

Estimating the Impact of a Gender-Neutral Quadrivalent Human Papillomavirus Vaccination Program in All HPV 6/11/16/18-Related Diseases in Colombia

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This study was funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ USA.

BACKGROUND

- Human papillomavirus (HPV) infection is a well-established cause of cervical cancer, genital warts (GW), and recurrent respiratory papillomatosis (RRP), and is associated with other malignancies (anus, vulva, vagina, penis, and head and neck cancers)¹
- HPV vaccines have the potential to reduce the burden of disease related to HPV in both genders²
- In 2012, Colombia introduced a publicly funded HPV immunization program for girls with a quadrivalent 6/11/16/18 HPV vaccine (4vHPV) through a school-based strategy³
 - The program successfully reached more than 85% of the target population in the first few years³
 - From 2014 to 2016, the vaccine coverage rate (VCR) has progressively decreased, reaching very low levels (<20%) among eligible girls⁴
- Several countries in Latin America have introduced gender-neutral vaccination (GNV) with the quadrivalent 6/11/16/18 vaccine (4vHPV) in their national immunization programs to strengthen vaccination program resilience, improve population-level HPV infection/disease prevention, and confer direct protection to males⁵
- The potential impact of extending the vaccination program to include boys in Colombia is unknown

OBJECTIVE

- We assessed the public health and economic impact of adding males to the existing 9- to 10-year-old female-only 4vHPV program (FOV) in Colombia

METHODS

- A published HPV-type dynamic transmission model⁶⁻¹⁰ was used to compare FOV and GNV with two-dose 4vHPV for the prevention of HPV-related cervical cancer, cervical intraepithelial neoplasia (CIN1/2/3), vaginal, vulvar, penile, anal, and head and neck cancers as well as GW and RRP, over a 100-year timeframe in Colombia
- The predicted health outcomes included HPV 6/11/16/18-related diseases and deaths averted [genital warts GW, RRP, CIN 1/2/3, and cervical, vaginal, vulvar, penile, anal, and head and neck cancers], direct healthcare cost prevented by vaccination, net cost of vaccination, and incremental cost-effectiveness ratios (ICERs)
- The model compared 35% VCR in FOV with GNV strategy at different VCRs: 35% GNV (scenario A), different VCRs between females/males (50% and 35%-scenario B), and 50% GNV (scenario C)
- For these analyses, it was used the VCR data for first and second dose, respectively, of 4vHPV in Colombia from 2012-2017: 98%, 88%, 81%, 61%, 14%, 30% and 88%, 60%, 24%, 45%, 5%, 14.9%¹¹
- Colombian-specific data were used in the model and consisted of demographic, epidemiological, screening, and economic parameters (**Tables 1 and 2**).¹²⁻¹⁷ The costs were based on national health care price tariffs used in Colombia (SOAT)¹⁸
- The model assumed a 100-year time-horizon, lifelong immunity following vaccination, herd immunity, ongoing cytology screening, and a discount rate of 5% for costs and benefits
- Incremental cost-effectiveness ratios (ICERs) were calculated by dividing the difference in accumulated costs by the QALY gained
 - Although there is no official cost-effectiveness threshold in Colombia, the HTA agency methodological manual suggests that for non-dominated technologies the ICER must be compared with 1 GDP per capita for Colombia or US \$6,408.9 and o 3 GDP per capita (less than US \$19,226.70)¹⁹⁻²¹
- The costs were converted from local currency (pesos colombianos) to US dollars (exchange rate 1 US\$ = 3137 COP)²²

Table 1. 2018 Burden of HPV-related Diseases in Colombia

		Burden of Disease	
		Incidence ^a	Mortality ^a
Female	Genital warts ^b	600	–
	RRP ^c	1.12	0.0531
	Cervical	15.3	7.10
	Vaginal	0.69	0.17
	Vulvar	1.40	0.30
	Anal	1.50	0.21
	Oral cavity	1.50	0.61
Male	Oropharynx	0.56	0.20
	Larynx	0.59	0.32
	Genital warts ^b	600	–
	RRP ^c	1.35	0.0635
	Penile	1.50	0.42
	Anal	0.71	0.12
	Oral cavity	1.90	0.82
	Oropharynx	1.85	0.48
	Larynx	2.90	1.40

^aCrude rate per 100,000 persons. ^bBrazil arm HIM study. ^cliterature data.

