Human papillomavirus (HPV) vaccination coverage of children in Slovakia

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Abstract

This report presents preliminary annual human papillomavirus vaccine coverage data of the 2-dose schedule fully reimbursed for girls and boys 12 years old in Slovakia. Human papillomavirus vaccination coverage of girls and boys in Slovakia based on health insurance data reported to the National Health Information Center. As of May 1, 2022, the Slovak Republic has joined other EU countries with full reimbursement of the nonavalent vaccine. This step was expected to rapidly increase vaccination coverage rates (VCRs) in this core cohort providing better health protection of the youth. However, the experience of the Bratislava Self-Governing Region (BSK) shows that self-payers are also interested in vaccination.

Keywords: vaccination, HPV, vaccination coverage rate, walk-in vaccination site

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1 Introduction

HPV stands for 'human papillomavirus', which is a group of more than 100 viruses. Some types of HPV infections cause warts, and some can cause different types of cancer.¹ These infections are often transmitted sexually or through other skinto-skin contact or mucous membranes. There is a well-established link between HPV and the development of cervical cancer, but HPV infection is also associated with vaginal and vulvar cancer, head and neck cancers as well as anal cancers in both sexes and penile cancer in men (Prue et al. (2018)). HPV DNA was detected in 90% of cervical, 91% of anal, 75% of vaginal, 70% of oropharyngeal, 69% of vulvar, 63% of penile, 32% of oral cavity, and 21% of laryngeal cancers, as well as in 99% of cervical cancer in situ (Saraiya et al. (2015)). The incidence of vaginal and vulvar cancer is about 2/100,000 in Denmark, Finland, Norway and Sweden (Hemminki et al. (2022)). The estimated age-standardized incidence rate by the world standard population today is 0.84 cases per 100 000 person-years (Cardona and García-Perdomo (2018)). Cervical cancer caused by HPV virus alone is the second most common type of cancer in Slovakia affecting women at reproductive age. Approximately 2 women are diagnosed daily with the disease. 2 In 2021, 215 women died from this diagnosis.³ Vaccination against HPV virus is the only available option in primary prevention of different types of cancers.

One of the priorities of the National Oncology Programme for 2021-2025 of the Slovak Republic is to increase vaccination rates of girls and boys against HPV.⁴ Europe's Beating Cancer Plan sets the target of VCR against HPV at 90 % for girls until year 2030 and calls for increase in VCRs for boys⁵ The first reimbursed vaccine against HPV was a four-valent vaccine with 10% reimbursement for 11 years old girls from April 1st, 2007 in Slovakia. In Slovakia, a bivalent vaccine against HPV

 $^{^1{\}rm Mayo}$ Clinic, HPV infection, https://www.mayoclinic.org/diseases-conditions/hpv-infection/symptoms-causes/syc-20351596

²European Cancer Information System, Estimated incidence of cervical cancer in Slovakia in 2020. https://ecis.jrc.ec.europa.eu.

³Štatistický úrad Slovenskej Republiky.

⁴Office of the government of the Slovak Republic (2021), Proposal for updating the Action Plans of the National Oncology Programme - new version, https://rokovania.gov.sk/RVL/ Material/26288/1..

⁵European Commission (2021), Europe's Beating Cancer Plan.https://ec.europa.eu

has been fully reimbursed and nonvalent vaccine partially reimbursed for 12 years old girls and boys since January 1, 2019. Vaccination requires a 2-dose schedule. The HPV immunization programme is part of a broader set of actions taken by the MoH towards cervical cancer elimination, together with raising awareness about HPV, increasing cervical cancer screening rates, implementation of a coordinated prevention and treatment strategy. As of May 1, 2022, the Slovak Republic has joined other EU countries with full reimbursement of the nonavalent vaccine. This step was expected to rapidly increase vaccination coverage rates in this core cohort providing better protection for the youth. HPV vaccination is recommended for the vaccination of 12 years old boys and girls in the Slovak Republic based on Decree of the MoH No. 585/2008 Coll.⁶

Currently, a bivalent vaccine and a nonavalent vaccine are available free of charge between the 12th and 13th birthday of the child.⁷ The first dose can be given at any time of age 12 years old. The second dose is also fully reimbursed and should be administered between 5 and 13 months after the first dose. The HPV vaccine is administered by paediatricians. HPV vaccination in other age groups (13 + years) is not fully reimbursed from public health insurance and these groups have to pay for it in pharmacies. HICs, however, provide some level of payback within their benefit programs for age groups 13 - 17.

