthy, N87 = precancerous state, C53 = cancerous state, D = dead.

The total costs assigned to states N87 (precancerous condition) and C53 (cervical carcinoma) may not fully encapsulate the expenses associated with these specific stages, as the costs for these diagnoses are already factored into the average total costs. It's important to note that the prevalence of women diagnosed with these conditions is relatively low in comparison to the total number of women insured by VZP. Additionally, the presented costs are not for individual diagnoses but rather for a broader group of related diagnoses. Despite this, it is posited that the costs associated with specific diagnoses are likely to be similar to those for the broader group, making this approach a valid approximation for the purposes of the analysis.

5 Results

5.1 Modelling process

To conduct a cost-effectiveness analysis, the costs and benefits of various vaccination strategies are calculated. The Incremental Cost-Effectiveness Ratio is utilized to evaluate the cost-effectiveness of each alternative relative to the current approach. Benefits are quantified by

multiplying the length of survival by the Health-Related Quality of Life, with survival duration derived from transition analysis. This analysis provides detailed insights into the duration of persistence in each health state, which, in turn, informs the cost calculations for these states. Assumptions regarding the costs associated with each state are detailed in Table 6.

In the proposed model, the cohort comprises thirteen-year-old girls who initially occupy the healthy state (H), reflecting the age at which health insurance companies in the Czech Republic fully reimburse HPV vaccination. The cohort size is established at 50,000 women to reflect the age composition of the population (Czech Statistical Office (CSU), 2020a). The model spans 68 cycles, corresponding to the average life expectancy of 81 years for Czech women (Czech Statistical Office (CSU), 2020b), subtracting the entry age of thirteen. Each cycle in the model equates to one year. In line with standard practices for cost-effectiveness analysis, a 3% discount rate is applied to both costs and effects. Additionally, sensitivity analyses are conducted using discount rates of 0% and 5% to evaluate the impact of these rates on the outcomes (State Institute for Drug Control (SUKL), 2020b).

To evaluate the benefits of HPV vaccination, two state-transition matrices are required. The matrix for unvaccinated women is derived from data supplied by UZIS, capturing state transitions for the general population, which includes both vaccinated and unvaccinated women. Given that HPV vaccination commenced in the Czech Republic in 2012, the impact of vaccinated women on the number of diagnosed cases and, consequently, on transition probabilities is considered marginal. This marginal impact is attributed to the extensive period required for the development of pre(cancerous) conditions. For vaccinated women, the matrix is adjusted by reducing the probability of transitioning from state H to states N87 and C53 by 90%, reflecting the assumed vaccine efficacy. To ensure the probabilities in the row sum up to one, the adjusted amounts are reallocated to the probability of remaining in state H. The probability of transitioning from state H to state D remains unchanged. These matrices depict the life-long transition probabilities for a cohort of women, tracking their movement among the states over 68 cycles, equivalent to years. The transition matrices for unvaccinated and vaccinated women are detailed in Table 3 and Table 4, respectively.

In each cycle, women residing in states H, N87, and C53 are credited with one year of life, whereas no years are added for those in state D. The accumulated years of life in each state, for every cycle, are then multiplied by the respective HRQoL scores, resulting in QALY as the measure of effect. The total costs are subsequently calculated by multiplying the duration of stay in each state by the corresponding state's total annual cost.The model was developed using the R software, employing the *heemod* package, which is specifically designed for constructing

Markov models for health economic evaluations (Filipovic-Pierucci *et al.*, 2017).

5.2 Proposed strategies

This subchapter outlines two vaccination strategies devised by the author to enhance HPV immunization coverage.

Strategy 1 aims to increase the vaccination rate among thirteen-year-olds from the current 65.8% (Hejduk *et al.*, 2018) to 80%. The calculation of costs and QALYs is adjusted based on the proportion of vaccinated women, with vaccination expenses incorporated into the total costs of the proposed strategy. Detailed calculations can be found in Appendix B. The anticipated boost in vaccination rates is attributed to a promotional campaign, estimated to cost 100,000,000 CZK. This figure is considered a high estimate for an HPV vaccination campaign, but it emphasizes the need for ongoing efforts to sustain increased coverage. The actual campaign costs are expected to be lower.

Strategy 2 suggests extending vaccination to include women aged thirteen to fifteen and aims to achieve a vaccination coverage of 80%. Unlike the first strategy, this approach necessitates a different model for the baseline scenario. Initially, 50,000 women are in state H, with an additional 50,000 women entering the model at the beginning of the first and second cycles, simulating a scenario where only thirteen-year-olds receive vaccination. This reflects the current practice. The costs include immediate expenses and those discounted for future cycles, representing the present vaccination strategy. Conversely, this strategy models a single cohort of 150,000 women, evenly divided among thirteen-, fourteen-, and fifteen-year-olds, with a third requiring three vaccine doses and the rest needing two. Cost calculations based on this setup are provided in Appendix C. Given the larger target group, the campaign's budget is set at 300,000,000 CZK, mirroring the cost for addressing a single age cohort but on a larger scale. This amount signifies the cost ceiling, with actual expenditures likely to be lower.

