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Cost-effectiveness of nonavalent vs bivalent HPV vaccine in Polish setting

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ABSTRACT

Objectives: Human papillomavirus (HPV) is a prevalent sexually transmitted infection with significant implications for public health. In Poland, a nationwide vaccination program offers a choice between the 9-valent (9v) and 2-valent (2v) HPV vaccines. We aimed to assess the cost-effectiveness of the 9v vs 2v vaccine from the public payer perspective in Poland.

Material and methods: A cost-effectiveness analysis was conducted to compare the public health and economic benefits of using 9v vs 2v vaccine in Poland over 100-year horizon using a previously published deterministic dynamic transmission model. A target population of girls and boys aged 12–13 years was considered. The model was populated with local epidemiological inputs, utilities, and costs, including vaccine and administration costs, as well as costs related to medical procedures for HPV-related diseases.

Results: The 9v vaccine reduced the prevalence of HPV infections and HPV-related diseases substantially more than 2v vaccine when both are compared to no vaccination strategy. The total discounted cost savings of using the 9v vaccine instead of 2v, excluding the vaccine costs, amounted to EUR 66 million. The incremental cost-effectiveness ratio amounted to 8094 EUR per quality-adjusted life year, much below the official cost-effectiveness threshold in Poland set up at the three times the annual gross domestic product per capita. 9v cost-effectiveness ratio remained unchanged when shorter time-horizons of 20, 40, 60, or 80 years were considered.

Conclusions: Using 9v HPV vaccine in Poland is highly cost-effective compared to the 2v vaccine.

Keywords: vaccine; human papillomavirus, cost-effectiveness, Poland

INTRODUCTION

Human papillomavirus (HPV) is the most common infection transmitted sexually [1]. The lifetime probability of being HPV-infected, assuming having at least one sexual partner of the opposite sex, has been estimated in the United States at 84.6% for women (95% confidence interval, 95% CI, equal to 53.6%–95%) and at 91.3% for men (95% CI = 69.5%–97.7%) [2]. The worldwide prevalence of HPV was estimated at 11.7% in women and at 21% in men in 2017 [3].

While about 90% of HPV infections clear up on their own, occasionally these infections persist and may result in various types of cancer, including the cervical, anal, vulva, oropharyngeal, oral cavity, or laryngeal cancer [4, 5]. In view of how widespread HPV is, it is responsible for a large share of cervical cancer (CC): the most carcinogenic types, HPV-16 and 18 cause almost 70% of CC worldwide, while the HPV types 31, 33, 45, 52, and 58 together account for an additional 15% of CC [3]. There are local differences in genotypes distribution, for example, in Poland HPV types 31 and 52 are both more prevalent than HPV 18 [6]. CC is the fourth most common cancer type in women and the second most common cancer type in women aged 15–44 [1]. The annual numbers of CC cases and related deaths were estimated at > 600 000 and > 340 000 in 2020, respectively [5]. Other types of HPV are also responsible for numerous disease cases. HPV types 6 and 11 are claimed to cause more than 90% of cases genital warts (GW) and recurrent respiratory papillomatosis (RRP) [7].

Meanwhile, HPV is a vaccine-preventable infection and HPV vaccines are available since 2006. The currently available vaccines in Poland protect against 2 types of HPV (16 and 18) or 9 types (6,11, 16, 18, 31, 33, 45, 52, and 58). The high efficacy, effectiveness, and safety of the vaccines have been demonstrated [8]. The vaccination coverage (as measured by the first dose received) varies substantially between the parts of the world (as defined by the World Health Organization [WHO] regions).

In Poland, the nation-wide program of HPV vaccination started in 2023. The program targets 12- and 13-year-old boys and girls and offers a choice between two doses of fully reimbursed either a bivalent (2v) or a nonavalent (9v) vaccine. As part of the free HPV vaccination program in Poland, from June 1 to November 29, 2023, 138,155 girls and boys aged 12 and 13 were vaccinated (about 90% with 9v vaccine), which constitutes around 17% vaccine coverage rate, far below the targeted 90% proposed by EU Beating Cancer Plan [9–11].

To help inform decision on choosing one vaccination strategy over another, additional evidence including cost-effectiveness is warranted.

Objectives

We aimed to assess the cost effectiveness of using 9v vs 2v HPV vaccine in Poland from the public payer perspective.

MATERIAL AND METHODS

Study design and model description

We conducted a cost-effectiveness analysis (CEA) to assess the public health and economic consequences under 9v and 2v HPV vaccination strategies targeting 12–13-year-old boys and girls in Poland. To provide a wider context for this comparison, also the public health consequences of no vaccination are presented. Incremental costs and quality adjusted life years (QALYs) were estimated based on the number of cases, morality rate, and costs associated with each vaccination strategy. We accounted for multiple types of cost incurred for public payer, including vaccine acquisition costs and administration as well as cost of medical procedures associated with managing HPV-related diseases (details follow). The indirect cost related to productivity loss has not been included.

We used a previously published and described CEA model [12, 13]: a population-based, deterministic, dynamic transmission model which reflects the natural history of HPV infection and HPV-related diseases. The model captures the clinical and financial consequences of using of either 2v or 9v HPV vaccines. The consequences are accrued over time using a system of equations that describe the spread of HPV in the population, the incidence of HPV-related diseases, and their consequences on the mortality, health-related quality of life, and cost. The model or its previous versions has been used previously in CEA of the 9v HPV vaccine. The present iteration of the model includes also considerations for infections associated with HPV types 31, 33, 45, 52, and 58, adding significant relevance to our research inquiries. The details of the previous version were published [14]. The model was populated with Polish-specific data on epidemiology, cost, and health state utilities.

