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### **Universal HPV vaccination programme**

Anticipated outcomes for the population and for the health care system in Poland

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# **Summary**

Human papillomavirus (HPV) is one of the most common viral infections that are primarily transmitted sexually. There are over 100 types of HPV, which can be divided into those of high or low oncogenic risk. Among the highly oncogenic types in the European population, eight are of particular importance (16, 18, 31, 33, 35, 45, 56 and 58), with types 16 and 18 responsible for approximately 73% of all cases of cervical cancer. Infections with these types of HPV can also cause other cancers, including cancers of the anus, penis, vulva, mouth and larynx.

In Poland, the highest incidence of all HPV-associated cancers in the female population is that of invasive and *in situ* cervical cancer. In 2020, it equalled approximately 10 and 5 cases per 100,000 women, respectively. The most common HPV-related malignancy among men is laryngeal cancer, which was diagnosed in about 7 per 100,000 men in 2020. Every year, about 4,400 women and 1,600 men in Poland are diagnosed with diseases that could nowadays be effectively prevented through vaccination. Existing vaccines have the potential to prevent approximately 54% of HPV-related cancer cases (75% in women and 35% in men), which would translate into 4,600 fewer cancer cases a year.

Currently, there are no active treatment options for HPV infections, but the risk of HPV infection can be significantly reduced, primarily through preventive vaccinations. In Poland, the strategic document dealing with HPV vaccination is the National Cancer Strategy for the years 2020-2030, in which HPV vaccination is one of the most important measures of cancer prevention. Currently, there are three vaccines available on the market to protect against HPV infection: Cervarix, Gardasil and Gardasil 9. Cervarix is publicly funded with a 50% reimbursement rate. In addition, since 1 June 2023, Cervarix and Gardasil 9 have been completely free of charge for children aged 12–13 years under the universal HPV vaccination programme.

Of the HPV-associated cancers, the highest incidence rates attributable to HPV are observed in cervical cancer *in situ* (99%), invasive cervical cancer (91%) and anal cancer (94% in men and 86% in women). Considered accountable for all HPV-related cancers, with the exception of laryngeal cancer, is the most oncogenic type of the virus – HPV 16. The present analysis concludes that over 90,000 or 114,000 cancer cases could have been avoided in the years 1999-2020 if the entire population of Poland had been vaccinated against HPV over the previous decades with either Cervarix or Gardasil 9, respectively.

An important element in the implementation of the HPV vaccination programme is a comprehensive approach based on cooperation of the general public, health care professionals and decision-makers within the health care system. This approach is essential to achieve the ambitious health goal of minimising HPV infections in the Polish population.

# **Scientific review**

The report provided for review, titled "Universal HPV vaccination programme — anticipated outcomes for the population and for the health care system in Poland," has been developed by the team of the Department of Systemic Analyses and Independent Research of the Medical Research Agency. The report addresses an extremely topical and important issue in public health.

The aim of the report is to estimate the potential health outcomes for the population and the impact on the Polish health care system depending on the HPV vaccine used. The analysis is based on data from the National Cancer Registry and focuses on HPV-related primary cancers. The research method adopted by the authors is described in detail and relevant for the purpose of the study.

The results of the report, including reasoning on the potential impact of preventive vaccination depending on anatomical site, are presented for 8 cancer profiles. The results of the analysis are well-ordered and logically presented.

The analysis carried out in the report concludes that preventive vaccination can be considered a key element of the HPV prevention strategy. However, the authors emphasise that the implementation of the HPV vaccination programme in Poland requires a comprehensive approach, hence the role of various groups of stakeholders to whom the recommendations contained in the report are addressed.

In conclusion, the report submitted for review is of paramount importance as it addresses the current challenges of public health. Thereby, it makes an important contribution to the scientific literature on epidemiology and the burden of HPV.

Associate Professor CPME Urszula Religioni, MD, PhD School of Public Health Centrum Medyczne Kształcenia Podyplomowego (Medical Centre for Postgraduate Education) In view of the lack of randomised trials comparing the efficacy of HPV vaccines of different valencies, the analysis presented is a valuable source of information on the potential ways of reducing the incidence of HPV-dependent malignancies with the use of 2-, 4-, and 9-valent vaccines as part of primary prevention. An additional advantage of the study is that it focuses on the Polish population, which is a primary topic of interest for researchers and decision-makers in the field of cancer prevention in Poland.

The authors emphasise the role of HPV infections in the pathogenesis of cervical cancer, as well as other cancers about which public awareness may be lower due to the higher incidence rates of cervical cancer and more commonly available methods of secondary and tertiary prevention focusing on this malignancy.

In the analysis, the authors make estimations on how many cancer cases could have been avoided if all residents of Poland had been vaccinated against HPV in past decades, and when to expect systemic effects of the universal HPV vaccination programme in terms of prevalence of cancers of the oral cavity, oropharynx, larynx, vulva, vagina, cervix, penis, and anus.

The results presented argue for further efforts to increase HPV vaccination coverage in relevant patient groups as part of prophylaxis of HPV-induced diseases, in accordance with national and international strategies to combat malignant tumours associated with available prevention opportunities, i.e. with: National Cancer Strategy for the years 2020–2030, Europe's Beating Cancer Plan, and the World Health Organization's global strategy for the elimination of cervical cancer with the 90-70-90 targets.

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# **Abbreviations**

AF	Attributable fraction
AOTMIT	Agency for Health Technology Assessment and Tariff System (Pol. Agencja Oceny Technologii Medycznych i Taryfikacji)
CDC	Centers for Disease Control and Prevention
HPV	Human papilloma virus
ICD-10	International Statistical Classification of Diseases and Related Health Problems
ICD-10: C01, C09-C10	Malignant neoplasms of the oropharynx
ICD-10: C02-C06	Malignant neoplasms of the oral cavity
ICD-10: C32	Malignant neoplasm of the larynx
ICD-10: C21	Malignant neoplasm of the anus
ICD-10: C51	Malignant neoplasm of the vulva
ICD-10: C52	Malignant neoplasm of the vagina
ICD-10: C53	Malignant neoplasm of the cervix uteri, invasive
ICD-10: C60	Malignant neoplasm of the penis
ICD-10: D06	Carcinoma <i>in situ</i> of the cervix uteri
KRN	National Cancer Registry (Pol. Krajowy Rejestr Nowotworów)
NHVP	Australian National HPV Vaccination Program
NSO	National Cancer Strategy (Pol. Narodowa Strategia Onkologiczna)
RCT	Randomised clinical trials

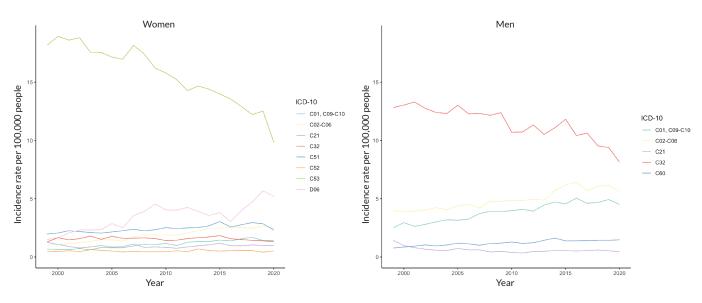
# **Glossary of Terms**

Attributable percentage	a proportion of cases in a group of patients that are caused by exposure to a spe- cific risk factor
Randomised clinical trial	the "gold standard" in clinical research; a trial in which the subjects are assigned randomly to one of two or more subgroups, of which at least one is subject to the intervention under investigation (e.g., a treatment method) and one to an alterna- tive or dummy intervention
Mortality	the number of deaths in relation to the number of people in a given population; in demographics and epidemiology, mortality is defined as the number of deaths caused by a given disease per 100,000 people in the observed population
Valency	number of strains (types) of the microorganism against which a vaccine is directed
Incidence rate	the number of new cases of a given disease in relation to the number of people at risk of falling ill in a given population, over a period of time (usually within a month or a year)