2 Methods of data collection

This interim report up to December 2022 presents detailed vaccination data for the first time in history of the HPV immunization programme in Slovakia. The data is collected based on healthcare claims data of all three health insurance companies which are provided to the National Health Information Center ⁸ The aim of this analysis is to show a trend in HPV VCRs based on reimbursed HPV vaccines in Slovakia.

 $^{^{6}}$ Decree of the MoH No. 585/2008 Coll

 $^{^7\}mathrm{MoH}\ \mathtt{https://www.health.gov.sk/?zoznam-kategorizovanych-liekov.}$

⁸HICs data sent to NHIC according to Section 15 (6) of Act No. 581/2004 Coll. on Health Insurance Companies, Health Care Supervision and on the Amendment and Supplementing of Certain Laws, as amended and pursuant to Act No. 153/2013 Coll. on the National Health Information System and on the Amendment and Supplementing of Certain Laws, as amended.

$$IR = \frac{Q}{N} \tag{1}$$

kde IR (incidence rate) is vaccination coverage rate, Q is the number of vaccines used and N is cohort population size. HPV vaccine coverage was calculated based on the total number of eligible girls and boys in the target population who received at least 1 dose (or 2 or 3) of the HPV vaccine in the years / months prior to October 2022. We assume that data in Q1 and Q2 of 2022 is complete and other quarters in 2022 will be updated.

Methodological issues:

- Given that claims represent the number of doses collected from pharmacies, and not the number of doses injected, there might be a slight overestimation of VCRs.
- On the other hand, our results presented in this report covered only reimbursed vaccines and do not include vaccination of older children or adults who pay for vaccines out-of-pocket. This could lead to some underestimation of VCRs.
- Age is calculated as the highest age within the observation period
- We assign a patient to a region based on the address of the pharmacy where the patient picked up the vaccine, not based on the patient's place of residence.

The variability in vaccination rates over months may also be explained by vaccine stock out, which we did not take into account in our report. The increased demand for the nonavalent vaccine was also due to the fact that in 2021, according to the available data, there were no imports of the bivalent vaccine. (C.1). Full data tables and codebook are available on the MoH website.⁹

⁹https://www.health.gov.sk/?iza

3 Results

This paper presents year-to-date (September 2022) HPV vaccine coverage data for the adolescent girls and boys of 2006-2010 birth cohorts of the 2-dose schedule. Since May 2022, the nonavalent vaccine if fully reimbursed for 12 years old girls and boys, driving a significant increase in uptake. Approximately 5,800 doses of HPV vaccines were administrated to adolescent girls and boys in May, which is 23% more than in January-April 2022 combined. In May, 92% of these vaccinations were 9-valent vaccines. The effect continued in Q2 and Q3, with data of 2022 significantly exceeding those of corresponding months in 2021. Overall, 53% more vaccines were reimbursed for in the first nine months of 2022 than in the same period of 2021 (figure 1).



FIGURE 1: REIMBURSED DOSES BY MONTH

Increased demand led to an improvement in VCRs in the first month after the program modification (figure 2A). VCRs more than doubled between April and May 2022: for girls born in 2009 from 9.2% to 18.5% (1st doses), for boys – from 2.7% to 6.0%. In June-September the trend continued with VCRs reaching 30.1% and 10.8% respectively.

Notes: Approximately 5,800 doses of HPV vaccines were administrated to adolescent girls and boys in May 2022, which is 23% more than in January-April 2022 combined. Overall, 53% more vaccines were reimbursed in the first nine months of 2022 than in the same period of 2021.