To fully account for life-time clinical benefits of vaccines, we used a 100-year time horizon. However, the results were also presented in shorter horizons. The future costs and effects were

discounted using the annual rate of 5% and 3.5% as required in CEA in Poland. In sensitivity analysis, the undiscounted results were presented.

In subsections below, we present how the parameters of the model were set, focusing on population size and mortality, sexual behaviour, clinical and screening information, vaccine efficacy, vaccination coverage rate, costs, and health state utility values. More detailed information was placed in the Supplementary Material.

Demographic and sexual behaviour

The demographic inputs on population size and age and gender structure were derived from the Demographic Yearbook 2022 from the Statistics Poland (Główny Urząd Statystyczny, GUS) [15]. Polish life tables were used to account for overall mortality [16]. In view of the lack of Polish-specific data, the information on sexual activity was based on a British study [17]. To describe sexual mixing, the model uses the standard approach in which partnership data and assumptions about the structure of gender mixing are used to calculate the number of partners in different age and sexual activity groups [18]. The inputs for sexual mixing were based on the US population study [19].

Clinical and screening inputs

The number of women receiving hysterectomy was estimated using the GUS demographic data and data from the National Health Fund (NFZ) on procedures M11, M12, M13, M20, and M21 [20]. Parameters related to CC and other cancer types of mortality were derived from the National Cancer Registry [21].

The proportion of women receiving a follow-up screening test after abnormal Pap Smear test result was based on the data on CC prevention program provided on the government website and MoH information on the National Oncological Strategy in 2021 [19, 22]. The report also included information on the approximate number of women who reported for further diagnostics after receiving abnormal cytological test results. These data allowed us to calculate the percentage of women with an abnormal result who underwent further diagnostics for cervical cancer (see Supplementary Material).

The data on the proportion of women screened for CC were derived from the report on the health status of the Polish population [23]. Polish-specific data were used for the diagnostic performance of CC Pap screening and colposcopy while French data were used on the diagnostic performance of cervical intraepithelial neoplasia PAP screening [24, 25].

Vaccine efficacy and vaccination coverage rate

The vaccine efficacy was assumed as in studies presenting the model. The vaccination coverage rates in females and males in different age groups for subsequent years of the analysis ranged from 20% to 60% and were derived from various publications, both Polish and foreign, depending on data availability. Vaccination rate model inputs along with the sources are described in detail in the Appendix. The proportion of both females and males aged 12-13 years who receive the 2nd dose of vaccine after receiving the 1st dose was assumed as 85%.

Costs

We assumed the cost of the vaccines proposed in public tender. The administration cost of vaccines has also been included into total vaccination cost (see Table A6 in the Supplementary Material).

Costs per episode of care for individual health states such as cervical intraepithelial neoplasia, CC and vaginal cancer, entailing the costs of diagnosing and treating the case, were derived from the available 2021 economic analysis for 2v HPV vaccine [26]. The same source was used to inform the model on costs of cytological examination, colposcopy and biopsy.

The costs of treatment of penile, head and neck cancer and viral pharyngeal warts were calculated using NFZ tariffs and claims data [27].

Prices given in PLN were converted into EUR at the exchange rate of approx. 4.59 PLN per EUR (as of 28th April 2023).

More cost-specific information is presented in the Supplementary Material.

Utilities

The health state utility values for the Polish population without HPV-related diseases come were based on the published population norms [28]. Due to the lack of Polish data, default decrements of the health status utility values for the non-Polish population suffering from HPV infection were used in the model input.

Model outputs

We present the results in terms of the number of HPV infections and related diseases. Regarding the cost, we present the total discounted cost over the time horizon of analysis separately for the cost of vaccines and the cost of treatment of the HPV-related diseases. As a

sensitivity analysis, we also present the results over various time horizons shorter than 100 years.

RESULTS

Clinical outcomes

HPV-vaccination with 9v vaccine – as compared to no vaccination – results approx. in a reduction of the HPV infections prevalence in females by 34% and in males by 26%. Vaccination with 2v vaccine resulted in approx. a 18% and a 10% reduction, respectively. It is important to note that the reduction is somewhat diminished by the conservative assumptions regarding the vaccination rate. The reduction mostly happens in the first 15 years of the analysed time horizon (see Figs. B1 and B2 in the Supplementary Material). In consequence, the incidence of HPV-related diseases is reduced as shown in Table I. The decrease mostly follows the decrease in HPV infections and mostly occurs between 30 and 60 years of the considered time horizon (see Fig. B3 in the Supplementary Material)

The largest relative benefit of 9v over 2v was observed for the cumulative percentage reduction in the incidence of HPV 6/11 related CIN 1, CIN2/3, genital warts (in women and man), and RRP.

It was estimated that using 9v vs 2v HPV vaccine reduced the number of deaths from HPV-related causes over given horizon by 6210 (CC), 130 (vaginal cancer) 224 (vulvar cancer), 101 and 60 (anal cancer in women and men, respectively), 126 (penile cancer), 1244 and 1122 (RRP in women and men, respectively).

In total, using 9v vs 2v yielded additional 163 QALYs per 100 000 people (in the whole population, not only in the vaccinated people).

Cost

The estimated cost savings related to HPV-related diseases avoided over time using 9v vaccine vs 2v vaccine are presented in Figure 1. In total, using a 9v vs 2v results in a discounted savings of approximately EUR 66 million (excluding the vaccine cost). In view of the discounting, in present value terms, the savings mostly occur between 10 and 30 years since the start of the analysed time horizon. The additional results are presented in Table B1 in Supplementary Material.

The total number of people receiving any dose in the analysed time horizon amounted to approx. 31.3 million people, for both 9v or 2v vaccine. The estimated incremental total discounted cost of using 9v vs 2v vaccine amounted to approx. EUR 569 million.