5.3 Cost-effectiveness results

Table 7 presents the ICER calculations for the first strategy, applying various discount rates to both costs and QALYs. As indicated in Table 7, Panel A, the ICER values fall below the cost-effectiveness threshold of 1.2 million CZK/QALY, marking the intervention as cost-effective with an ICER of 327,868 CZK/QALY using a 3% discount rate. Notably, the intervention remains cost-effective under alternative discount rates of 0% and 5%, chosen for sensitivity analysis in alignment with standard cost-effectiveness assessment methods (State Institute for Drug Control (SUKL), 2020b). Given the established vaccine efficacy against precancerous

stages, the analysis was reiterated under the assumption of an 80% vaccine efficacy. Table 7, Panel B, demonstrates that the intervention retains its cost-effectiveness relative to the 1.2 million CZK/QALY threshold, even with reduced vaccine efficacy.

Table 7: ICER computation - Strategy 1

Discount rate	0%	3%	5%
Panel A: 90% vaccine efficacy			
Δ C [CZK]	71,907,936	105,312,653	113,545,063
Δ QALY	487	321	252
ICER [CZK/QALY]	147,637	327,868	450,081
Panel B: 80% vaccine efficacy			
Δ C [CZK]	78,368,191	107,979,623	115,277,062
Δ QALY	432	285	224
ICER [CZK/QALY]	181,483	379,073	515,435

Note: The table displays ICER computation for 90% and 80% vaccine efficacy. The campaign costs were added to the total costs of Strategy 1 and thus are included in the ICER calculation. C = costs, QUALY = Quality-adjusted life year, ICER = Incremental cost-effectiveness ratio.

Strategy 2 also demonstrates cost-effectiveness in the base-case analysis, using a 3% discount rate, with an ICER of 50,877 CZK/QALY. Table 8, Panel A, illustrates the ICER values across different discount rates, while Panel B assesses the strategy under the assumption of 80% vaccine efficacy. In both cases, the strategy remains cost-effective when evaluated against the cost-effectiveness threshold of 1.2 million CZK/QALY. Given the ICER values for both strategies, we recommend a policy shift regarding HPV vaccination in the Czech Republic. Expanding reimbursement for vaccination to include women aged thirteen to fifteen and/or enhancing vaccination coverage would yield significant health benefits.

6 Conclusion

This paper evaluates the cost-effectiveness of HPV vaccination for women in the Czech Republic, where HPV is identified as the primary cause of the majority of cervical cancer cases. Albright & Ondrus (2021a) highlights the significance of HPV vaccination as a pivotal global prevention program over the past decade.To determine cost-effectiveness, we simulate the survival and health state transitions of a cohort of women. A multistage homogeneous Markov model is employed, delineating four health states: cervical precancerous condition, cervical cancer, death, and healthy living without cancer or precancerous conditions. Assigned to each state are the

Table 8: ICER computation - Strategy 2

Discount rate	0%	3%	5%
Panel A: 90% vaccine efficacy			
Δ C [CZK]	306,156,596	696,091,339	795,551,553
Δ QALY	1,743	13,682	16,502
ICER [CZK/QALY]	175,688	50,877	48,209
Panel B: 80% vaccine efficacy			
Δ C [CZK]	325,921,761	704,480,901	801,796,162
Δ QALY	1,571	13,564	16,383
ICER [CZK/QALY]	207,510	51,937	48,941

Note: The table displays ICER computation for 90% and 80% vaccine efficacy. The campaign costs were added to the total costs of Strategy 2 and thus are included in the ICER calculation. C = costs, QUALY = Quality-adjusted life year, ICER = Incremental cost-effectiveness ratio.

total average costs per cycle and the health-related quality of life values. Transition probabilities between all possible states are calculated using data from UZIS. The outcomes of the model, encompassing total costs and quality-adjusted life years (QALYs), facilitate the calculation of the incremental cost-effectiveness ratio (ICER).