FIGURE 2: EVOLUTION OF VCRs IN HPV IN 2022 - AT LEAST 1ST DOSE

It is important to note that children born in 2009-2010 continue to be vaccinated throughout the year with the main focus of the paediatricians being on children close to 13 years of age due to reimbursement conditions. For the 2010 birth cohort, VCRs in May 2022 increased almost 9 times – from 0.3% to 2.6%for girls and 8 times for boys from 0.1% to 0.8%. (figure 2B). By end of September 1st dose VCRs for 2010 birth cohort girls and boys reached 10.1% and 3.5% respectively. By comparison, last year VCRs for girls aged 12 (2008 birth cohort) at the end of the year (1st doses) peaked at 24.9% and 8.0% for boys. This means that this year the coverage rates from last December were already surpassed in June, suggesting stellar end of year expected results (figure 3). However, there is a significant missed opportunity for birth cohorts 2007 and younger, where VCRs stay limited (21.5% for 2007 birth cohort, 11.7% for 2006 birth cohort for girls, single digit numbers for boys, 1st dose). Adherence to the vaccination schedule in recent years was approximately 80% for both genders. This is a relatively low compliance compared to other European programmes for girls, where median adherence is around 93%, and at the level of what 's observed for boys - 83%. (figure B5).

These results are also due to joint efforts of the MoH, Ministry of Education, Science, Research and Sport, National Oncology Institute, health insurance companies, patients' organizations, scientific societies, and municipalities in raising awareness about HPV and HPV vaccination.



FIGURE 3: NATIONAL VCRS BY BIRTH COHORT AND DOSE

Despite the marked increase in VCR at the national level, there is a significant difference at the regional level. VCRs vary more than twice from 43.3% in the Bratislava region to 21.3% in the Košice region (2009 birth cohort girls, 1st doses) (figure 4A). The difference for boys is similar, although the overall level is lower - from 14.7% to 6.8% in the mentioned locations. Overall, the western part of the country has higher VCRs compared to the eastern part.Within the 2010 birth cohort, Trenčín region leads the regional ranking with 13.5% of VCRs for girls and 5.1% for boys (1st dose). Košice region again has the lowest VCRs with 7.7% and 2.9% respectively(figure4B).



A: CHILDREN BORN IN 2009





FIGURE 4: REGIONAL DIFFERENCES IN HPV VACCINATION COVERAGE OF CHILDREN WITH AT LEAST ONE DOSE

In addition to the results at the county level, differences in vaccination rates by district should be considered. Figure 5A shows significant differences between VCRs in districts within the same region for girls born in 2009. The highest vaccination rate among girls was in the districts of Humenné, Ružomberok, Banská Štiavnica, Bratislava, where it reached 50% VCRs. The lowest rates were in Stropkov (6%), Gelnica (9%) and Kežmarok (10%).

Most boys were vaccinated in Žiar nad Hronom, Žarnovica, Ružomberok and Bytča, where the overall vaccination rate in this age cohort was above 30%. The 0% vaccination rate was in Stropkov (figure 5B).



Map data: ZBGIS® • Created with Datawrapper



Map data: ZBGIS® • Created with Datawrapper

B: Boys

Figure 5: Comparison of vaccination coverage of at least one dose in girls and boys born in 2009 by district

 $\it Notes:$ Bratislava and Košice were taken as a whole in the data and not divided into individual city districts.

While the results are promising, there is still room for improvement to ensure that the HPV immunization programme reaches the goals of the National Oncology Plan and Europe's Beating Cancer which set at 90% VCR. (Figure 6) presents a comparison of Slovak VCRs for the primary cohort with other neighbouring countries (where data available). The Czech Republic has VCRs for girls 2.6 times higher, Hungary 3.1 times higher.



FIGURE 6: NATIONAL VCRs FOR PRIMARY BIRTH COHORT IN 2021, 1ST DOSE, MARKETS WITH GENDER-NEUTRAL HPV PROGRAMME

Notes: WHO HPV Immunization data, Association of Innovate Pharmaceutical Industry (Czech Republic data), Slovakia - health insurance data reported to the National Health Information Center.

SK – Slovakia, DE – Germany, CZ – Czech Republic, HU – Hungary, IE – Ireland, UK - United Kingdom of Great Britain and Northern Ireland, BE – Belgium, SE – Sweden, DK – Denmark, NO – Norway.