## Introduction

Human papilloma virus (HPV) is a DNA virus that infects stratified epithelium cells. HPV infection can be asymptomatic, and lesions usually develop slowly in the infected area. However, the process may be faster in people with immunodeficiencies. There are over one hundred types of HPV that cause infection in the skin and mucous membranes. These include high-oncogenic and low-oncogenic types. Among the highly oncogenic types in the European population, eight are of particular importance (16, 18, 31, 33, 35, 45, 56 and 58), with types 16 and 18 responsible for approximately 73% of all cases of cervical cancer. HPV can also induce other cancers, including cancers of the anus, penis, vulva, mouth and larynx. The low-oncogenic types, in particular types 6 and 11, are mainly responsible for the formation of genitourinary warts (genital warts). The main risk factors for HPV infection are: early sexual initiation, having multiple sexual partners, having a high-risk partner (one who is infected with HPV or has had multiple sexual partners), coexistence of other sexually transmitted infections, smoking, long-term use of hormonal contraception, immunodeficiency (e.g. HIV infection, use of immunocompromising drugs).1-3

According to the National Cancer Registry, in the years 1999-2020, the highest incidence of all HPV-associated cancers in the female population in Poland was that of cervical cancer - invasive (C53) and insitu (D06). In 1999, the incidence rate of the invasive form was nearly 18 cases/100,000 women, which gradually fell in the later years to reach the lowest level in 2020 (9 cases/100,000). In the same period, the incidence rate of in situ cervical cancer mostly remained at below 5 cases/100,000 women, but after 2015, it began to increase rapidly and in 2020 stood at approximately 6 cases per 100,000 women. This change in incidence rates of cervical cancers, i.e. the drop in case numbers of the invasive form and the rise of the in situ form, has been associated with earlier detection of the disease as a result of cervical screening tests. The incidence of other HPV-associated cancers in the female population remained quite constant in the analysed period, staying significantly below 5 cases/100,000 women, with slight fluctuations during this time. Of these neoplasms, the highest incidence was observed in malignant neoplasms of the vulva (C51), and the lowest in malignant neoplasms of the vagina (C52) (Figure 1).

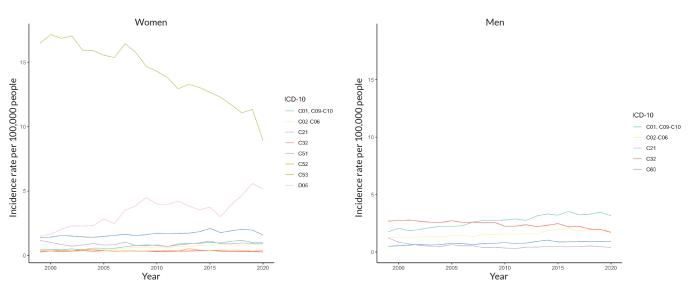


**Figure 1.** The incidence rates\* of HPV-related malignant neoplasms in the Polish population, by sex, 1999–2020. Cancer sites according to the ICD-10 terminology: C01, C09-C10 – oropharynx; C02-C06 – oral cavity; C32 – larynx; C21 – anus; C51 – vulva; C52 – vagina; C53 – cervix, invasive; C60 – penis; D06 – cervix, in situ. \* Based on data from the National Cancer Registry (onkologia.org.pl/raporty).



As regards the male population, in the years 1999–2020, the highest rates of HPV-associated neoplasms were observed for malignant neoplasms of the larynx (C32). At the beginning of the study period — in 1999 — the incidence rate of laryngeal cancer was approximately 13 cases/100,000 men, while in 2020 it was about 8 cases/100,000. The incidence rates of most other HPV-related cancers in the male population remained below 5 cases per 100,000, with the exception of malignant neoplasms of the oral cavity, where this limit was exceeded around 2015 (*Figure 1*).

HPV-attributable incidence of malignant neoplasms in women in Poland exhibits similar trends as total incidence of HPV-associated cancers. HPV-attributable incidence of cervical cancer shows a decrease with regard to the invasive form (C53) and an increase with regard to the *in situ* form (D06), as is the case with total HPV-associated cancers (*Figures 1 and 2*). Conversely, HPV-attributable incidence of malignant neoplasms in men is considerably lower than that of HPV-associated cancers in general — fewer than 5 cases/100,000 men for each of the analysed malignancies. These incidence rates remained at a similar level over the study period, with minor fluctuations in the most common cancers attributable to HPV in men, namely neoplasms of the larynx (C32) (a slight decrease) and of the oropharynx (C09-C10) and oral cavity (C02-C06) (slight increase) (*Figure 2*).



**Figure 2.** HPV-attributable incidence rate of malignant neoplasms in the Polish population, by sex and cancer site, 1999–2020. Cancer sites according to the ICD-10 terminology: C01, C09-C10 – oropharynx; C02-C06 – oral cavity; C32 – larynx; C21 – anus; C51 – vulva; C52 – vagina; C53 – cervix, invasive; C60 – penis; D06 – cervix, in situ. Note: The y axis is different for both sexes

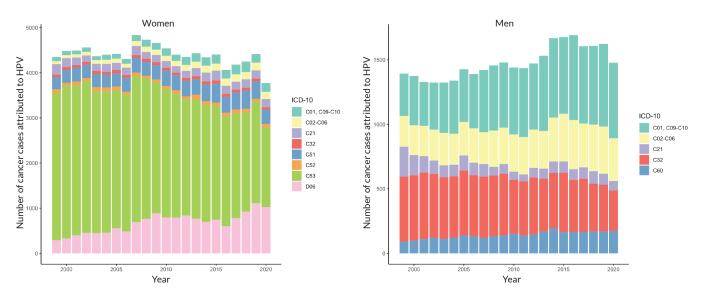
Over the years 1999–2020, clearly the highest raw number of cases attributable to HPV in the female population pertained to cervical cancer in both forms: invasive (C53) and *in situ* (D06), as well as malignant neoplasms of the vulva (C51) (*Figure 3*). In the male population, the most cases of malignant neoplasms attributable to HPV were oropharyngeal (C01, C09-C10), laryngeal (C32) and oral (C02-C06) cancers (*Figure 3*). Currently, **there are no active treatment options for HPV infection**. In clinical practice, only topical treatment of viral lesions is used:

- invasive by way of surgical excision, cryotherapy, electrocoagulation, laser therapy,
- conservative topical application of immunomodulators (interferon alfa, imiquimod), antiproliferative drugs (podophyllotoxin, 5-fluorouracil), keratolytic drugs (salicylic acid, trichloroacetic acid, dichloroacetic acid), sinecatechin (a drug with a complex mechanism of action).<sup>1</sup>



The risk of HPV infection can be significantly reduced, primarily through preventive vaccinations. Vaccinations, combined with preventive screening tests, provide the best possible protection against cervical cancer, as well as other HPV-associated malignancies.