The Incremental Cost-Effectiveness Ratio (ICER) serves as a comprehensive metric for evaluating the cost-effectiveness of a health intervention relative to the existing approach. In this study, the author proposes two targeted strategies. The first strategy aims to enhance vaccination coverage among thirteen-year-old girls, for whom vaccination costs are entirely covered by health insurance. This increase in coverage is anticipated to be supported by a vaccination promotion campaign. The second strategy suggests extending vaccination coverage, with full reimbursement, to include girls aged thirteen to fifteen, alongside a supportive vaccination campaign. Both proposed strategies are deemed cost-effective when measured against the established cost-effectiveness threshold of 1.2 million CZK/QALY, aligning with findings from the existing literature.

While the findings align with existing literature, the analysis encounters several limitations. Firstly, challenges were faced in acquiring the necessary data. The information sourced from the NZIS does not accurately capture the epidemiology of cervical cancer and cervical precancerous conditions. A more detailed modeling of transitions among states would benefit from clinical data. Furthermore, the absence of certain cost data could have enhanced the precision of the analysis. Despite these discrepancies, the data are considered representative for assessing the financial impact of the current situation versus the proposed change, focusing mainly on cost-related outcomes. Secondly, the analysis does not account for the decline in Health-Related

Quality of Life following the disease's resolution. A critical assumption is that a woman free from either the precancerous or cancerous stages of cervical carcinoma possesses an HRQoL equivalent to perfect health. Consequently, preventing the disease would also prevent a significant drop in HRQoL. However, in reality, the prevented decrease in HRQoL would likely not be as substantial. The third and potentially most consequential limitation of this study is that, until January 1, 2024, HPV vaccination coverage in the Czech Republic was confined to individuals aged 13. A recent policy alteration has expanded this coverage to include ages 11 to 15. This significant shift in vaccination policy reflects evolving strategies aimed at improving public health outcomes. Notably, the expanded age range for vaccination aligns with the proposed policy change based on the findings of our analysis.

In conclusion, despite encountering challenges in acquiring precise epidemiological and clinical data and the assumptions concerning Health-Related Quality of Life changes, this study provides meaningful contributions and tackles an essential issue. Evaluating the cost-effectiveness of HPV vaccination for women in the Czech Republic illuminates the possible advantages of various vaccination strategies and lays the groundwork for policy advice. It's important to acknowledge that this analysis utilizes data collected before the most recent policy amendments, offering insights into the cost-effectiveness landscape under the former vaccination reimbursement scheme.The analysis remains crucial for understanding the efficacy of vaccination strategies and may offer valuable insights for policymakers and, notably, may be applicable to other nations confronting similar public health dilemmas. This research serves as a valuable resource for guiding informed decisions in public health policy, particularly in the domain of cervical cancer prevention.

References

Albright, M. & J. Ondrus (2021a): "Očkování proti HPV | HPV College." `https://www.hpv-college.cz/ockovani-proti-hpv`, Last accessed on 2021-07-01.

Albright, M. & J. Ondrus (2021b): "Prevence | HPV College." `https://www.hpv-college.cz/prevence`, Last accessed on 2021-07-06.

Austrian Institute for Health Technology Assessment (2018): "Prevention of cervical cancer in Austria – Implementation of HPV testing into the existing screening programme." `https://aihta.at/page/praevention-zervix-karzinom-implementierung-eines-hpv-screenings/en`, Last accessed on 2021-07-11.

Boiron, L., E. Joura, N. Largeron, B. Prager, & M. Uhart (2016): "Estimating the cost-effectiveness profile of a universal vaccination programme with a nine-valent HPV vaccine in Austria." *BMC Infectious Diseases* **16(1)**: p. 153.

Bruni, L., G. Albero, B. Serrano, M. Mena, D. Gomez, J. Munoz, X. Bosch, & S. de Sanjose (2019): "Human Papillomavirus and Related Diseases in Europe: Summary Report."

Coalfield Brotherhood Cash Office, a health insurance compan (RBP) (2021): "Preventivní a bonusový program." `https://www.rbp213.cz/pojistenci/bonusy-a-prevence/preventivni-a-bonusovy-program/a-55/`, Last accessed on 2021-07-09.

Czech Industry Health Insurance Fund (CPZP) (2021): "Preventivní programy." https://www.cpzp.cz/preventivni-programy, Last accessed on 2021-07-09.

Czech Statistical Office (CSU) (2020a): "Věkové složení obyvatelstva - 2020." https://www.czso.cz/csu/czso/vekove-slozeni-obyvatelstva-2020, Last accessed on 2021-07-24.

Czech Statistical Office (CSU) (2020b): "Úmrtnostní tabulky za ČR, regiony soudržnosti a kraje - 2019–2020." https://www.czso.cz/csu/czso/umrtnostni-tabulky-za-cr-regiony-soudrznosti-a-kraje-i09aftm7w4, Last accessed on 2021-07-24.