Cost-effectiveness results with sensitivity analysis

Accounting for both the incremental cost of vaccination and the avoided cost of diseases, the total additional cost of using 9v instead of 2v amounts to approx. EUR 503 million in the base-case in 100-year time horizon.

The incremental cost and QALY gains per person amount to EUR13.26 and 0.00164, respectively. In consequence, the incremental cost-effectiveness ratio (ICER) equals 8094 EUR/QALY.

When shorter time horizons are considered, the results do not account for the benefits accrued over time, which reduces the cost-effectiveness of 9v vaccine. For the time horizons equal to 20, 40, 60, and 80 years, the ICER coefficients amount to approx. 38,481, 16,638, 11,253, and 9077 EUR/QALY, respectively, which is still substantially below the official acceptability threshold in Poland.

Conversely, when the future cost and effects are not discounted, the benefits obtained in the future gain more weight, and the cost-effectiveness of the 9v vaccine increases. For the 100-year time horizon, the ICER amounts to only 4583 EUR/QALY.

In the base-case analysis, the impact of 9v on head and neck cancer was not included. When the impact of 9v on this type of cancer is accounted for in the modelling, the ICER changes to 8022 EUR/QALY, with discounting and in the 100-year time horizon.

DISCUSSION

In the paper, we compared the cost and effects of two HPV vaccines – the 2v and the 9v one – currently offered in Poland within the national, non-mandatory vaccination program. The effects were expressed as QALYs, by far the most widely used measure of clinical effects in CEA. Using QALYs allows for measuring the benefits of improving both the survival and the health-related quality of life and also for the aggregation of health benefits across a multitude of possible clinical conditions resulting from HPV infection.

In Poland, there is a precisely defined threshold for the cost per QALY to be used in health technology assessment in public decision-making process (for most of the countries the thresholds are estimated based on historical decisions or are only indicated as ranges [29,30]).

The value of the threshold in Poland is defined as three times the annual Gross Domestic Product per capita, and as of 31st October 2023, it amounts to 190,380 PLN/QALY, or approx. 41 500 EUR/QALY as per exchange rate used in all calculations for the present paper. The obtained ICER is well below this threshold, which clearly indicates that using the 9v instead of 2v vaccine is well justified from an economic point of view. From a purely clinical perspective, the 9v vaccine allow for preventing more cases of HPV-related diseases and deaths than the 2v vaccine.

Nevertheless, we understand the rationale for how the prevention program is currently organised, *i.e*., the possibility for the person to choose the vaccine they feel matches their medical needs and preferences most. This is especially the case if the public having a choice may decrease the vaccine hesitancy and in consequence increase the overall vaccination coverage, which currently seems below expectations [9]. From the perspective of the person being offered the vaccine, the results support the continued provision of the 9v vaccine in the national program free of charge, even more so that it is currently being chosen by approx. 90% of the program participants.

Our study is subject to additional limitations. First, for many parameters, Polish-specific values were lacking. Seeing that public decisions need to be made nonetheless; we think it is warranted to use best available source of data instead. For this reason, we decided to use foreign data, for instance, the British and US data on the sexual behaviour. Obtaining credible Polish-specific data would require large samples and be challenging in view of how sensitive aspects these data relate to. For this reason, such efforts go beyond the scope of the present study and constitute an important area of further research.

Another limitation is that the actual cost of the vaccines is subject to non-disclosure agreements between the pharmaceutical companies and Ministry of Health. In view of this limitation, we decided to calculate the vaccines cost for the National Immunization Program based on the data derived from the public tender platform where the exact prices are not listed.

The public-payer perspective has been adopted to reflect the preferred approach for cost-effectiveness studies run in Poland for the sake of the decision making. The societal perspective including indirect cost would highly likely increase the cost-effectiveness outcomes.

Regarding the modelling assumptions, we see how using a 100-year horizon may be challenged, as it differs from the time-horizons typically used in CEA of other, non-vaccine health technologies, where often life-time horizons are used but the age of patients effectively implies that at most a couple of decades are accounted for. The reason for using the 100-year horizon is that the effects of any prophylactic health technologies are only observed in the longer horizon than for curative medical technologies. While it might be deemed somewhat simplistic to believe that the assumptions used in the analysis will hold valid in such long a time horizon, the results of the analysis allow to understand the justification for using the 9v vaccine in the present setting. Moreover, it is important to notice that the impact of future cost and effects is diminished by the discounting. Finally, the results obtained for limited time-horizons continue to demonstrate the cost-effectiveness of 9v vs 2v HPV vaccine delivering the ICER below the official cost-effectiveness threshold in Poland. It is of great importance to monitor the impact of the current vaccination program over the long term in terms of the health and cost utility outcomes.

Our results resemble those obtained with the same economic model in other countries. In Norway, the ICER of 9v vs 2v for a 100-year horizon amounted to approx. 10,000 EUR, which only slightly exceeds the value obtained in the present study [12]. Importantly, our results tend to correspond with those using other modelling approaches than we applied. For instance, in a study in India using different economic model, all types of vaccines, 2v, quadrivalent, and 9v, were found to be cost-effective as compared to no-vaccination, with ICERs as low as being in approx. 330-430 USD/QALY range [31]. When one compares the reported cost and disability-adjusted life years between the 2v and 9v vaccine, the 9v is dominant, i.e. it offers greater clinical benefit while reducing the total cost from both the health care and societal perspective. More results on the cost-effectiveness of 9v HPV vaccine against the quadrivalent vaccine or no-vaccination are available, including systematic reviews [32–34]. Most published data, as synthesized in systematic reviews, indicates less favourable cost-effectiveness outcomes for the bivalent HPV vaccine than for the other HPV vaccines [35].