4 Conclusions

The MoH is actively engaged in various initiatives aimed at raising awareness of HPV related diseases, education about HPV vaccines, the effectiveness of vaccination campaigns at national, regional and municipality level. These initiatives are carried out in collaboration with patient organizations, paediatric societies, HICs and various NGO associations and include, but are not limited to:

- support of municipality vaccination days, as piloted in Bratislava,
- reminders and recall programmes for the parents of adolescents, as initiated by HICs,
- ongoing discussions on expanding reimbursement to older adolescent categories.

Key recommendations going forward for precise vaccination coverage tracking

- Expand data collection on HPV vaccination and ensure that data will be publicly available and updated on quarterly basis
- Add health insurance companies (HICs) data about number of 13-17 years old girls and boys who have had access to vaccination through partial payment via HICs benefits to get more complete VCR data in all children.
- Include an HPV vaccine administration-specific code in the system to monitor vaccination rate across all cohorts regardless of vaccine reimbursement.
- Open discussion on expanding reimbursement to children 13 to 18 years old (or at least to 15 years old) based on the positive impact on acceleration of VCR after implementation of full reimbursement of nonavalent vaccine and consider a program for older birth cohorts.
- Extend HICs' systems of automatic invitations for 1st dose of HPV vaccination, also with implementation of reminders for 2nd dose to increase adherence to at least 90%.

- Support GPs (e.g. technically or with behavioural interventions) to increase uptake and compliance with 2nd dose.
- Support municipalities in implementation of HPV prevention programmes, including mass HPV vaccination events to increase HPV vaccination coverage. Target areas with lower vaccination rates.
- Include a new parameter for the evaluation of ambulances by HICs.
- Increase communication on prevention, awareness-raising campaign at national level.
- Given the successes of HPV vaccination rates from other countries, consider introducing a vaccination programme in schools/in cooperation with schools.

As of May 1, 2022, the Slovak Republic has joined other EU countries with full reimbursement of the nonavalent vaccine. This step was expected to rapidly increase VCRs in this core cohort providing better health protection of the youth. Despite the marked increase in VCR at the national level, there is a significant difference at the regional level. The differences are also significant at the district level. Adherence to the vaccination schedule was approximately 80% for both genders in Slovakia. This is a relatively low compliance compared to other European programmes for girls, where median adherence is around 93%, and at the level of what's observed for boys – 83%. There is still room for improvement.

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Appendix A

A.1 A case study: Experience of Bratislava self-governing region with the HPV Vaccination Day

Prevention is one of the key goals of the health department at Bratislava selfgoverning region as included in draft of Strategy for development of healthcare in Bratislava self-governing region for 2022-2026.¹⁰ The accelerating moment for HPV vaccination was the inclusion of nonavalent vaccine into the reimbursement list. To increase awareness and vaccination uptake, Bratislava self-governing region held two¹¹ events of barrier-free vaccination against HPV in June and September 2022. HPV vaccination was available to the public through a designated healthcare provider - Poliklinika Karlova Ves. The key to building a simplified vaccination process was creating a free and transparent booking system. Thanks to it the organizers were able to estimate the interest in vaccination and thus order required vaccine quantities from a pharmacy. An agreement with a distributor allowed the pharmacy to return unused vaccines back to the distributor thus reducing the risk for all payers in the value chain. Outreach to potential people who would like to be vaccinated was done mainly through social media. The Vaccination Day was also supported by non-government organizations (NIE RAKOVINE, League against Cancer) and several influencers. The Ministry of Health and Slovak Society of Primary Paediatric Care provided patronage. Out of 272 registered persons, 162 people (60%) arrives at the healthcare center. Another 18 people who came without prior registration were also vaccinated. The age-gender split of the vaccinated is shown in Figure A1.