Damm, O., J. Horn, R. T. Mikolajczyk, M. E. E. Kretzschmar, A. M. Kaufmann, Y. Deleré, B. Ultsch, O. Wichmann, A. Krämer, & W. Greiner (2017): "Cost-effectiveness of human papillomavirus vaccination in Germany." *Cost Effectiveness and Resource Allocation* **15(1)**: p. 18.

Debicki, D., N. Ferko, N. Demarteau, S. Gallivan, C. Bauch, A. Anonychuk, L. Mantovani, S. Capri, C.-Y. Chou, B. Standaert, & L. Annemans (2008): "Comparison of detailed and succinct cohort modelling approaches in a multi-regional evaluation of cervical cancer vaccination." *Vaccine* **26**: pp. F16–F28.

Demarteau, N., G. Van Kriekinge, & P. Simon (2013): "Incremental cost-effectiveness evaluation of vaccinating girls against cervical cancer pre- and post-sexual debut in Belgium." *Vaccine* **31(37)**: pp. 3962–3971.

Duskova, J., A. Bekova, V. Dvorak, O. Majek, & L. Dusek (2014): "Results of the czech national cervical cancer screening programme." *Klinicka Onkologie: Casopis Ceske a Slovenske Onkologicke Spolecnosti* **27**: pp. 79–86.

Elbasha, E. H., E. J. Dasbach, & R. P. Insinga (2007): "Model for Assessing Human Papillomavirus Vaccination Strategies." *Emerging Infectious Diseases* **13(1)**: pp. 28–41.

European Centre for Disease Prevention and Control (ECDC) (2021): "Human Papillomavirus Infection: Recomended vaccinations." https://vaccine-schedule.ecdc.europa.eu/Scheduler/ByDisease?SelectedDiseaseId=38&SelectedCountryIdByDisease=-1, Last accessed on 2021-07-11.

European Medicines Agency (2007): "Medicines: Gardasil." https://www.ema.europa.eu/en/medicines/human/EPAR/gardasil, Last accessed on 2021-07-23.

European Medicines Agency (2008): "Medicines: Cervarix." https://www.ema.europa.eu/en/medicines/human/EPAR/cervarix, Last accessed on 2021-07-23.

European Medicines Agency (2015): "Medicines: Gardasil 9." https://www.ema.europa.eu/en/medicines/human/EPAR/gardasil-9, Last accessed on 2021-07-23.

Favato, G., G. Baio, A. Capone, A. Marcellusi, S. Costa, G. Garganese, M. Picardo, M. Drummond, B. Jonsson, G. Scambia, P. Zweifel, & F. S. Mennini (2012): "Novel health economic evaluation of a vaccination strategy to prevent HPV-related diseases: the BEST study." *Medical Care* **50(12)**: pp. 1076–1085.

Ferlay, J., M. Ervik, F. Lam, M. Laversanne, M. Colombet, L. Mery, M. Pineros, A. Znaor, I. Soerjomataram, & F. Bray (2021): "Global cancer observatory: Cancer today. lyon, france: International agency for research on cancer. data visualization tools for exploring the global cancer burden." http://gco.iarc.fr/today/home, Last accessed on 2021-07-26.

Filipovic-Pierucci, A., K. Zarca, & I. Durand-Zaleski (2017): "Markov Models for Health Economic Evaluations: The R Package heemod." DOI: https://doi.org/10.48550/arXiv.1702.03252.

General Health Insurance Company of the Czech Republic (VZP) (2020): "VZP ČR Ročenka 2019." https://media.vzpstatic.cz/media/Default/rocenky/rocenka_vzp_2019.pdf, Last accessed on 2021-06-06.

General Health Insurance Company of the Czech Republic (VZP) (2021): "Výhody a příspěvky." https://www.vzp.cz/pojistenci/vyhody-a-prispevky, Last accessed on 2021-07-09.

Gray, A. M., P. M. Clarke, J. L. Wolstenholme, & S. Wordsworth (2011): *Applied Methods of Cost-effectiveness Analysis in Healthcare*. OUP Oxford. ISBN: 978-0-19-922728-0.

Hejduk, K., L. Mandelova, O. Ngo, R. Chloupkova, T. Vyskot, J. Gregor, & O. Majek (2018): "Národní screeningové centrum ÚZIS ČR: Očkování dívek i chlapců proti lidským papilomavirům (HPV) zabraňuje vzniku řady vážných nádorových onemocnění a chrání lidské životy." https://nsc.uzis.cz/index.php?pg=aktuality&aid=29, Last accessed on 2021-07-02.

Ibe, O. (2013): *Markov Processes for Stochastic Modeling.* Elsevier insights. Elsevier Science. ISBN: 978-0-12-407795-9.