It needs to be underlined that presented results are specific to the Polish setting. The results may not be directly generalizable to other countries as they may differ in terms of their healthcare systems, epidemiological profiles, and economic context.

Offering to the people the choice between different vaccines could decrease their vaccine hesitancy and boost the vaccination coverage. Nevertheless, the broadest possible protection

and compatibility with the local epidemiology surveillance data need to be carefully considered.

CONCLUSIONS

Using a 9v HPV vaccine is highly cost-effective option as compared to the 2v vaccine in Poland since the calculated incremental cost per QALY (8094 EUR/QALY) amounts to less than 1 annual GDP per capita, i.e., far below the official acceptability threshold in Poland set to 3 annual GDP per capita (41 500 EUR/QALY). Our study provides insights that can inform reimbursement allocation decisions and enhance the cost-effectiveness of resource utilization.

Article information and declarations

Data availability statement

The data presented in this study are available on reasonable request from the corresponding author.

Ethics statement

The study only used parameters found in the literature. Therefore, in our opinion, ethical committee approval was not required.

Author contributions

Michal Jakubczyk — 12.5% — concept, analysis & interpretation of data, article draft; Joanna Bieganska — 12.5% — concept, searching for data sources & preparing input parameters, critical review; Katarzyna Kowalczuk — 12.5% — concept, searching for data sources & preparing input parameters, critical review; Rafal Jaworski — 12.5% — concept, searching for data sources & preparing input parameters, critical review; Marcin Czech — 12.5% — concept, help with data sources & preparing input parameters, critical review; Andrew Pavelyev — 12.5% — model calibration & running, critical review; Vincent Daniels — 12.5% — model calibration & running, critical review; Maciej Niewada — 12.5% — concept, help with data sources & preparing input parameters, critical review, corresponding author.

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None.

Conflict of interest

M. Niewada, J. Bieganska, K. Kowalczuk, and M Jakubczyk are employed (or were employed at the time of the analysis) by HealthQuest – a company that prepares health technology assessment reports for different entities, including MSD Poland. R. Jaworski is an employee of MSD Poland. M. Czech reports honoraria for the lectures and participation in scientific

meetings for different pharmaceutical entities as a consultant. A Pavelyev is a contractor for Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, U.S.A. and ownws stock in Merck & Co., Inc., Rahway, NJ, U.S.A. V Daniels is an employee of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, U.S.A. and owns stock in Merck & Co., Inc., Rahway, NJ, U.S.A. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or material discussed in the manuscript apart from those disclosed.

Supplementary material

Supplementary material for publication with article is provided.

Table 1. Cumulative reduction and cumulative percent reduction (in parentheses) of the disease incidence cases for 9v vs 2v depending on the time horizon of analysis

	Time horizon			
	5 years	25 years	50 years	100 years
Cervical				
Cancer	0 (0.0)	156 (0.2)	2 557 (2.1)	14 346 (7.3)
CIN 1	491 (0.7)	63 317 (21.1)	167 330 (29.4)	373 190 (33.6)
CIN 2/3	349 (0.5)	39 975 (13.6)	105 059 (19.6)	234 332 (22.8)
Vaginal				
Cancer	0 (0.0)	0 (0.0)	23 (0.8)	358 (8.1)
VAIN 1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
VAIN 2/3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vulvar				
Cancer	0 (0.0)	0 (0.0)	18 (0.5)	317 (5.6)
VIN 1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
VIN 2/3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Genital Warts and HPV 6/11-related CIN 1				
Genital Warts (female)	1 961 (1.8)	108 798 (20.3)	341 398 (31.9)	860 129 (40.1)
Genital Warts (male)	926 (1.3)	62 055 (17.6)	196 514 (27.8)	495 326 (35.0)
CIN 1	1029 (0.7)	150 101 (19.6)	502 593 (32.8)	1 283 883 (41.8)
Anal				
Cancer (female)	0 (0.0)	0 (0.0)	12 (0.2)	177 (1.6)
Cancer (male)	0 (0.0)	0 (0.0)	5 (0.2)	85 (1.8)
Penile Cancer	0 (0.0)	1 (0.0)	35 (1.3)	362 (10.6)
RRP				
RRP (female)	18 (0.5)	2 437 (12.9)	10 015 (26.5)	27 763 (36.8)
RRP (male)	13 (0.4)	2 137 (12.2)	8 989 (25.7)	25 093 (35.9)

Cases are rounded to the nearest 1, and percentages are rounded to the nearest 0.1