**Figure 3.** The numbers of malignant neoplasms attributable to HPV in the Polish population, by sex and cancer site, 1999–2020. Cancer sites according to the ICD-10 terminology: C01, C09-C10 – oropharynx; C02-C06 – oral cavity; C32 – larynx; C21 – anus; C51 – vulva; C52 – vagina; C53 – cervix, invasive; C60 – penis; D06 – cervix, in situ. Note: The y axis is different for both sexes

Currently, there are three vaccines available on the market that protect against HPV infection: Cervarix, Gardasil and Gardasil 9 (*Table 1*), of which both vaccines Gardasil are targeted against types of both low and high oncogenic risk (types 6 and 11, and 16 and 18, respectively). Gardasil 9 also contains L1 proteins of other highly oncogenic HPV types - 31, 33, 45, 52, and 58.

**Table 1.** Anti-human papillomavirus (HPV) vaccines available on prescription on the Polish market in 2023 (Official Journal of<br/>the Minister of Health 2023, item 70).

Trade name	Manufacturer (country of the manufacturer)	Out of pocket cost	Valency	HPV types
Cervarix	GlaxoSmithKline Biologicals (Belgium)	50% (PLN 138.18)	2	16 18
Gardasil *		100%	4	6 11 16 18
Gardasil 9	MSD Vaccins (Netherlands)	100%	9	6 11 16 18 31 33 45 52 58

\* In September 2018, the trade name of this 4-valent HPV vaccine was changed in Poland from Silgard to Gardasil; from 2023, the availability of the quadrivalent Gardasil preparation is suspended on the polish market.

According to the announcement of the Minister of Health of 20 June 2023 on the list of reimbursed medicinal products, foods for particular nutritional uses and medical devices as of 1 July 2023 (Official Journal of the Minister of Health 2023, item 70), **the HPV vaccine currently subject to reimbursement in Poland is Cervarix**. The product is reimbursed at 50% in all registered indications as of the date of the decision, i.e. in the prevention of premalignant genito-anal lesions and



cervical and anal cancers causally related to certain oncogenic HPV types, from the age of 9.4 Cervarix has been evaluated in terms of meeting health needs, efficacy, safety, and availability by the Transparency Council of the Agency for Health Technology Assessment and Tariff System (AOTMiT) in its opinion of 31 July 2023<sup>5</sup> on medicinal products used in children and adolescents under 18 years of age. The vaccine was found to be highly effective and safe, of moderate significance in terms of the health needs of the population in question, and of moderate availability. In 2021, the president of AOTMiT<sup>6</sup> issued a conditional recommendation to expand reimbursement coverage to include Gardasil, "a vaccine against human papillomavirus [types 6, 11, 16, 18] indicated from the age of 9 for the prevention of: premalignant genital lesions, premalignant anal lesions, cervical cancers and anal cancers causally related to certain oncogenic HPV types, and genital warts causally related to specific HPV types." The president of AOTMiT also noted that "(...) no data are available comparing the product's

efficacy versus the vaccine currently under reimbursement in Poland, namely Cervarix. The available RCTs making direct comparisons between Gardasil and Cervarix only focus on the safety and immunogenicity of these vaccines." Subsequently, in 2022, the Transparency Council of AOTMiT issued opinion No. 180/2022<sup>7</sup> assessing favourably the efficacy of Cervarix and Gardasil 9 for the prevention of cervical cancer and pointing out that there was no evidence of clinical superiority of either of them.

The first country in the world to initiate public funding of HPV vaccination as part of a universal programme was Australia, which launched the Australian National HPV Vaccination Program (NHVP) in 2007, effectively reducing the incidence of the types of HPV targeted by the vaccines. The NHVP included routine vaccinations for girls aged 12–13 and booster vaccinations for women aged 14–26 by 2009, as well as vaccinations for boys aged 12–13 by 2013, and aged 14–15 by the end of 2025.<sup>8</sup>

In the UK, the HPV vaccination programme has almost completely eliminated cervical cancer in women born after 1 September 1995.<sup>9</sup>

The efficacy of three doses of 4-valent Gardasil in women aged 16-23 years in the Nordic countries has been estimated at over 90%, with protection sustained for at least 10 years,<sup>10</sup> while clinical trials in Costa Rica, India and Fiji revealed a high level of efficacy even with a single dose of the anti-HPV-16/18 vaccine<sup>11,12</sup> up to eight years after administration,<sup>13</sup> which may provide a solution to the logistical and financial challenges associated with the use of multiple doses. Considering the high importance of the health challenge that is HPV, in 2020, the World Health Assembly approved a strategic plan defining HPV vaccination objectives to be met in Member States by 2030. These objectives include, among other things, vaccinating programme in accordance with the National Cancer Strategy. As part of the programme, free HPV vaccinations were initiated on 1 June 2023 available to girls and boys aged 12 and 13. The programme offers 2 vaccines: 2-valent Cervarix and 9-valent Gardasil 9.<sup>15</sup>



Poland has joined the ranks of countries offering free HPV vaccination as part of a nationwide, universal vaccination programme.

It is also worth mentioning the economic benefits for the health care system resulting from increased anti-HPV vaccination coverage. According to a report by prof. Ewelina Nojszewska<sup>15</sup> from the Warsaw School of Economics, the costs of treating cervical cancer alone incurred by the National Health Fund in 2010–2014 amounted to over PLN 307 million. In addition to reducing the burden on the state budget associated with hospital care, vaccinations would also help to avoid economic losses and hence a potential decline in gross domestic product caused by incapacity to work and premature deaths.

The aim of this analysis is to estimate the potential health outcomes for the population and the impact on the Polish health care system depending on the HPV vaccine used.

# **Materials and Methods**

#### **Sources of Data**

This analysis is based on data from the National Cancer Registry (KRN), an institution supervising statistical and epidemiological research focused on cancer in Poland. Detailed information on KRN's operation is available from other sources.<sup>16,17</sup> Our analysis focuses on primary cancers associated with HPV, categorised according to the International Statistical Classification of Diseases and Related Health Problems ICD-10: oral cavity (C02-C06), oropharynx (C01, C09-C10), larynx (C32), vulva (C51), vagina (C52), cervix, in situ (D06), cervix, invasive (C53), penis (C60), and anus (C21). The analysis includes all cases of primary malignant neoplasms potentially associated with HPV. It should be noted that a patient with two or more distinct concomitant HPV-associated cancers may be included in the analysis multiple times. The study covers the period from 1 January 1999 to 31 December 2020. Data on the number of cases and age at diagnosis were sourced from the KRN website (www.onkologia.org.pl/raporty) in an anonymised and aggregated form.

To assess the potential impact of HPV vaccines on HPV-related cancers and the health system in Poland, we used data on the specific types of HPV present in patients diagnosed with primary HPV-related cancers before the introduction of vaccines. Due to the unavailability of Polish data, we based our analysis on the results of a study conducted in the United States by the Centers for Disease Control and Prevention (CDC) in cooperation with seven regional US cancer registries.<sup>18</sup> The US study used archival tissue samples from patients diagnosed in the years 1993–2005. The study used material from 2,670 people diagnosed with cancer, a group carefully selected to be representative in terms of age and sex. The analysis included demographic and clinical factors, stratified by tumour location and HPV status. DNA collected from these samples was genotyped with the HPV Linear Array assay (LA, Roche Diagnostics, Indianapolis, USA), and the samples that first tested negative for HPV were re-tested using HPV INNO-LiPA genotyping (LiPA, Innogenetics, Gent, Belgium).

#### **Statistical Analysis**

The HPV-attributable fraction (AF) of malignant tumours by anatomical site and sex was determined on the basis of literature.<sup>18</sup> In addition, literature data<sup>18</sup> were used to calculate the percentages attributable to the types of HPV targeted by each vaccine (Cervarix, Gardasil, Gardasil 9).