Institute of Health Information and Statistics of the Czech Republic (UZIS) (2021): "MKN-10 klasifikace diagnóz." https://mkn10.uzis.cz/, Last accessed on 2021-07-22.

Komorowski, M. & J. Raffa (2016): "Markov Models and Cost Effectiveness Analysis: Applications in Medical Research." In "Secondary Analysis of Electronic Health Records," pp. 351–367. Springer International Publishing.

Majek, O., V. Dvorak, O. Ngo, L. Dusek, J. Muzik, L. Snajdrova, & K. Hejduk (2021a): "Cervix.cz – program cervikálního screeningu v České republice: Prevence a screening rakoviny děložního čípku." https://www.cervix.cz/cs/verejnost/prevence-a-screening-rakoviny-delozniho-cipku/, Last accessed on 2021-07-01.

Majek, O., V. Dvorak, O. Ngo, L. Dusek, J. Muzik, L. Snajdrova, & K. Hejduk (2021b): "Cervix.cz – Program cervikálního screeningu v České republice: Rakovina děložního čípku." https://www.cervix.cz/cs/verejnost/rakovina-delozniho-cipku/, Last accessed on 2021-06-25.

Markowitz, L. E. (2007): "HPV Vaccines—Prophylactic, Not Therapeutic." *JAMA* **298(7)**: pp. 805–806.

Military Health Insurance Company of the Czech Republic (VoZP) (2021): "Příspěvky na prevenci." https://www.vozp.cz/prispevky-na-prevenci, Last accessed on 2021-07-09.

Ministry of Health, CR (2019): "Regulation No. 269/2019 Coll. amending regulation no. 134/1998 coll., which issues a list of medical procedures with point values, as amended."

Ministry of Health, CR (2020): "Regulation No. 428/2020 Coll. setting point values, reimbursement levels for covered services and regulatory limits for 2021."

Ministry of the Interior Health Insurance Fund (ZPMV) (2021): "Program prevence infekčních onemocnění - očkování." https://www.zpmvcr.cz/pojistenci/bonusy-na-prevenci/program-prevence-infekcnich-onemocneni-ockovani, Last accessed on 2021-07-09.

Mohan, H. (2018): *Textbook of pathology.* Jaypee Brothers Medical Publishers. ISBN: 978-93-5270-547-4.

National Cancer Institute (NCI) (2021): "Definition of catch-up vaccination - NCI Dictionary of Cancer Terms." https://www.cancer.gov/publications/dictionaries/cancer-terms/def/catch-up-vaccination, Last accessed on 2021-07-11.

Occupational Health Insurance Company for Employees of the Banking, Insurance and Building Industry (OZP) (2021): "Benefity OZP." https://www.ozp.cz/benefity/benefityozp, Last accessed on 2021-07-09.

Olsen, J. A. (2009): *Principles in health economics and policy.* Oxford University Press.

Prieto, L. & J. A. Sacristan (2003): "Problems and solutions in calculating quality-adjusted life years (QALYs)." *Health and Quality of Life Outcomes* **1**: p. 80.

Russell, L. B. (1996): "The Role of Cost-effectiveness Analysis in Health and Medicine." *JAMA: The Journal of the American Medical Association* **276(14)**: p. 1172.

Serrano, B., S. de Sanjose, S. Tous, B. Quiros, N. Munoz, X. Bosch, & L. Alemany (2015): "Human papillomavirus genotype attribution for HPVs 6, 11, 16, 18, 31, 33, 45, 52 and 58 in female anogenital lesions." *European Journal of Cancer* **51(13)**: pp. 1732–1741.

Skoda Employees Health Insurance Fund (ZPS) (2021): "Příspěvky na očkování." http://www.zpskoda.cz/pro-pojistence/zdravotni-programy-2021/prispevky-na-ockovani, Last accessed on 2021-07-09.

State Institute for Drug Control (SUKL) (2019): "Dodávky léčiv - se zaměřením na léčivé přípravky." https://www.sukl.cz/2019, Last accessed on 2021-07-08.

State Institute for Drug Control (SUKL) (2020a): "Dodávky léčiv - se zaměřením na léčivé přípravky." https://www.sukl.cz/2020, Last accessed on 2021-07-08.

State Institute for Drug Control (SUKL) (2020b): "Postup pro posuzování analýzy nákladové efektivity,." Methodological procedure SP-CAU-028-W, Last accessed on 2021-07-24.

State Institute for Drug Control (SUKL) (2021): "Databáze léků." https://www.sukl.cz/modules/medication/search.php, Last accessed on 2021-07-07.