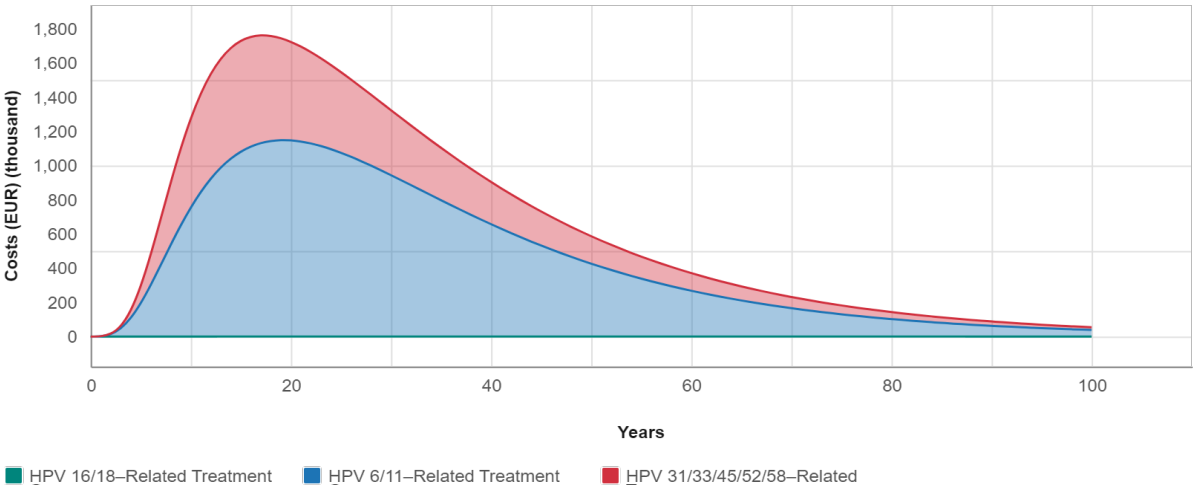

Figure 1. The estimated avoided healthcare cost by HPV genotype as generated over time within the considered time horizon (discounted)

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Supplementary material

A. Additional information on input parameters

A.1. Mortality inputs and calculations

Mortality was calculated using the following formula:

-1 * (a – b) * (1/c), where

- a denotes the number of people (per 100 000) who lived to the beginning of the next age range;
- b denotes number of people who lived to the beginning of the considered age range
- c denotes the number of years in the considered range

The calculation was based on the data coming from Life expectancy tables of Poland 2021 [1]. The results are presented in Table A1.

Table A1. Annual all-cause mortality rates for the general population

Age group (years)	Males	Females
<1	0.00209	0.00175
1-8	0.00016	0.00012
9-10	0.00009	0.00008
11-12	0.00011	0.00010
13-14	0.00017	0.00013
15-17	0.00034	0.00020
18	0.00052	0.00024
19	0.00063	0.00027
20-24	0.00087	0.00029
25-26	0.00108	0.00031
27-29	0.00125	0.00036

30-34	0.00165	0.00051
35-39	0.00241	0.00076
40-44	0.00362	0.00124
45-49	0.00568	0.00212
50-54	0.00908	0.00344
55-59	0.01431	0.00571
60-64	0.02266	0.00976
65-69	0.03465	0.01586
70-74	0.04945	0.02521
75-79	0.07186	0.04090
80-84	0.10828	0.07037
>85	1.00000	1.00000

A.2. Number of hysterectomies

In Table A2, we present the NFZ statistics for the number of hysterectomies per age group split by DRG codes.

Table A2. The number of hysterectomies in 2020 split by diagnosis related group codes

	Number of procedures by procedure code						
Age group	**M11**	**M12**	**M13**	**M20**	**M21**	**Sum**	**Percent of all hysterectiomies**
<1	0	0	0	0	0	0	0.00%
1-6	0	0	0	0	0	0	0.00%
7-17	0	0	14	0	0	14	0.03%
18-40	4	0	264	0	0	268	0.65%
41-60	327	35	10 267	53	2	10 684	25.74%
61-80	2148	330	17 887	365	42	20 772	50.05%
>81	2943	563	4832	706	112	9156	22.06%
No data	222	50	241	78	15	606	1.46%

[2]

Percent of female population receiving hysterectomy over the course of 1 year was calculated using the sum of all hysterectomies in a given age range and the

population size in the ranges considered by the model. The calculations took into account the fact that the National Health Fund statistics presented results for age ranges wider than those included in the model.

The following formula was used to calculate percent of female population receiving Hysterectomy over the course of 1 year:

$a/(b*c)$, where:

- a denotes the total number of hysterectomies in a given age group reported by NFZ
- b denotes the population size for the age ranges included in the model
- c denotes the number of age ranges included in the model that fall within the corresponding age range presented in NFZ statistics

Table A3. Population size and percent of female population receiving hysterectomy over the course of 1 year

Age group	Population size	Percent receiving hysterectomy
<1	158 281	0.00000
1-8	1 476 064	0.00000
9-10	382 753	0.00001
11-12	413 238	0.00001
13-14	406 953	0.00001
15-17	539 521	0.00001
18	170 679	0.00022
19	172 084	0.00022
20-24	934 320	0.00004
25-26	419 119	0.00009
27-29	707 716	0.00005
30-34	1 352 188	0.00003
35-39	1 580 374	0.00002
40-44	1 529 062	0.00175
45-49	1 391 073	0.00192
50-54	1 167 265	0.00229
55-59	1 161 620	0.00230
60-64	1 366 295	0.00380
65-69	1 387 413	0.00374
70-74	2 958 313	0.00176
75-79	739 578	0.00702
80-84	739 578	0.00619
>85	739 578	0.00619

[3]

A.3. Percent of females receiving a follow-up screening test after abnormal PAP smear diagnosis

According to the information on the prevention program website, approximately 1.5-2% of the PAP smear test results are abnormal [4]. The number of all cytologies performed in 2021 based on the report of the Ministry of Health amounted to 376 791 [5]. Using the value of 2%, the number of abnormal test results was estimated as 7536. The number of women who reported for further diagnostics after receiving abnormal cytological test results in year 2021 was 1698, which is approximately 22.5% of total number of women with abnormal test results.

A.4. Vaccination coverage rate in females

Parameters and references for vaccination coverage rate adopted in model input are shown in Tables A4 and A5.