The number of cancer cases attributable to HPV infections was calculated by multiplying the number of new registered cases by the specific attributable fraction for all HPV-related tumour sites. To assess the potential impact of the immunisation programme, the number of new registered cancer cases was multiplied by the attributable percentages for the HPV types targeted by each vaccine.

In addition, in order to assess the burden of HPV-related cancers on the Polish health care system, we calculated what percentage of all malignant neoplasms diagnosed in a given calendar year were HPV-related cancer cases.

The statistical analysis was performed with R (version 2023.06.0+421).

#### **Compliance with Ethical Standards**

This analysis was a re-evaluation of existing sets of publicly available data from the sources listed in the Sources of Data section. Due to the nature of the analysis, it was not necessary to seek formal approval from an ethics committee or request an exemption from this requirement.

# Results

#### **HPV-Related Cancers – Anatomical Organs**

The proportion of cancer cases attributable to HPV infection varies by organ. In the US population,<sup>18</sup> the largest proportion of cases can be attributed to HPV infections in cervical cancers (in situ (D06) – 99%, invasive (C53) – 91%). As regards the remaining HPV-related cancers, the percentage is slightly lower: anal cancer (C21) – 94% in women, 86% in men; vaginal cancer (C52) – 75%; oropharyngeal cancers (C09-C10) – 70%, vulvar cancer (C51) – 69%, and penile cancer (C60) – 63%. Of all HPV-related cancers, the least dependence on HPV was found in cancers of the oral cavity (C02-C06) – 32% and the larynx (C32) – 21%.

#### **Oncogenicity of Individual Types of HPV**

According to literature,<sup>18</sup> the most oncogenic type of HPV is type 16 (*Table 2*). With regard to most of the above-mentioned organs — with the exception of the oral cavity and larynx — this type is implicated in more than half of all malignant tumour cases and can therefore be considered to play a major role in the process of carcinogenesis. In oral cavity and laryngeal cancers, in which HPV infection is not the primary risk factor, it remains the most commonly associated type of HPV.

#### Potential Protective Effect of Vaccinations by Anatomical Sites

Based on data from the US population, HPV vaccination has been estimated to have the highest potential protective effect against anal cancers (up to 92% in females and up to 84% in males; *Table 3*). As regards the most common HPV-associated cancer, i.e. cervical cancer, the figure is up to 82% for the *in situ* form and 81% for the invasive form.

The data presented in Table 3 show that the attributable percentage depends proportionally on the vaccine's valence. However, attention should be paid to the possibility of cross-protection against virus genotypes other than those contained in the vaccine  $^{19-21}$ .

#### Burden of HPV-Associated Cancers for the Health Care System

Nationally, HPV-associated cancers that can be prevented by prophylactic vaccination account for about 4% of all malignancies diagnosed annually (7% of female cancers and 2% of male cancers; *Table S1*). Over the past two decades, approximately 6,000 new cancer cases could be directly attributed to HPV infection. This means that each year approximately 4,400 women and 1,600 men were diagnosed with a disease that could have been effectively prevented by vaccination. Existing vaccines have the potential to prevent approximately 54% of HPV-related cancer cases (75% in women and 35% in men), which in turn would translate into 4,600 fewer cancer cases a year.

# Time and Extent of Expected Systemic Effects of the Preventive Vaccination Programme

HPV-related malignancies, with the exception of cervical cancers, are usually diagnosed at an older age. Therefore, real-world population effects of the preventive vaccination programme that addresses adolescents aged 12–13 can only be assessed several decades from now. This does not mean, however, that one cannot try to predict the potential impact of the programme. Using the epidemiological data on the number of HPV-associated cancer cases that have been diagnosed in Poland so far and the literature on the percentage of these types of cancers where HPV has been detected, it is possible to estimate the impact of the measures undertaken on the health care system in the future.

The proportion of diagnoses associated with HPV infection varies from one organ to another. The age at which a given cancer is most often diagnosed also varies. Therefore, assessing the impact of vaccination on the epidemiological landscape and determining the timepoint when systemic effects of the universal HPV vaccination will become noticeable should address each organ separately.

For the reader's convenience, reasoning on the potential impact of preventive vaccination depending on anatomical site is presented in the form of 'cancer profiles'. Each profile answers the following questions: how many cancer cases could have been avoided had the entire population of Poland been vaccinated against HPV in the past decades, and when to expect systemic effects of the universal HPV vaccination programme.



Anatomical site		Sov	HPV-attributable percentage by type of HPV (%) Sex									
Anatomical site	Anatomical site		6	11	16	18	31	33	45	52	58	total
Oral cavity	C02-C06	both	1.4	0.7	19.9	2.1	0.0	0.7	0.0	3.5	0.0	32.0
Oropharynx	C01, C09-C10	both	0.0	0.2	58.2	2.0	0.2	4.3	0.5	0.5	0.2	70.1
Larynx	C32	both	1.4	0.7	5.9	1.7	0.0	4.6	0.0	0.0	0.0	20.9
Vulva	C51	female	0.6	0.0	48.1	0.6	1.1	9.3	0.6	2.7	0.6	68.8
Vagina	C52	female	0.0	0.0	53.4	1.7	0.0	11.6	3.3	1.7	1.7	75.0
Cervix (in situ)	D06	female	0.6	0.0	53.5	6.3	6.6	5.2	2.2	4.0	3.4	98.8
Cervix (invasive)	C53	female	0.1	0.4	50.1	16.1	2.1	3.5	5.5	1.8	1.8	90.6
Penis	C60	male	1.3	0.0	45.2	2.7	0.0	5.1	2.7	1.3	0.0	63.3
		female	1.4	0.0	78.5	1.1	1.2	8.4	0.0	0.0	1.1	86.2
Anus	C21	male	1.4	0.0	75.3	3.8	0.0	1.9	0.0	1.9	0.0	93.8
		both	1.4	0.0	77.3	2.1	0.8	6.1	0.0	0.7	0.7	91.1

Table 2. Human papillomavirus (HPV)-attributable percentage\* of cancer cases by anatomical site and sex.

\* HPV-attributable proportion of all HPV-related cancers

Table 3. Percentage attributable to human papillomavirus (HPV)\* in cancer cases by anatomical site and sex<sup>18</sup> and percentage attributable to HPV types targeted by the vaccines (Cervarix, Gardasil, Gardasil 9).

A metomoio		Sex	н	IPV-attributabl	e percentage (S	%)
Anatomic	Anatomical Site		HPV total	Cervarix	Gardasil	Gardasil 9
Oral an its	C02-C06	female	32.0	22.0	24.1	28.3
Oral cavity	CU2-CU6	male	32.0	22.0	24.1	28.3
	CO1 CO0 C10	female	70.1	60.2	60.4	66.1
Oropharynx	C01, C09-C10	male	70.1	60.2	60.4	66.1
	C32	female	20.9	7.6	9.7	14.3
Larynx		male	20.9	7.6	9.7	14.3
Vulva	C51	female	68.8	48.7	49.3	63.6
Vagina	C52	female	75.0	55.1	55.1	73.4
Cervix (in situ)	D06	female	98.8	59.8	60.4	81.8
Cervix (invasive)	C53	female	90.6	66.2	66.7	81.4
Penis	C60	male	63.3	47.9	49.2	58.3
A	C01	female	86.2	79.6	81.0	91.7
Anus	C21	male	93.8	79.1	80.5	84.3

\* HPV-attributable proportion of all HPV-related cancers



#### **PROFILE 1. Malignant Neoplasms of the Oral Cavity**

ICD-10: C02-C06 Sex: female, male Sites: tongue except base, gums, floor of mouth, palate, other parts of mouth

How many oral cavity cancer cases could have been avoided had the entire population of Poland been vaccinated against HPV in the past decades?