Westra, T. A., M. H. Rozenbaum, R. M. Rogoza, H. W. Nijman, T. Daemen, M. J. Postma, & J. C. Wilschut (2011): "Until Which Age Should Women Be Vaccinated Against HPV Infection? Recommendation Based on Cost-effectiveness Analyses." *The Journal of Infectious Diseases* **204(3)**: pp. 377–384.

Whitehead, S. J. & S. Ali (2010): "Health outcomes in economic evaluation: the QALY and utilities." *British Medical Bulletin* **96(1)**: pp. 5–21.

A Request for the data from NZIS

1. The number of women who had a reported diagnosis of C53 at any time during the year 2018 and at the same time did not have a reported diagnosis of N87. Only women who did not die in 2018 and were born before 2018 would be identified.

    - The number of women from part 1., who had a reported diagnosis of C53 in 2019 as well. At the same time, they did not have a reported diagnosis of N87 and did not die in 2019.
    - The number of women from part 1., who had a reported diagnosis of N87 in 2019 and did not die in 2019. (These women may or may not have a reported diagnosis of C53 in 2019.)
    - The number of women from part 1., who did not have a reported diagnosis of either C53 or N87 in 2019 and did not die in 2019.
    - The number of women from part 1., who died in 2019.

    Each woman from part 1., would thus fall into just one of the above sub-points.

2. The number of women who had a reported diagnosis of N87 at any time during the year 2018 and at the same time did not have a reported diagnosis of C53. Only women who did not die in 2018 and were born before 2018 would be identified.

    - The number of women from part 2., who had a reported diagnosis of N87 in 2019 as well. At the same time, they did not have a reported diagnosis of C53 and did not die in 2019.
    - The number of women from part 2., who had a reported diagnosis of C53 in 2019 and did not die in 2019. (These women may or may not have a reported diagnosis of N87 in 2019.)
    - The number of women from part 2., who did not have a reported diagnosis of either C53 or N87 in 2019 and did not die in 2019.
    - The number of women from part 2., who died in 2019.

    Each woman from part 2., would thus fall into just one of the above sub-points.

3. The number of women who did not have a reported diagnosis of either N87 or C53. Only women who did not die in 2018 and were born before 2018 would be identified.

- The number of women from part 3., who had a reported diagnosis of N87 in 2019. At the same time, they did not have a reported diagnosis of C53 in 2019 and did not die in 2019.
- The number of women from part 3., who had a reported diagnosis of C53 in 2019 and did not die in 2019. (These women may or may not have a reported diagnosis of N87 in 2019.)
- The number of women from part 3., who did not have a reported diagnosis of either C53 or N87 in 2019 and did not die in 2019.
- The number of women from part 3., who died in 2019.

Each woman from part 3., would thus fall into just one of the above sub-points.

B Calculations of costs and QALY for strategy 1

Table B.1: Total costs and QALY of the whole cohort assuming the efficacy of the vaccine to be 90%

	90%	Costs 0%	QALY 0%	Costs 3%	QALY 3%	Costs 5%	QALY 5%
Calculation basis							
0% VACC		55,302	2,459,371	26,009	1,157,091	18,248	812,018
100% VACC		54,901	2,462,801	25,843	1,159,353	18,140	813,795
Current setup							
Vaccinated	0.658	36,125	1,620,523	17,005	762,854	11,936	535,477
Unvaccinated	0.342	18,913	841,105	8,895	395,725	6,241	277,710
SUBTOTAL		55,038	2,461,628	25,900	1,158,579	18,177	813,187
VACC	32,900	134		134		134	
TOTAL		55,172		26,034		18,310	
Intervention							
Vaccinated	0.8	43,921	1,970,241	20,675	927,482	14,512	651,036
Unvaccinated	0.2	11,060	491,874	5,202	231,418	3,650	162,404
SUBTOTAL		54,981	2,462,115	25,877	1,158,901	18,161	813,440
VACC	40,000	162		162		162	
TOTAL		55,144		26,039		18,329	

Note: The table displays the calculation of total costs and QALY for strategy 1 as well as for the current situation. The campaign costs were added when calculating the ICER and, thus are omitted here. 90% vaccine efficacy was assumed. The percentages of vaccinated and unvaccinated women were calculated proportionally according to the top part of the table representing 0% and 100% vaccination coverage. The vaccination costs were added.