Table A4 Vaccination coverage rate in females

Year	12 year olds	13 year olds	Source(s)
1	22.0%	22.0%	Low boundary estimate for EU National Programs (recalculated for half year)
2	44.0%	44.0%	Low boundary estimate for EU National Programs
3	57.0%	57.0%	Max VCR in municipality programs in Poland (published by Polish HTA Agency)
4	58.0%	58.0%	[6]; VCR in Czech Rep after 4 years with two vaccines available
5	59.0%	59.0%	Assumption based on data regarding years 4 and 6+
6+	60.0%	60.0%	Polish National Oncology Strategy target

Table A5. Expected vaccination coverage rate in males

Year	12 year olds	13 year olds	Reference(s)
1	18.0%	18.0%	Low boundary estimate for EU National Programs (recalculated for half year)
2	35.0%	35.0%	Low boundary estimate for EU National Programs
3	50.0%	50.0%	Max VCR in municipality programs in Poland (published by Polish HTA Agency)
4	58.0%	58.0%	[6]; VCR in Czech Rep after 4 years with two vaccines available
5	59.0%	59.0%	Assumption based on data regarding years 4 and 6+
6+	60.0%	60.0%	Polish National Oncology Strategy target

A.5. Costs

The costs of the vaccines are based on public tenders and are presented in Table A6 below.

Table A6. Cost of vaccines

Price	Vaccine	PLN (EUR)	Reference
Listed official price per dose	Gardasil 9	486.22 (105.93)	[7]
Listed official price per dose	Cervarix	245.16 (53.41)	[8]
Visible contract price	Gardasil 9	335.00 (73.00)	[9]
Visible contract price	Cervarix	130.00 (28.33)	[9]
Vaccine administration cost per dose	Both vaccines	29.74 (6.48)	[10]

Other costs adopted in the model are presented in tables below.

Table A7. Cost per episode of care

Parameter	Cost (EUR)	Reference(s)
CIN 1	211.34	[11]
CIN 2	285.07	[11]
CIN 3, CIS	285.07	[11]
Cervical cancer, local disease*	1544.46	[11]
Cervical cancer, regional disease*	1544.46	[11]
Cervical cancer, distant disease*	1544.46	[11]
VaIN 1	112.57	[12]
VaIN 2	112.57	[12]
VaIN 3, CIS	112.57	[12]
Vaginal cancer, local disease*	4530.79	[11]
Vaginal cancer, regional disease*	4530.79	[11]
Vaginal cancer, distant disease*	4530.79	[11]
Vulvar cancer, local disease*	4939.95	[11]
Vulvar cancer, regional disease*	4939.95	[11]
Vulvar cancer, distant disease*	4939.95	[11]

CIN – cervical intraepithelial neoplasia; VaIN – Vaginal intraepithelial neoplasia

* Disease stages can be related to the traditional Tumour-Node-Metastasis (TNM) classification system as followed:

- "Local disease" corresponds to stages I and II TNM classification, i.e., localized primary tumour;
- "Regional disease" corresponds to stage III TNM classification system, i.e., metastasis to regional lymph nodes;
- "Distant disease" corresponds to stage IV TNM classification system, i.e., distant metastatic disease.

Table A8. Cost per episode of care

Parameter	Cost (EUR)	Reference(s)
Penile cancer, local disease*	495.00	[12]
Penile cancer, regional disease*	495.00	[12]
Penile cancer, distant disease*	495.00	[12]
Anal cancer, local disease*	3909.75	[11]
Anal cancer, regional disease*	3909.75	[11]
Anal cancer, distant disease*	3909.75	[11]
Head & Neck cancer, local disease*	4797.65	[12]
Head & Neck cancer, regional disease*	4797.65	[12]
Head & Neck cancer, distant disease*	4797.65	[12]
Genital warts	54.99	[11]
Recurrent respiratory papillomatosis	2832.33	[12]

Table A9 Screening and diagnostic tests (for cervical and vaginal cancers only)

Parameter	Cost (EUR)	Reference(s)
Screening (PAP smear) + consultation	5.21	[11]
Colposcopy	24.56	[11]
Biopsy	69.23	[11]

CIN – cervical intraepithelial neoplasia; VaIN – Vaginal intraepithelial neoplasia

A.6. Utilities

Table A10 Health utility values by age and gender for individuals without HPV disease [13]

Age range	Men	Women
<1	0.967	0.959
1-8	0.967	0.959
9-10	0.967	0.959
11-12	0.967	0.959
13-14	0.967	0.959
15-17	0.967	0.959
18	0.967	0.959
19	0.967	0.959
20-24	0.967	0.959
25-26	0.958	0.948
27-29	0.958	0.948
30-34	0.958	0.948
35-39	0.942	0.934
40-44	0.942	0.934
45-49	0.910	0.887
50-54	0.91	0.887
55-59	0.851	0.861
60-64	0.851	0.861
65-69	0.837	0.793
70-74	0.837	0.793
75-79	0.74	0.715
80-84	0.740	0.715
>85	0.740	0.715

B. Additional results

Table B1. Estimated cumulative cost of HPV-related diseases at the population level (discounted, in EUR)

	Considered vaccination alternative		% reduction when using 9v vs 2v
	2v	9v	
Cervical			
Cancer	76 495 853	75 317 545	1.5
CIN 1	49 738 823	39 006 462	21.6
CIN 2/3	64 309 887	55 514 346	13.7
Vaginal			
Cancer	5 475 243	5 422 257	1.0
VAIN 1	0	0	99.8
VAIN 2/3	0	0	100.0
Vulvar			
Cancer	7 261 414	7 212 609	0.7
VIN 1	0	0	-
VIN 2/3	0	0	-
Genital Warts and HPV 6/11-related CIN 1			
CIN 1	87 815 332	67 105 132	23.6
CIN 2/3	9 872 735	7 561 476	23.4
Genital Warts (male)	11 859 022	9 375 656	20.9
Genital Warts (female)	17 984 116	13 643 840	24.1
Anal			
Cancer (male)	4 857 931	4 847 334	0.2
Cancer (female)	11 390 174	11 367 223	0.2
Penile Cancer	543 147	536 217	1.3
RRP	83 730 834	68 410 707	18.3
Total Disease Costs	431 334 511	365 320 805	15.3

Costs are discounted a 5% annual rate. Percentages are rounded to nearest 0.1%.