Approximately 32% of cancers of the oral cavity are associated with HPV infection (*Table 4*). Protective vaccinations should be able to prevent 22–28% of all cases of these neoplasms. Hence, if all Polish residents had received HPV vaccination in the past decades, approximately 6,000–8,000 cases of oral cavity cancer could have been avoided in the years 1999–2020.

**Table 4.** Malignant neoplasms of the oral cavity – total number of cases, cases attributable to human papillomavirus (HPV), cases that could have been prevented depending on the vaccine used (Cervarix, Gardasil 9); Poland, 1999–2020.

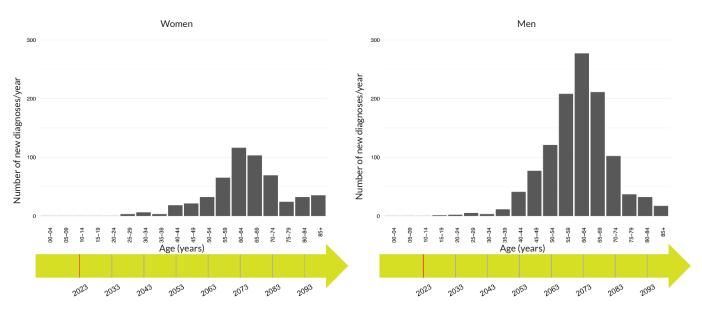
Sex		Cocce attribu	Avoidable cases				
	Total cases*	Cases attributable to HPV		Cer	varix	Gardasil 9	
		Number	Percent	Number	Percent	Number	Percent
female	8,170	2,614	32.0%	1,795	22.0%	2,314	28.3%
male	20,083	6,426	32.0%	4,420	22.0%	5,683	28.3%

\* Based on data from the National Cancer Registry (onkologia.org.pl/raporty).



# When are systemic effects of the universal HPV vaccination programme to be expected?

Oral cavity cancers are most often diagnosed at the age of 50–70 (*Figure 4*). Therefore, the first effects of vaccination should become noticeable around 2053. The greatest effect for the health care system will be visible around 2073.



**Figure 4.** Potential distribution of malignant neoplasms of the oral cavity (C02-C06) in the current population of 10–14 year-olds assuming no vaccination against HPV (females, males).



#### **PROFILE 2. Malignant Neoplasms of the Oropharynx**

ICD-10: C01, C09-C10 Sites: base of the tongue, tonsil, oropharynx Sex: female, male

How many oropharyngeal cancer cases could have been avoided had the entire population of Poland been vaccinated against HPV in the past decades?

Approximately 70% of cancers of the oropharynx are associated with HPV infection (*Table 5*). Protective vaccinations should be able to prevent 60–66% of all cases of these neoplasms. Hence, if all Polish residents had received HPV vaccination in the past decades, approximately 12,000–13,000 cases of oropharyngeal cancer could have been avoided in the years 1999–2020.

**Table 5.** Malignant neoplasms of the oropharynx – total number of cases, cases attributable to human papillomavirus (HPV), cases that could have been prevented depending on the vaccine used (Cervarix, Gardasil 9); Poland, 1999–2020.

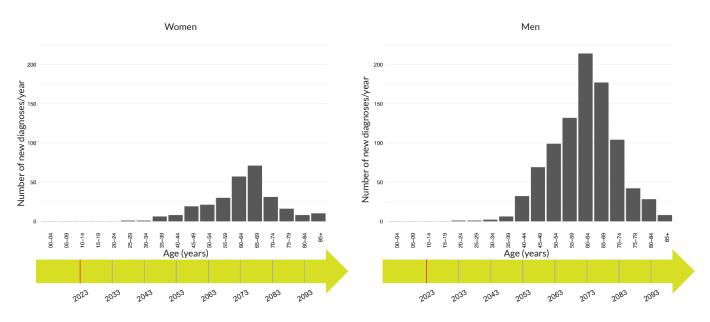
Sex		Cocce attribu	table to LIDV		Avoidable	cases	
	Total cases*	Cases attributable to HPV		Cer	varix	Gardasil 9	
		Number	Percent	Number	Percent	Number	Percent
female	4,710	3,304	70.1%	2,836	60.2%	3,112	66.1%
male	15,691	10,998	70.1%	9,446	60.2%	10,372	66.1%

\* Based on data from the National Cancer Registry (onkologia.org.pl/raporty).



# When are systemic effects of the universal HPV vaccination programme to be expected?

Oropharyngeal cancers are most often diagnosed at the age of 60–70 (*Figure 5*). Therefore, the first effects of vaccination should become noticeable around 2053. The greatest effect for the health care system will be visible around 2073.



**Figure 5.** Potential distribution of malignant neoplasms of the oropharynx (C01, C09-C10) in the current population of 10–14 year-olds assuming no vaccination against HPV (females, males).



#### **PROFILE 3. Malignant Neoplasms of the Larynx**

ICD-10: C32 Sites: glottis, epiglottis, infraglottic cavity Sex: female, male

How many laryngeal cancer cases could have been avoided had the entire population of Poland been vaccinated against HPV in the past decades?

Approximately 21% of cancers of the larynx are associated with HPV infection (*Table 6*). Protective vaccinations should be able to prevent 8–14% of all cases of these neoplasms. Hence, if all Polish residents had received HPV vaccination in the past decades, approximately 4,000–8,000 cases of laryngeal cancer could have been avoided in the years 1999–2020.

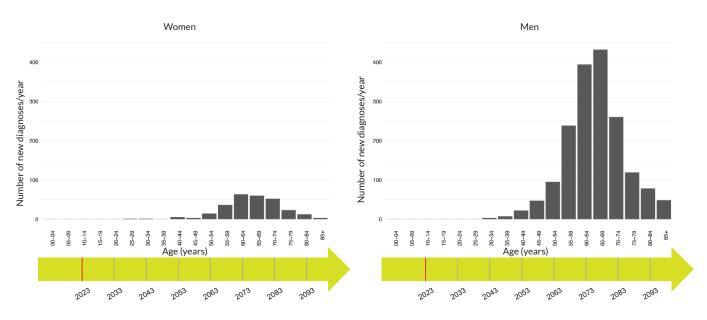
**Table 6.** Malignant neoplasms of the larynx – total number of cases, cases attributable to human papillomavirus (HPV), cases that could have been prevented depending on the vaccine used (Cervarix, Gardasil 9); Poland, 1999–2020.

Sex		Casas attribu	table to LIDV		Avoidable	cases	
	Total cases*	Cases attributable to HPV		Cerv	varix	Gardasil 9	
		Number	Percent	Number	Percent	Number	Percent
female	6,788	1,420	20.9%	519	7.6%	969	14.3%
male	46,964	9,816	20.9%	3,569	7.6%	6,716	14.3%

\* Based on data from the National Cancer Registry (onkologia.org.pl/raporty).

When are systemic effects of the universal HPV vaccination programme to be expected?

Laryngeal cancers are most often diagnosed at the age of 60–70 (*Figure 6*). Therefore, the first effects of vaccination should become noticeable around 2058. The greatest effect for the health care system will be visible around 2078.



**Figure 6.** Potential distribution of malignant neoplasms of the larynx (C32) in the current population of 10–14 year-olds assuming no vaccination against HPV (females, males).



#### **PROFILE 4. Malignant Neoplasms of the Vulva**

ICD-10: C51 Sites: labia, clitoris Sex: female

How many vulvar cancer cases could have been avoided had the entire female population of Poland been vaccinated against HPV in the past decades?