Table B.2: Total costs and QALY of the whole cohort assuming the efficacy of the vaccine to be 80%

	80%	Costs 0%	QALY 0%	Costs 3%	QALY 3%	Costs 5%	QALY 5%
Calculation basis							
0% VACC		55,302	2,459,371	26,009	1,157,091	18,248	812,018
100% VACC		54,947	2,462,412	25,862	1,159,097	18,152	813,593
Current setup							
Vaccinated	0.658	36,155	1,620,267	17,017	762,686	11,944	535,344
Unvaccinated	0.342	18,913	841,105	8,895	395,725	6,241	277,710
SUBTOTAL		55,068	2,461,372	25,912	1,158,411	18,185	81,3055
VACC	32,900	134		134		134	
TOTAL		55,202		26,046		18,318	
Intervention							
Vaccinated	0.8	43,957	1,969,930	20,690	927,278	14,522	650,875
Unvaccinated	0.2	11,060	491,874	5,202	231,418	3,650	162,404
SUBTOTAL		55,018	2,461,804	25,892	1,158,696	18,171	813,278
VACC	40,000	162		162		162	
TOTAL		55,180		26,054		18,334	

Note: The table displays the calculation of total costs (in millions) and QALY for strategy 1 as well as for the current situation. The campaign costs were added when calculating the ICER and, thus are not included here. 80% vaccine efficacy was assumed. The percentages of vaccinated and unvaccinated women were calculated proportionally according to the top part of the table representing 0% and 100% vaccination coverage. The vaccination costs were added.

C Calculations of costs and QALY for strategy 2

Table C.1: Total costs and QALY for current setting assuming 90% vaccine efficacy

	90%	Costs 0%	QALY 0%	Costs 3%	QALY 3%	Costs 5%	QALY 5%
Calculation basis: 13 only							
Inflow	I	6,085	272,367	5,815	260,249	5,645	252,686
Inflow	II	160,601	7,141,114	72,276	3,214,450	48,978	2,178,618
0% VACC		166,686	7,413,481	78,091	3,474,699	54,624	2,431,304
Inflow	I	6,075	272,716	5,805	260,581	5,636	253,007
Inflow	II	159,418	7,151,216	71,799	3,220,859	48,674	2,183,529
100% VACC		165,494	7,423,932	77,604	3,481,440	54,311	2,436,537
Current setup							
Vaccinated	0.658	108,895	4,884,947	51,064	2,290,788	35,736	1,603,241
Unvaccinated	0.342	57,007	2,535,410	26,707	1,188,347	18,681	831,506
SUBTOTAL		165,901	7,420,358	77,771	3,479,135	54,418	2,434,747
VACC	32,900	401		389		382	
TOTAL		166,302		78,160		54,800	

Note: The table displays the calculation of total costs(in millions) and QALY for the current situation. 90% vaccine efficacy was assumed. The percentages of vaccinated and unvaccinated women were calculated proportionally according to the rows representing 0% and 100% vaccination coverage. The vaccination costs were added.

Table C.2: Total costs and QALY for Strategy 2 assuming 90% vaccine efficacy

13 - 15	90%	Costs 0%	QALY 0%	Costs 3%	QALY 3%	Costs 5%	QALY 5%
Calculation basis: 13 - 15							
Inflow	I	6,629	296,499	6,343	283,695	6,164	275,696
Inflow	II	160,070	7,117,204	72,039	3,203,641	48,818	2,171,269
0% VACC		166,6995	7,413,703	78,382	3,487,336	54,982	2,446,964
Inflow	I	6,616	296,957	6,330	284,130	6,152	276,116
Inflow	II	158,885	7,127,243	71,559	3,210,057	48,512	2,176,204
100% VACC		165,500	7,424,200	77,889	3,494,187	54,663	2,452,320
Intervention							
Vaccinated	0.8	132,400	5,939,360	62,311	2,795,349	43,730	1,961,856
Unvaccinated	0.2	33,340	1,482,741	15,676	697,467	10,996	489,393
SUBTOTAL		165,740	7,422,100	77,988	3,492,817	54,727	2,451,249
VACC	120,000	568		568		568	
TOTAL		166,308		78,556		55,295	

Note: The table displays the calculation of total costs (in millions) and QALY for strategy 2. 90% vaccine efficacy was assumed. The percentages of vaccinated and unvaccinated women were calculated proportionally according to the rows representing 0% and 100% vaccination coverage. The vaccination costs were added.