Table B2. Estimated quality-adjusted life year (QALY) gains when comparing 9v vs 2v vaccine per 100,000 individuals per disease type

Disease type	QALY gain
Cervical	50.47
Vaginal	0.43
Vulvar	0.54
Genital warts	66.14
Anal	0.28
Penile	0.48
RRP	44.96
Total	163.30

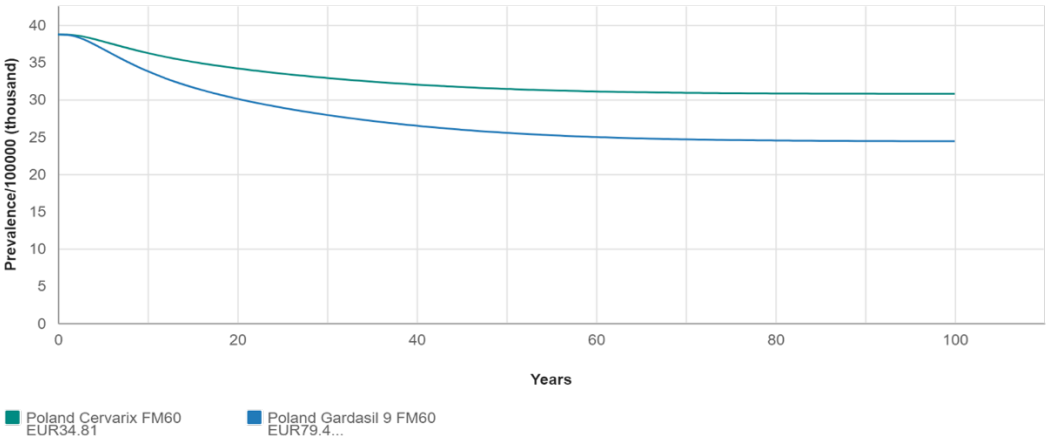

Fig. B1. The estimated HPV infection prevalence among females

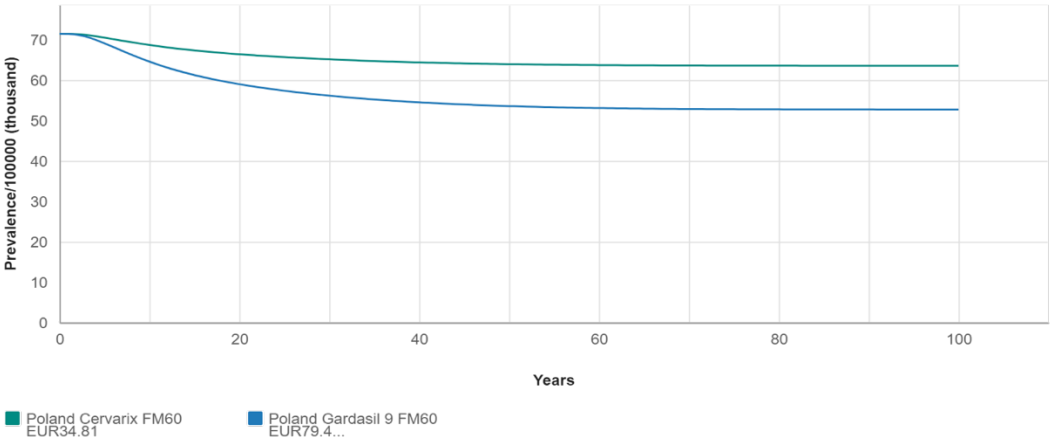

Fig. B2. The estimated HPV infection prevalence among males

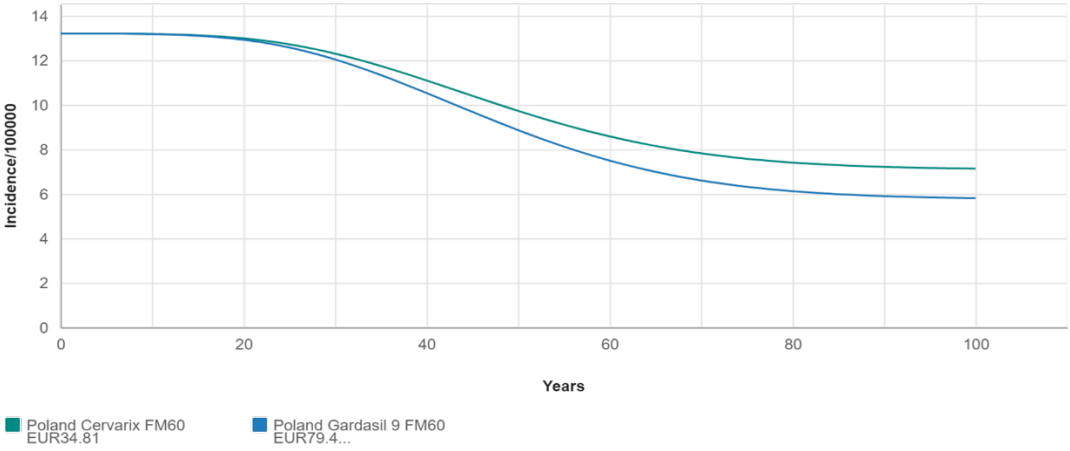

