

# Cost Effectiveness and Public Health Impact of Implementing Gender-Neutral Vaccination with the 9-Valent Human Papillomavirus Vaccine in Türkiye

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## Background and Objectives

### Background

Human Papillomavirus (HPV) is a family of viruses comprising over 100 genotypes and responsible for significant proportion of cancers and precancerous lesions of the cervix, vulva, vagina, anus, penis, head & neck, and genital warts. Global Health Organizations and Scientific Societies have set HPV elimination as a public health priority. Vaccination is among the most effective measures to prevent HPV infection and is included in the World Health Organization (WHO) guidelines on Comprehensive Cervical Cancer control.<sup>1</sup>

However, issues of affordability and budget constraints in the healthcare sector are more prominent than ever. As such, the cost-effectiveness of HPV vaccination also needs to be assessed in specific local contexts.

### Objectives

Cervical cancer is the most common HPV-related cancer in Türkiye, with 2,532 diagnoses and 1,245 deaths in 2020.<sup>2</sup> In Türkiye, HPV vaccines are not included in the National Immunization Program (NIP) yet. The aim of this study to assess the cost-effectiveness and public health impact of the inclusion of 9-Valent HPV (9vHPV) gender-neutral vaccination (GNV) in the NIP of Türkiye for individuals aged 11-12 years old.

## Methods

To assess the public health impact and the cost-effectiveness of a GNV strategy with 9vHPV, a published and validated HPV dynamic transmission model, built in Mathematica®<sup>3</sup>, was adapted and calibrated for Türkiye.

- Turkish-specific data have been used where available, i.e., demographic<sup>4,5</sup>, epidemiological, and economic parameters. However due to the lack of availability of certain other data sources, inputs from similar countries<sup>6</sup> have been used in such cases. The data have been thereafter reviewed and validated with physicians at an advisory board.
- The model was used to simulate the natural history of HPV infections and estimate potential economic and health impacts of inclusion of 9vHPV in the NIP. HPV related diseases associated with the following HPV genotypes (6/11/16/18/31/33/45/52/58) have been included in the model for both genders. Diseases included were: Cervical, vaginal, vulvar, anal, penile, head and neck cancers, genital warts, and cervical intraepithelial neoplasia (CIN1/2/3).
- Screening, utilities, clinical, and behavioral data were extracted from the literature. A 2-dose schedule and a vaccination coverage rate (VCR) of 90% were used in the base case analysis. The model used a time horizon of 100 years. Outcomes included quality-adjusted life-years (QALYs), cost for each vaccination strategy, and reduction in HPV related cancer incidence and mortality. Costs were calculated based on the Social Security Institute (SSI) perspective. Costs and outcomes were discounted by 3%.
- Model Structure: The transmission in the open population-based model is set on three building blocks:
  - A demographic module that defines birth, ageing, death, and sexual behavior of the population and describes how persons enter, age within, and exit the model.
  - An epidemiological module simulates the spread of HPV infection and resulting HPV-related diseases: cervical, vaginal, vulvar, anal, H&N, penile cancers, genital warts.
  - A cost-effectiveness module can compare two or more prevention strategies, assess their impact on costs (including screening, vaccination, and management of the disease costs) and quality of life.

## Results

The results show that over 100 years, GNV may result in significant decrease in incidence and mortality of many types of cancers. According to the calculations of the model, GNV may result in avoiding 86,736 cases and 37,155 deaths of cervical cancer; 39,181 cases and 11,721 deaths of head & neck cancer; 5,670 cases and 1,847 deaths of anal cancer; 2,074 cases and 529 deaths of vaginal cancer; 1,224 cases and 335 deaths of vulvar cancer; and avoiding 5,695,781 genital warts (as shown in Table 1) compared to no vaccination, with an incremental cost-effectiveness ratio (ICER) of 3,744 \$/QALY (Table 3), significantly lower than the estimated 3xGDP Per capita willingness-to-pay (WTP) threshold of 31,965\$ per QALY in Türkiye. Additionally, as indicated in Table 2, a total gain of 1,539.21 QALYs per 100,000 persons was calculated.

Table 1: Estimated Reduction in Incidence and Mortality due to GNV with 9vHPV Vaccination over 100 Years

Sex	HPV-related diseases	Incidence		Mortality	
		Cases prevented	%*	Deaths prevented	%*
Female	Cervical Cancer	86,736	38.4	37,155	33.7
	Vaginal Cancer	2,074	30.0	529	25.3
	Vulvar Cancer	1,224	26.2	335	22.6
	Genital Warts	3,018,214	60.1	-	-
	Anal Cancer	2,917	29.2	910	27.7
	Head & Neck Cancer	5,106	27.6	1,849	23.9
Male	Genital Warts	2,677,567	53.2	-	-
	Anal Cancer	2,753	32.7	937	31.2
	Head & Neck Cancer	34,075	34.7	9,872	31.1
	Penile Cancer	484	48.1	119	43.6

\*Cumulative Percentage Reduction. Percentages rounded to nearest 0.1.

Table 2. Cumulative QALYs Gained per 100,000 by HPV 6/11/16/18/31/33/45/52/58-Related Disease Over 100 Years Relative to No Vaccination Scenario

HPV-related diseases	QALYs Gained per 100,000
Cervical Cancer	102.38
Vaginal Cancer	1.29
Vulvar Cancer	0.70
Genital Warts*	1407.57
Anal Cancer	3.63
Head and Neck Cancer	23.28
Penile Cancer	0.35
Total Disease QALYs	1539.21

\*Includes HPV 6/11-related CIN1.

Table 3. Cost-effectiveness Analysis of HPV Vaccination Strategy

Scenario	Discounted Total Costs/Person (USD)*	QALYs/Person (QALY)**	Costs/Person (USD)*	Incremental QALYs/Person (QALY)**	Costs/QALYs (USD/QALY)***
Screening only	72.14	27.28520	-	-	-
9vHPV, Age 11-12	129.76	27.30060	57.62	0.01539	3,744

\* Costs rounded to 0.01.  
\*\*QALYs rounded to 0.00001.  
\*\*\* Costs/QALY rounded to 1.

## Limitations

- Direct medical costs associated with potential complications, and palliative care in HPV-related cancers are not included in the model. This may result in cost underestimation of treatment.
- Indirect costs were not taken into consideration.

## Conclusions

- GNV with the 9vHPV vaccine is a highly cost-effective public health intervention compared to no-vaccination and results in greater improvement of the public health and economic impact in both women and men. HPV disease prevention should be a public health priority in Türkiye and 9vHPV vaccination should be considered for NIP inclusion. Furthermore, significant catch-up vaccination initiatives are essential to reverse the deficit created during the pandemic and prevent long-term public health and economic consequences.

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