Table 2. Cost Parameters per Episode-of-Care

Parameter	Costs (US \$)
CIN 1	245.19
CIN 2	763.95
CIN 3	1,198.88
Cervical cancer	3,213.17
VaIN 2/3	763.95
Vaginal cancer	2,906.39
Vulvar cancer	2,918.71
Penile cancer	3,188.73
Anal cancer	3,612.15
Head & Neck cancer	2,361.38
Genital warts	302.63
RRP	1,070.13

CIN, cervical intraepithelial neoplasia; RRP, recurrent respiratory papillomatosis; VaIN, vaginal intraepithelial neoplasia.

RESULTS

HPV-related Disease

- The 3 GNV scenarios (A,B, and C) are estimated to provide faster and greater reductions in the incidence of HPV 6/11/16/18-related diseases relative to FOV at 35% VCR, mainly the scenarios B and C (**Figure 1** and **Table 3**)
- The greatest cumulative reductions of HPV 6/11/16/18-related diseases were seen in scenario C relative to FOV at 35% VCR at year 100:
 - A total of 39,969 avoided cancer cases: 28,001 cervical cancer (CC) cases and 11,968 non-CC cases (4,753 in females and 7,215 in males)
 - Percentage reductions of GW and all HPV-related diseases can be seen in **Figure 1** and **Table 3**, respectively
 - A total of 15,541 avoided deaths: 12,882 in females and 2,259 in males (**Table 4**)

Figure 1. Estimated HPV 6/11-related Genital Warts Incidence in Scenarios A (F35M35), B (F50M35), and C (F50M50) Compared With FOV at 35% VCR Over 100 Years

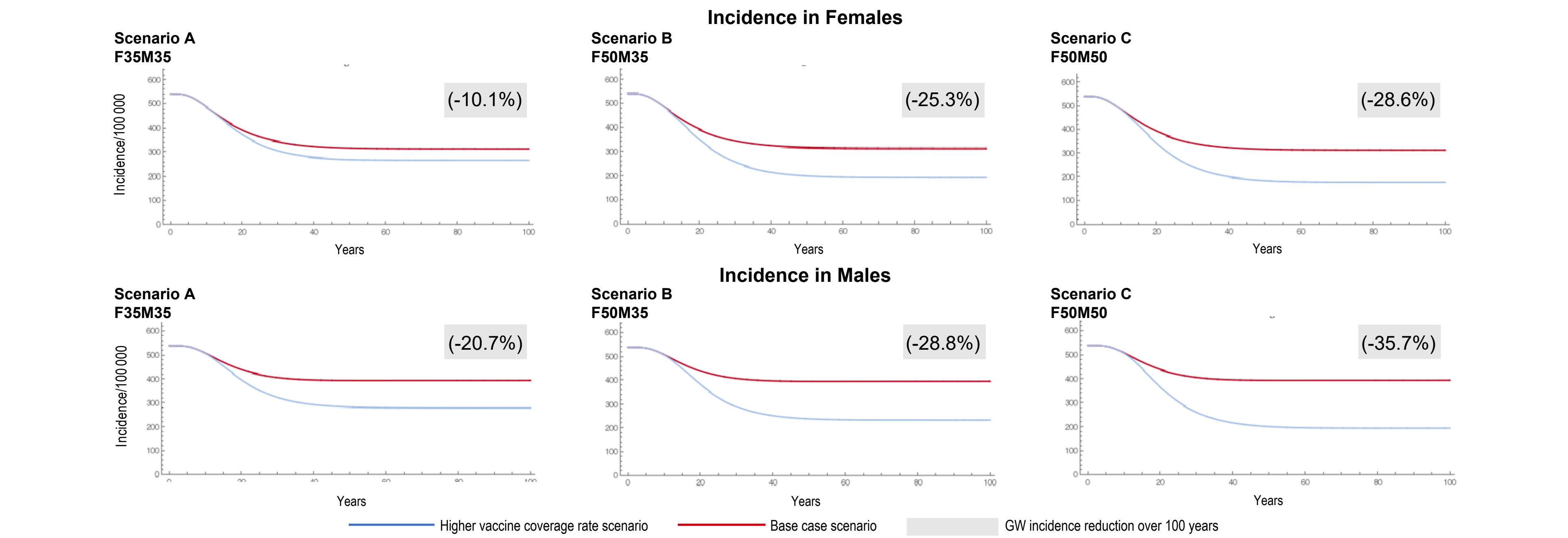


Table 3. Cumulative Percentage Reduction of HPV 6/11/16/18-related Diseases in Scenarios A (F50M35), B (F50M35) and C (F50M50) Compared With FOV at 35% VCR Over 100 Years