Approximately 69% of cancers of the vulva are associated with HPV infection (*Table 7*). Protective vaccinations should be able to prevent 49–64% of all cases of these cancers. Hence, if all women in Poland had received HPV vaccination in the past decades, approximately 5,000–7,000 cases of vulvar cancer could have been avoided in the years 1999–2020.

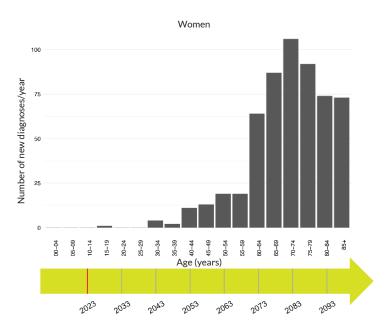
**Table 7.** Malignant neoplasms of the vulva – total number of cases, cases attributable to human papillomavirus (HPV), cases that could have been prevented depending on the vaccine used (Cervarix, Gardasil 9); Poland, 1999–2020.

Sex		Casas attribu	table to LIDV/		Avoidable	cases	
	Total cases*	Cases attributable to HPV		Cerv	varix	Gardasil 9	
		Number	Percent	Number	Percent	Number	Percent
female	10,511	7,233	68.8%	5,118	48.7%	6,685	63.6%

\* Based on data from the National Cancer Registry (onkologia.org.pl/raporty).

When are systemic effects of the universal HPV vaccination programme to be expected?

Vulvar cancers are most often diagnosed at the age of 65–80 (*Figure 7*). Therefore, the first effects of vaccination should become noticeable around 2063. The greatest effect for the health care system will be visible around 2083.



**Figure 7.** Potential distribution of malignant neoplasms of the vulva (C51) in the current population of 10–14 year-olds assuming no vaccination against HPV.



#### **PROFILE 5. Malignant Neoplasms of the Vagina**

ICD-10: C52 Sites: vagina Sex: female

How many vaginal cancer cases could have been avoided had the entire female population of Poland been vaccinated against HPV in the past decades?

Approximately 75% of cancers of the vagina are associated with HPV infection (Table 8). Protective vaccinations should be able to prevent 55–73% of all cases of these cancers. Hence, if all women in Poland had received HPV vaccination in the past decades, approximately 1,200–1,600 cases of vulvar cancer could have been avoided in the years 1999–2020.

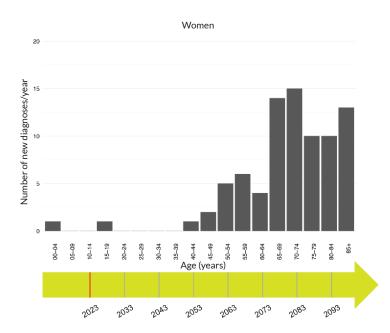
**Table 8.** Malignant neoplasms of the vagina — total number of cases, cases attributable to human papillomavirus (HPV), cases that could have been prevented depending on the vaccine used (Cervarix, Gardasil 9); Poland, 1999–2020.

Sex		Casas attribu	table to LIDV/		Avoidable	cases	
	Total cases*	Cases attributable to HPV		Cer	varix	Gardasil 9	
		Number	Percent	Number	Percent	Number	Percent
female	2,214	1,661	75.0%	1,221	55.1%	1,625	73.4%

\* Based on data from the National Cancer Registry (onkologia.org.pl/raporty).

When are systemic effects of the universal HPV vaccination programme to be expected?

Vaginal cancers are most often diagnosed at the age of 65–75 (*Figure 8*). Therefore, the first effects of vaccination should become noticeable around 2063. The greatest effect for the health care system will be visible around 2083.



**Figure 8.** Potential distribution of malignant neoplasms of the vagina (C52) in the current population of 10–14 year-olds assuming no vaccination against HPV.



#### **PROFILE 6.** Malignant and *In Situ* Neoplasms of the Cervix

ICD-10: C53 (invasive form), D07 (*in situ* form) Sites: mucosa of the cervical canal and the outer surface of the cervix Sex: female

How many cervical cancer cases could have been avoided had the entire female population of Poland been vaccinated against HPV in the past decades?

Approximately 91% of cancers of the cervix are associated with HPV infection (*Table 9*). Protective vaccinations should be able to prevent approximately 65–82% of all cases of these cancers. Hence, if all women in Poland had received HPV vaccination in the past decades, approximately 54,000–68,000 cases of cervical cancer could have been avoided in the years 1999–2020.

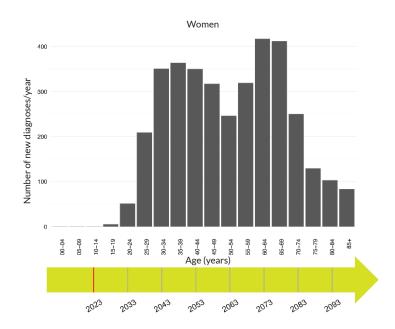
**Table 9.** Malignant and *in situ* neoplasms of the cervix – total number of cases, cases attributable to human papillomavirus (HPV), cases that could have been prevented depending on the vaccine used (Cervarix, Gardasil 9); Poland, 1999–2020.

Sex		Casas attribu	table to LIDV		Avoidable	cases	
	Total cases*	Cases attributable to HPV		Cerv	varix	Gardasil 9	
		Number	Percent	Number	Percent	Number	Percent
female	83,264	76,666	90.6%	54,160	65.0%	67,838	81.5%

\* Based on data from the National Cancer Registry (onkologia.org.pl/raporty).

When are systemic effects of the universal HPV vaccination programme to be expected?

Cervical cancers are most often diagnosed at the age of 25–75 (*Figure 9*). Therefore, the first effects of vaccination should become noticeable around 2033. The greatest effect for the health care system will be visible around 2073.



**Figure 9.** Potential distribution of malignant neoplasms of the cervix (C53) in the current population of 10–14 year-olds assuming no vaccination against HPV.



#### **PROFILE 7. Malignant Neoplasms of the Penis**

ICD-10: C60 Sites: foreskin, glans penis and body of penis Sex: male

How many penile cancer cases could have been avoided had the entire male population of Poland been vaccinated against HPV in the past decades?

Approximately 63% of cancers of the penis are associated with HPV infection (*Table 10*). Protective vaccinations should be able to prevent approximately 48–58% of all cases of these cancers. Hence, if all men in Poland had received HPV vaccination in the past decades, approximately 2,300-2,900 cases of penile cancer could have been avoided in the years 1999–2020.

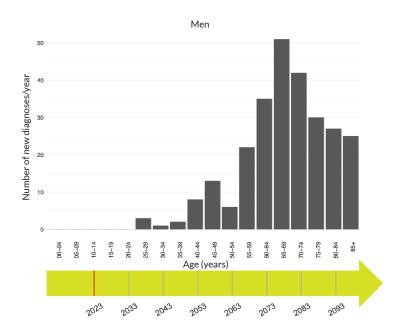
**Table 10.** Malignant neoplasms of the penis – total number of cases, cases attributable to human papillomavirus (HPV), cases that could have been prevented depending on the vaccine used (Cervarix, Gardasil 9); Poland, 1999–2020.

		Cases attribu	table to LIDV/		Avoidable	cases	
Sex	Total cases*	Cases attribu		Cerv	varix	Gard	lasil 9
		Number	Percent	Number	Percent	Number	Percent
male	4,909	3,110	63.3%	2,351	47.9%	2,860	58.3%

\* Based on data from the National Cancer Registry (onkologia.org.pl/raporty).

When are systemic effects of the universal HPV vaccination programme to be expected?