Table C.3: Total costs and QALY for current setting assuming 80% vaccine efficacy

	80%	Costs 0%	QALY 0%	Costs 3%	QALY 3%	Costs 5%	QALY 5%
Calculation basis: 13 only							
Inflow	I	6,085	272,367	5,815	260,249	5,645	252,686
Inflow	II	160,601	7,141,114	72,276	3,214,450	48,978	2,178,618
0% VACC		166,686	7,413,481	78,091	3,474,699	54,624	2,431,304
Inflow	I	6,076	272,677	5,806	260,544	5,636	253,007
Inflow	II	159,553	7,150,095	71,854	3,220,142	48,709	2,182,980
100% VACC		165,630	7,422,772	77,660	3,480,686	54,345	2,435,987
Current setup							
Vaccinated	0.658	108,984	4,884,184	51,100	2,290,292	35,759	1,602,879
Unvaccinated	0.342	57,007	2,535,410	26,707	1,188,347	18,681	831,506
SUBTOTAL		165,991	7,419,594	77,807	3,478,639	54,441	2,434,385
VACC	32,900	401		389		382	
TOTAL		166,392		78,196		54,822	

Note: The table displays the calculation of total costs (in millions) and QALY for the current situation. 80% vaccine efficacy was assumed. The percentages of vaccinated and unvaccinated women were calculated proportionally according to the rows representing 0% and 100% vaccination coverage. The vaccination costs were added.

Table C.4: Total costs and QALY for Strategy 2 assuming 80% vaccine efficacy

	80%	Costs 0%	QALY 0%	Costs 3%	QALY 3%	Costs 5%	QALY 5%
Calculation basis: 13 - 15							
Inflow	I	6,629	296,499	6,343	283,695	6,164	275,696
Inflow	II	160,070	7,117,204	72,039	3,203,641	48,818	2,171,269
0% VACC		166,699	7,413,703	78,382	3,487,336	54,982	2,446,964
Inflow	I	6,617	296,906	6,331	284,082	6,153	276,069
Inflow	II	159,020	7,126,125	71,614	3,209,338	48,547	2,175,650
100% VACC		165,637	7,423,031	77,945	3,493,420	54,699	2,451,719
Intervention							
Vaccinated	0.8	132,510	5,938,424	62,356	2,794,736	43,760	1,961,375
Unvaccinated	0.2	33,340	1,482,741	15,676	697,467	10,996	489,393
SUBTOTAL		165,849	7,421,165	78,033	3,492,203	54,756	2,450,768
VACC	120,000	568		568		568	
TOTAL		166,417		78,601		55,324	

Note: The table displays the calculation of total costs (in millions) and QALY for strategy 2. 80% vaccine efficacy was assumed. The percentages of vaccinated and unvaccinated women were calculated proportionally according to the rows representing 0% and 100% vaccination coverage. The vaccination costs were added.

IES Working Paper Series

2024

1. Nino Buliskeria, Jaromir Baxa, Tomáš Šestořád: *Uncertain Trends in Economic Policy Uncertainty*
2. Martina Lušková: *The Effect of Face Masks on Covid Transmission: A Meta-Analysis*
3. Jaromir Baxa, Tomáš Šestořád: *How Different are the Alternative Economic Policy Uncertainty Indices? The Case of European Countries.*
4. Sophie Ghvanidze, Soo K. Kang, Milan Ščasný, Jon Henrich Hanf: *Profiling Cannabis Consumption Motivation and Situations as Casual Leisure*
5. Lorena Skufi, Meri Papavangjeli, Adam Gersl: *Migration, Remittances, and Wage-Inflation Spillovers: The Case of Albania*
6. Katarina Gomoryova: *Female Leadership and Financial Performance: A Meta-Analysis*
7. Fisnik Bajrami: *Macroprudential Policies and Dollarisation: Implications for the Financial System and a Cross-Exchange Rate Regime Analysis*
8. Josef Simpart: *Military Expenditure and Economic Growth: A Meta-Analysis*
9. Anna Alberini, Milan Ščasný: *Climate Change, Large Risks, Small Risks, and the Value per Statistical Life*
10. Josef Bajzík: *Does Shareholder Activism Have a Long-Lasting Impact on Company Value? A Meta-Analysis*
11. Martin Gregor, Beatrice Michaeli: *Board Bias, Information, and Investment Efficiency*
12. Martin Gregor, Beatrice Michaeli: *Board Compensation and Investment Efficiency*
13. Lenka Šlegerová: *The Accessibility of Primary Care and Paediatric Hospitalisations for Ambulatory Care Sensitive Conditions in Czechia*
14. Kseniya Bortnikova, Tomas Havranek, Zuzana Irsova: *Beauty and Professional Success: A Meta-Analysis*
15. Fan Yang, Tomas Havranek, Zuzana Irsova, Jiri Novak: *Where Have All the Alphas Gone? A Meta-Analysis of Hedge Fund Performance*
16. Martina Lušková, Kseniya Bortnikova: *Cost-Effectiveness of Women's Vaccination Against HPV: Results for the Czech Republic*

Univerzita Karlova v Praze, Fakulta sociálních věd
Institut ekonomických studií [UK FSV – IES] Praha 1, Opletalova 26
E-mail : ies@fsv.cuni.cz http://ies.fsv.cuni.cz