Adolescents aged 12 (i.e. before their 13th birthday) are entitled to full reimbursement of the vaccine from public health insurance and are therefore expected to comprise the majority within this group. However, only 48 of them (27%) were aged 12. The majority of those vaccinated were adults (113 individuals, 63%). The oldest people were a 56-year-old lady and a 52-year-old gentleman. The median

¹⁰Bratislava self-governing region https://bratislavskykraj.sk/wp-content/uploads/ 2022/06/strategia-rozvoja-zdrav-star-bsk-zverej.pdf

 $^{^{11}\}mathrm{Third}$ vaccination day 16/12/2022 organized by BSK is not included in this report

age of woman was 26.8 years, men 29.2 years.



FIGURE A1: BRATISLAVA BARRIER FREE VACCINATION EVENTS – SPLIT OF VACCINATED BY GENDER AND AGE

Notes: 12 years: two-dose scheme, the only cohort that is mandatorily covered by the VZP, 13-14 years: two-dose scheme, 15-18 years: three-dose scheme. 19-59 years: adults, three-dose scheme.

Why did people use the option of vaccination within the event?

- Their GP does not vaccinate adults
- Their doctors ask for a fee to administer the vaccine,
- The GP is far away, vaccination at central location is more convenient.

All respondents agreed that they would like to have follow up doses of the vaccination schedule administered in the same way. This requires reminding them about the date of the next dose and organization of the next vaccination day. Conclusion and recommendation:

- Walk-in vaccination sites play a key role in increasing vaccination of population.
- Even though only a certain part of the population is entitled to full coverage of the vaccine from public health insurance, a dedicated vaccination site was also attractive for self-payers of both genders and all ages.
- By using the self-service booking system, citizens had the option of choosing a convenient time slot for vaccination and the organizers got contact details for follow up and reminding of the next dose within the vaccination scheme.

Appendix B

B.1 Additional details on VCRsi



FIGURE B1: NATIONAL VCRS BY BIRTH COHORT



B: Full course

FIGURE B2: REGIONAL VCRs by birth cohort: Girls



FIGURE B3: REGIONAL VCRS BY BIRTH COHORT: BOYS





FIGURE B4: REGIONAL ADHERENCE RATES BY BIRTH COHORT AND GENDER

 $Notes:\ 2009\mathchar`-2010$ adherence rates not representative as most of second doses are expected to happen in 2022.



FIGURE B5: Adherence comparison, primary birth cohort, markets with gender-neutral HPV programme

Notes: Boys' vaccination only started in Germany in 2021, so adherence may not be representative for Year 1 of the programme. Hungarian data may require additional validation. SK – Slovakia, DE – Germany, HU – Hungary, UK - United Kingdom of Great Britain and Northern Ireland, BE – Belgium, IE – Ireland, DK – Denmark, NO – Norway, SE – Sweden, non-SB – non-school based Source: WHO Immunization data.

Appendix C

C.1 Data about imported and reimbursed number of HPV vaccines in Slovakia

TABLE C1: DATA ABOUT IMPORTED AND REIMBURSED NUMBER OF HPV VACCINES IN SLOVAKIA

	2021				2022			
Number of units	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Panel A. Imported number of units of HPV vaccines reported by distributors ¹								
Nonavalent	1 136	8951	820	7 052	$6\ 804$	$22 \ 409$	$11 \ 074$	$6\ 180$
Bivalent					2888	$3\ 184$		375
Total	1 136	$8\ 951$	820	$7\ 052$	9692	25 593	$11 \ 074$	6555
Panel B. Reimbursed number of units of HPV vaccines based on insurance $claims^2$								
Nonavalent	1 696	$2 \ 247$	1 859	$2 \ 412$	$2 \ 207$	9088	$5\ 220$	0
Bivalent	2617	2978	$1 \ 315$	223	1 107	1 508	264	0
Total	$4 \ 313$	$5\ 225$	$3\ 174$	2635	$3 \ 314$	10 596	$5\ 484$	0

Notes: HICs data sent to NHIC according to Section 15 (6) of Act No. 581/2004 Coll. on Health Insurance Companies, Health Care Supervision and on the Amendment and Supplementing of Certain Laws, as amended and pursuant to Act No. 153/2013 Coll. on the National Health Information System and on the Amendment and Supplementing of Certain Laws, as amended.

¹ Reported by State Institute of Drug Control, not completed data.

² Reported by NHIC, not completed data.