Penile cancers are most often diagnosed at the age of 55–70 (*Figure 10*). Therefore, the first effects of vaccination should become noticeable around 2063. The greatest effect for the health care system will be visible around 2078.



**Figure 10.** Potential distribution of malignant neoplasms of the penis (C60) in the current population of 10–14 year-olds assuming no vaccination against HPV.



#### **PROFILE 8. Malignant Neoplasms of the Anus**

ICD-10: C21 Sites: anal canal, cloacogenic zone Sex: female, male

> How many anal cancer cases could have been avoided had the entire population of Poland been vaccinated against HPV in the past decades?

Approximately 87–94% of cancers of the anus are associated with HPV infection (*Table 11*). Protective vaccinations should be able to prevent approximately 80–92% of all cases of these cancers. Hence, if all Polish residents had received HPV vaccination in the past decades, approximately 5,000-6,000 cases of anal cancer could have been avoided in the years 1999–2020.

**Table 11.** Malignant neoplasms of the anus — total number of cases, cases attributable to human papillomavirus (HPV), cases that could have been prevented depending on the vaccine used (Cervarix, Gardasil 9); Poland, 1999–2020.

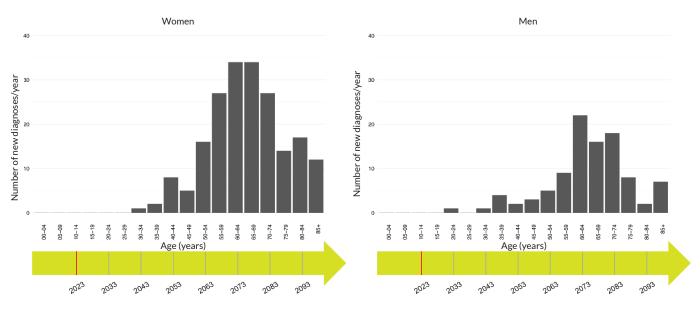
		Cases attribu	table to LIDV		Avoidable	cases	
Sex	Total cases*	Cases attribu	table to HPV	Cer	varix	Garc	lasil 9
		Number	Percent	Number	Percent	Number	Percent
female	4,135	3,878	93.8%	3,292	79.6%	3,793	91.7%
male	2,473	2,132	86.6%	1,958	79.2%	2,086	84.4%

\* Based on data from the National Cancer Registry (onkologia.org.pl/raporty).



# When are systemic effects of the universal HPV vaccination programme to be expected?

Anal cancers are most often diagnosed at the age of 55–75 (*Figure 11*). Therefore, the first effects of vaccination should become noticeable around 2063. The greatest effect for the health care system will be visible around 2073.



**Figure 11.** Potential distribution of malignant neoplasms of the anus (C21) in the current population of 10–14 year-olds assuming no vaccination against HPV (females, males).

# Conclusions

Introducing a vaccines against HPV into general practice could drastically reduce the incidence of HPV-related cancers. In Poland, malignant cancers closely related to the presence of HPV account annually for approximately 4,400 cases in women and 1,600 cases in men. Still, with a pro-vaccine stance and public cooperation, these numbers can be significantly reduced. Protective vaccination is a key element of prophylaxis strategies as a means to prevent these diseases and reduce the overall number of cases.

Introducing an HPV vaccination programme in Poland is a process that requires perseverance and patience. Changes in public health are never immediate but rather gradual over decades. Research and observations suggest that the first significant reductions in cervical cancer incidence can be observed approximately 10 years after the introduction of vaccination. The anticipated changes in the incidence rates of other HPV-related cancers will also take time and are expected to peak in about 40–50 years. Achieving full protective effects that ensure long-term public health benefits requires involving the health care sector and promoting social education. This way, by taking steps to implement HPV vaccination, Poland is demonstrating its ability to take strategic actions for the benefit of future generations.

# **Directions of Expected Actions**

An important element in the implementation of HPV vaccination programme as a means to prevent HPV-associated cancers is a comprehensive approach based on cooperation of the general public, health care professionals and decision-making bodies within the health care system. Initiating and completing certain activities addressed at these three groups seems to be essential to achieve the ambitious health goal of minimising HPV infections in the Polish population. Below we discuss the directions of the expected change which follow from this analysis, in relation to these target groups and the associated activities. These directions seem justified from the point of view of maximising anti-HPV vaccination coverage, as well as reducing the burden of HPV-related diseases in the Polish population.

#### **The General Public**

- Recommending that in the absence of medical contraindications — all parents/guardians have their children vaccinated against HPV as part of a universal, free immunisation programme.
- Working to educate the general public, in particular the target groups, i.e. children, adolescents and their guardians, about the health benefits of HPV vaccination, and about the myths surrounding the HPV virus and vaccines.
- Education of target groups, in accordance with the community-based concept of health promotion, should be conducted primarily in schools and medical offices, which will ensure comprehensive community education tailored to local needs. The availability of information and support from teachers, medical staff and family doctors plays a key role in shaping an informed society and promoting the benefits of a universal HPV vaccination program.
- Building public confidence in vaccination. According to the latest Polish recommendations on prophylactic vaccination against HPV (2022)<sup>22</sup>, educational measures "(...) should be undertaken at the central level (media campaigns), regional/local level (scientific and training conferences, educational and information initiatives of the manufacturers), and individual level (at clinics and doctors' offices) in order to maximise the transmission of reliable information on the benefits of HPV vaccination."

#### **Health Care Professionals**

- Routine communication of the health benefits of HPV vaccination and general information on HPV in particular to patients with children at the age of vaccination. During a pediatric visit, it is important to provide parents with this information. In addition, it is essential that healthcare professionals are involved as much as possible in encouraging patients to be vaccinated, including gynecologists (especially during teenagers' first visits), nurses and midwives.
- Undertaking activities to promote and improve awareness among health care professionals of the health benefits resulting from HPV vaccination and effective methods of educating patients and their caretakers.

#### **Decision-Makers**

- Ensuring financial, organisational and infrastructural stability to provide for the continued operation of the universal HPV vaccination programme in Poland.
- Recommending for HPV vaccinations to be introduced into the mandatory vaccination calendar in Poland while simplifying the immunisation procedure, for example by including schools a vaccination sites. Facilitating access to medical services by rationalizing the vaccination model for both healthcare providers and parents is one of the key success factors, as the current one, based on part of primary health care clinics, does not ensure full accessibility.
- Ensuring financial, organisational and legal resources necessary to carry out extensive educational activities on the health benefits of HPV vaccination. It is important to organize a social media campaign, addressed separately to teenagers and parents, engaging people with high social influence.
- Promoting and funding research on the health outcomes of HPV vaccination, as well as on health interventions aimed to increase vaccination coverage.
- Continuous monitoring of the effectiveness of the universal HPV vaccination programme, and in the event of the vaccination coverage falling or stabilising at an unsatisfactory level – undertaking corrective measures.
- Including information on primary prevention of cancer, mainly based on the European Code Against Cancer, in curriculum in schools. Such activities should be carried out, for example, as part of biology lessons, and in the future by building knowledge, skills and competences as part of planned health lessons.