		Cumulative HPV 6/11/16/18-related Disease Reduction		
		Over 100 Years		
		Scenario A F35M35	Scenario B F50M35	Scenario C F50M50
Female		%	%	%
Cervical cancer		5.4	15.7	17.2
CIN 1 related HPV 16/18		8.1	22.6	24.8
CIN 2/3		7.4	21.3	23.4
Vaginal cancer		5.4	13.1	14.6
VaIN		5.9	14.3	15.9
Vulvar cancer		5.2	12.9	14.3
Anal cancer		6.8	13.7	15.6
Head/Neck cancer		6.4	12.7	14.3
CIN related HPV 6/11		7.4	22.2	24.9
Genital warts		10.1	25.3	28.6
RRP		10.8	25.2	28.8
Male				
Anal cancer		13.5	17.6	21.6
Head/Neck cancer		13.0	17.1	20.8
Penile cancer		15.3	16.6	22.1
Genital warts		20.7	28.8	35.7
RRP		17.0	27.3	32.9

F, female; M, male; FOV, female-only vaccination; RRP, recurrent respiratory papillomatosis.

Table 4. Cumulative Case Reduction in HPV 6/11/16/18-related Deaths in Scenarios A (F35M35), B (F50M35), and C (F50M50) Compared With FOV at 35% VCR Over 100 Years

		Over 100 Years					
		Scenario A F35M35		Scenario B F50M35		Scenario C F50M50	
Female		AD	%	AD	%	AD	%
Cervical cancer		3714	4.8	10800	13.8	11684	15.2
Vaginal cancer		38	5.1	92	12.4	102	13.8
Vulvar cancer		72	5.0	177	12.3	197	13.6
Anal cancer		201	6.5	404	13.1	459	14.8
Head/Neck cancer		89	5.9	178	11.8	201	13.3
RRP		90	9.9	210	23.1	239	26.4
Male							
Anal cancer		240	13.0	312	16.9	383	20.8
Head/Neck cancer		411	12.2	542	16.1	660	19.6
Penile cancer		589	14.8	639	16.0	849	21.3
RRP		188	15.6	305	25.2	367	30.4

F, female; M, male; FOV, female-only vaccination; RRP, recurrent respiratory papillomatosis; AD, avoided deaths.

Cost Analysis

- A GNV strategy with the 4vHPV vaccine is projected to decrease cumulative HPV 6/11/16/18-related disease health care costs by 4.6%, 8.1%, and 9.7% compared with the FOV at 35% VCR for Scenarios A, B, and C, respectively (**Table 5**)
- The greatest projected reductions in health care costs are attributable to costs associated with the treatment of HPV-6/11 diseases (approximately 90% for all scenarios)
- Male costs accounted for approximately 38% of the total costs in the 3 GNV scenarios analyzed
- The direct health care cost prevented by vaccination varied from 87.9 (scenario A) to 184.5 million (scenario C) relative to FOV at 35%
- The net costs of vaccination varied from 29.3 (scenario A) to 80.2 million (scenario C) (**Table 5**)
- The ICER for all scenarios was <0, indicating that under the model assumptions, it is cost-saving to implement a GNV-4vHPV in Colombia

Table 5. Net Cost of Vaccination (US \$) in Scenarios A (F35M35), B (F50M35), and C (F50M50) at the Population Level Compared With FOV at 35% VCR Over 100 Years

	Scenario A F35M35	Scenario B F50M35	Scenario C F50M50
Estimated vaccination costs (vaccine + administration) ^a	58,556,992	79,078,535	104,293,231
Estimated HPV 6/11/16/18 disease costs avoided ^a	87,910,368	154,485,657	184,499,192
Estimated net cost of vaccination ^a	(29,353,377)	(75,407,123)	(80,205,962)

^aCost rounded to 0.01.

LIMITATIONS

- Currently, HPV vaccines are not indicated for the prevention of penile cancer, RRP, and head and neck cancers
- Model does not assess possible changes to cervical cancer screening methods over the course of the 100 years
- Direct medical costs associated with outpatients visits, 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

- In Colombia, a model-based analysis suggests that GNV-4vHPV program is a cost-saving strategy and could result in a greater improvement of the public health impact in both females and males compared with FOV with 35% VCR

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