Fig. B3. The estimated HPV-related incidence of cervical cancer among females

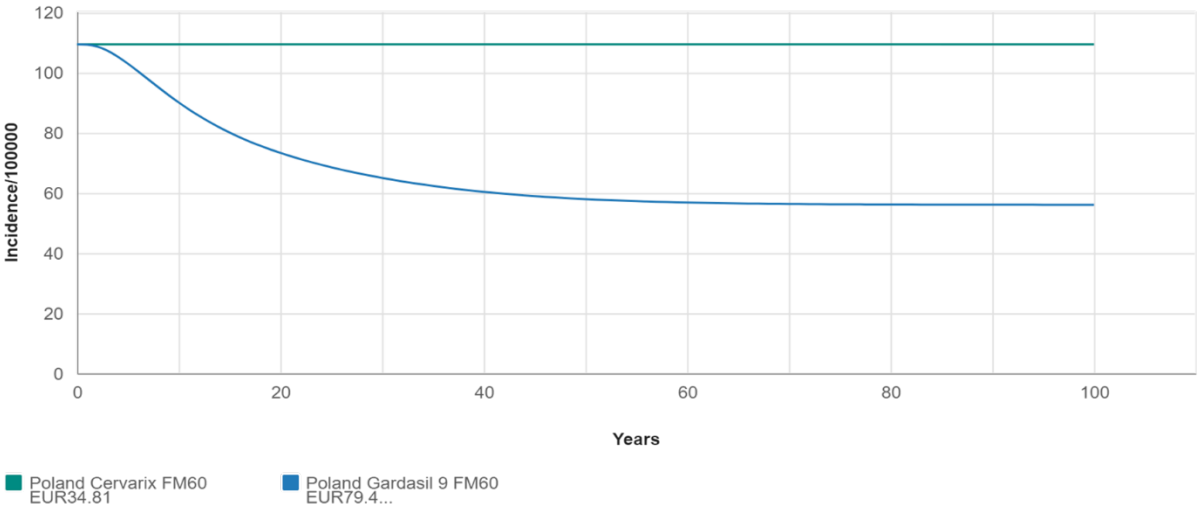

Fig. B4. The estimated HPV-related incidence of genital warts among females

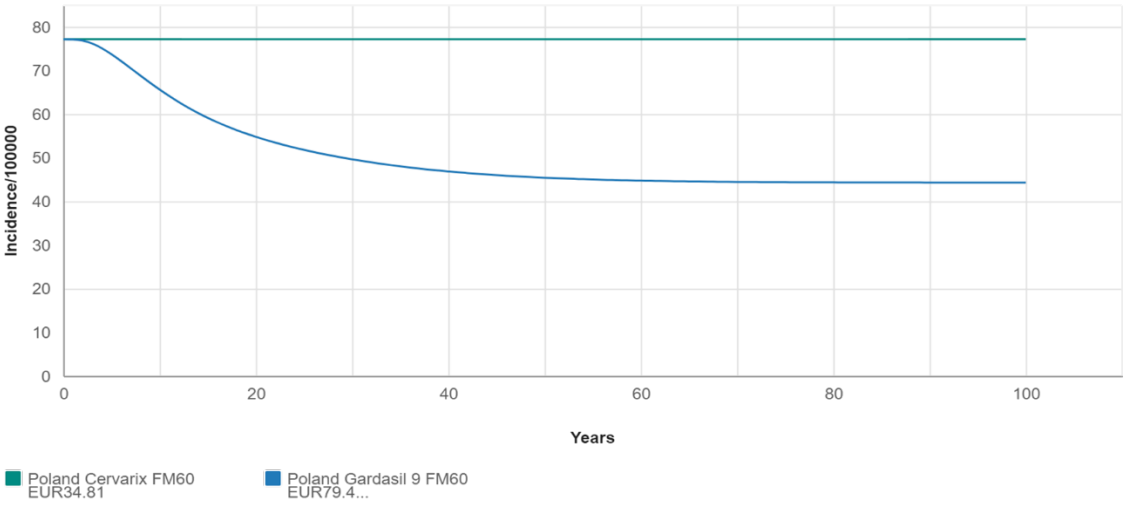

Fig. B5. The estimated HPV-related incidence of genital warts among males

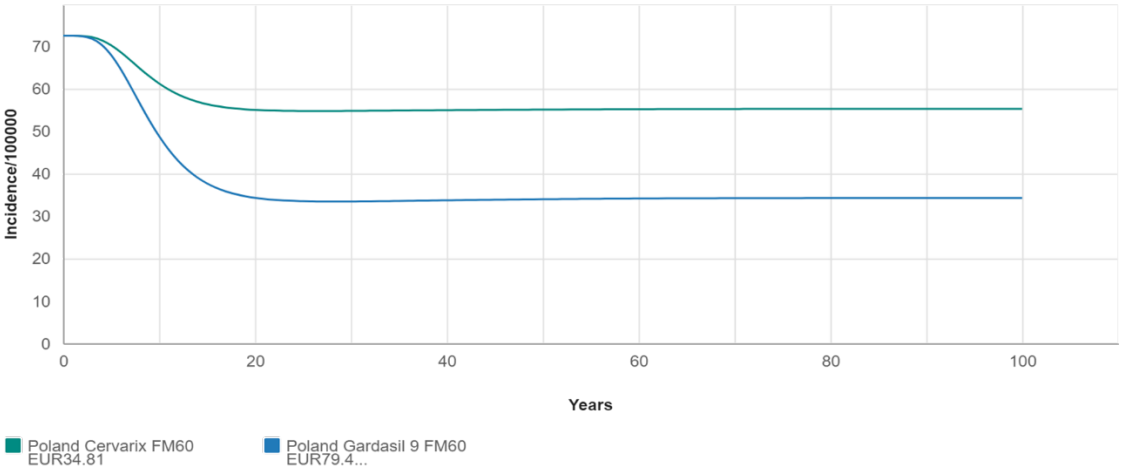

Fig. B6. The estimated HPV 16/18/31/33/45/52/58-related incidence of CIN 1 among females

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