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# Appendix 1

Table S1. Total numbers of cancer cases, numbers of HPV-associated neoplasms, HPV-attributable fractions, total number of neoplasms attributable to HPV, and numbers and propor-tions of cancer cases that could have been prevented depending on the vaccine used (Cervarix, Gardasil 9) in the entire Polish population.

tions of Câ	ancer cases	s that could have	ve been preventet	a depending on the va	tions of caricer cases that could have been prevented depending on the vaccine used (Cervarix, Gardash 7) in the entire Polish population.	ווו או אומסמפט	the entire P	ollsn populati	ion.		
								Potentially p	Potentially preventable cancer cases	ases	
Year	Sex	Cancer cases in total	HPV-associated cancers	HPV-attributable percentage in total	HPV-attributable cases in total	Number	ber	Percentage associa	Percentage relative to HPV- associated cancers	Percentage malignant	Percentage relative to all malignant neoplasms
						Cervarix	Gardasil 9	Cervarix	Gardasil 9	Cervarix	Gardasil 9
	female	55,564	5,242	83%	4,352	3,154	3,912	%09	75%	6%	7%
1999	male	59,518	4,038	35%	1,394	912	1,177	23%	29%	2%	2%
	total	115,082	9,280	62%	5,746	4,066	5,089	44%	55%	4%	4%
	female	58,079	5,441	82%	4,482	3,234	4,021	59%	74%	6%	7%
2000	male	60,934	4,028	34%	1,375	891	1,156	22%	29%	1%	2%
	total	119,013	9,469	62%	5,857	4,125	5,177	44%	55%	3%	4%
	female	59,815	5,434	83%	4,494	3,232	4,026	59%	74%	5%	7%
2001	male	62,405	4,003	33%	1,328	841	1,107	21%	28%	1%	2%
	total	122,220	9,437	62%	5,822	4,073	5,133	43%	54%	3%	4%
	female	61,605	5,533	82%	4,562	3,271	4,080	59%	74%	5%	7%
2002	male	63,953	3,940	34%	1,323	844	1,107	21%	28%	1%	2%
	total	125,558	9,473	62%	5,885	4,115	5,187	43%	55%	3%	4%
	female	62,178	5,363	81%	4,369	3,129	3,909	58%	73%	5%	6%
2003	male	65,685	3,919	34%	1,324	852	1,111	22%	28%	1%	2%
	total	127,863	9,282	61%	5,693	3,981	5,020	43%	54%	3%	4%
	female	62,947	5,382	82%	4,401	3,163	3,943	59%	73%	5%	6%
2004	male	66,709	3,908	34%	1,339	865	1,124	22%	29%	1%	2%
	total	129,656	9,290	62%	5,740	4,028	5,067	43%	55%	3%	4%
	female	66,926	5,432	81%	4,421	3,155	3,945	58%	73%	5%	6%
2005	male	69,893	4,156	34%	1,427	926	1,202	22%	29%	1%	2%
	total	136,819	9,588	61%	5,848	4,081	5,147	43%	54%	3%	4%



Gardasil 9 Percentage relative to all malignant neoplasms %9 2% 4% %9 2% 4% 2% %9 2% 4% 2% 4% %9 %9 2% 4% 5% 3% 5% 2% 3% Cervarix 1%1%5% 1%3% 5% 3% 5% 1%3% 4% 1%3% 4% 1%3% 4% 3% 4% 1%3% Potentially preventable cancer cases Percentage relative to HPV. Gardasil 9 54% 31% 31% 54% 73% 29% 73% 30% 56% 73% 30% 55% 73% 30% 54% 72% 55% 72% 55% 71% 31% associated cancers Cervarix 43% 59% 23% 44% 44% 23% 43% 24% 44% 24% 44% 57% 24% 43% 58% 58% 23% 58% 23% 58% 58% Gardasil 9 3,852 1,1724,317 5,519 4,212 5,448 4,142 1,253 5,276 3,916 1,228 5,1445,024 1,202 1,236 5,395 4,043 1,233 3,870 1,255 5,125 Number Cervarix 3,086 3,452 4,389 3,362 4,323 4,273 3,223 4,192 3,116 4,082 3,079 4,064 3,991 3,297 905 976 969 996 985 937 961 HPV-attributable cases in total 4,310 1,389 5,699 4,834 6,255 6,188 4,662 1,478 6,140 4,400 1,435 5,835 1,421 4,541 1,4415,982 4,352 1,472 4,731 1,4575,824 HPV-attributable percentage in total 61% 81%35% 62% 81%36% 61% 82% 35% 82% 35% 63% 35% 82% 81%36% 62% 80% 36% 62% 63% **HPV-associated** cancers 5,278 4,019 5,900 5,808 5,713 4,190 5,415 3,950 9,365 9,512 9,297 4,129 9,903 3,956 9,533 5,424 4,088 4,031 9,931 9,937 5,577 Cancer cases in total 136,949 143,193 149,875 140,675 145,514 66,948 69,989 74,206 147,687 158,271 70,686 71,156 72,037 72,753 72,761 74,804 78,965 70,001 73,481 75,071 79,306 female female female female Sex female female female male male male male male male total total total total male total total total Year 2006 2007 2008 2009 2010 2011 2012

Appendix 1

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MEDICAL RESEARCH AGENCY	
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								Potentially p	Potentially preventable cancer cases	ases	
Year	Sex	Cancer cases in total	HPV-associated cancers	HPV-attributable percentage in total	HPV-attributable cases in total	Number	ber	Percentage associat	Percentage relative to HPV- associated cancers	Percentage I malignant	Percentage relative to all malignant neoplasms
						Cervarix	Gardasil 9	Cervarix	Gardasil 9	Cervarix	Gardasil 9
	female	80,027	5,559	80%	4,432	3,148	3,949	57%	71%	4%	5%
2013	male	80,452	4,060	38%	1,531	1,049	1,320	26%	33%	1%	2%
	total	160,479	9,619	62%	5,963	4,197	5,269	44%	55%	3%	3%
	female	82,462	5,506	%6 <i>L</i>	4,344	3,094	3,878	56%	70%	4%	5%
2014	male	82,262	4,411	38%	1,668	1,145	1,439	26%	33%	1%	2%
	total	164,724	9,917	61%	6,012	4,239	5,317	43%	54%	3%	3%
	female	84,351	5,612	78%	4,405	3,134	3,932	56%	70%	4%	5%
2015	male	84,975	4,560	37%	1,676	1,135	1,438	25%	32%	1%	2%
	total	169,326	10,172	%09	6,081	4,269	5,370	42%	53%	3%	3%
	female	84,180	5,194	78%	4,064	2,902	3,632	56%	70%	3%	4%
2016	male	85,649	4,426	38%	1,691	1,174	1,467	27%	33%	1%	2%
	total	169,829	9,620	%09	5,755	4,076	5,099	42%	53%	2%	3%
	female	84,740	5,309	%6 <i>L</i>	4,181	2,968	3,726	56%	70%	4%	4%
2017	male	85,256	4,254	38%	1,605	1,104	1,387	26%	33%	1%	2%
	total	169,996	9,563	61%	5,786	4,072	5,113	43%	53%	2%	3%
	female	86,466	5,368	79%	4,248	3,004	3,780	56%	70%	3%	4%
2018	male	86,642	4,151	39%	1,608	1,124	1,398	27%	34%	1%	2%
	total	173,108	9,519	62%	5,856	4,128	5,178	43%	54%	2%	3%
	female	88,137	5,529	80%	4,418	3,097	3,911	56%	71%	4%	4%
2019	male	88,073	4,166	39%	1,623	1,140	1,415	27%	34%	1%	2%
	total	176,210	9,695	62%	6,041	4,237	5,326	44%	55%	2%	3%
	female	74,277	4,773	79%	3,773	2,641	3,340	55%	70%	4%	4%
2020	male	73,467	3,737	40%	1,477	1,043	1,290	28%	35%	1%	2%
	total	147,744	8,510	62%	5,250	3,684	4,630	43%	54%	2%	3%

Appendix 1

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