

Orengo JC<sup>1</sup>; Pavelyev A<sup>2</sup>; Daniels V<sup>3</sup>; Saxena K<sup>4</sup>; Jalil HA<sup>4</sup>; Acevedo R<sup>4</sup>; Lima BC<sup>5</sup>; Parellada C<sup>5</sup>

<sup>1</sup>MSD (IA) LLC, Puerto Rico; <sup>2</sup>Atlas Data Systems, Berkeley Heights, NJ, USA; <sup>3</sup>Merck & Co., Inc.,Rahway, NJ, USA; <sup>4</sup>MSD Mexico, Ciudad de Mexico, Mexico; <sup>5</sup>MSD Brazil, São Paulo, Brazil

Background

- In Mexico, human papillomavirus (HPV) female-only vaccination (FOV) in the national immunization program has been available since 2012. Vaccination coverage rates were higher than 90% between 2012 and 2019<sup>1</sup>.
- The HPV vaccination program was interrupted in 2021 due to supply issues but resumed in November 2022 with one dose-HPV quadrivalent vaccine FOV (4vHPV FOV) program. In 2023, eligibility for HPV vaccination included 11-year-old girls in public high school (fifth grade) <sup>1</sup>
- HPV vaccination for boys is only available in private market and vaccination coverage rates (VCR) is estimated in only 1% in 11-year-old boys

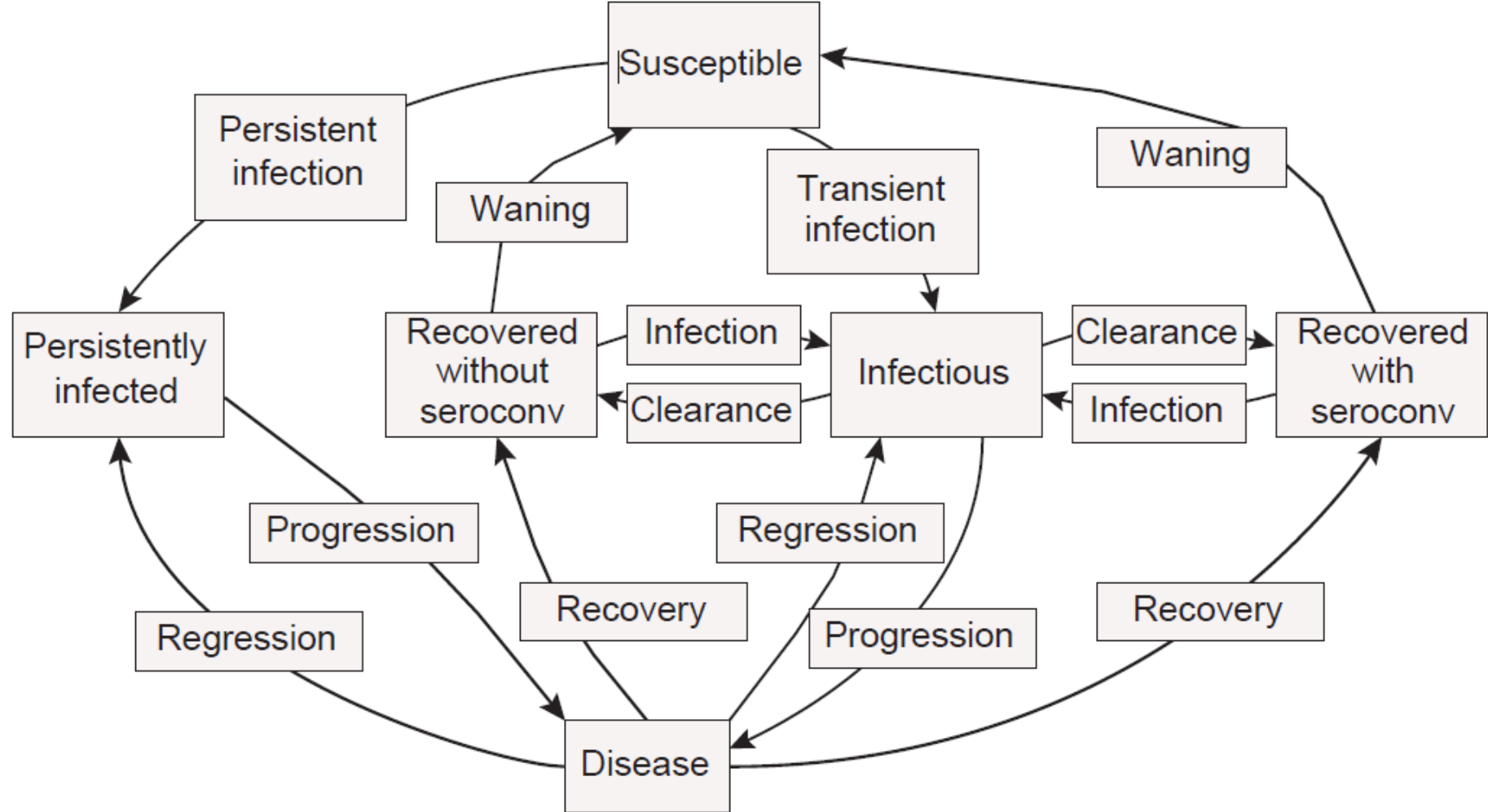
Objective

- To estimate the public health impact for switching from a 4vHPV FOV (base-case) to a 9-valent HPV vaccine (9vHPV) in 11-year-old 9vHPV FOV and 11-year-old 9vHPV gender-neutral vaccination (GNV) programs

Methods

- A previously published dynamic model of HPV disease transmission was calibrated to simulate the natural history of HPV and associated disease burden in Mexico <sup>2-5</sup> (**Figure 1**)
- The model assumed a two-dose schedule over a 100-year time horizon, lifetime immunity after vaccination, continuous cytology screening, 94% VCR for females, and herd immunity in all scenarios. In both base-case and scenario with 9vHPV FOV, it was considered 1% VCR for males (private market) and in scenario with 9vHPV GNV, 60% of VCR for males
- The diseases considered in the model are cervical, head & neck, penile, anal, vaginal, and vulvar cancers, genital warts, recurrent respiratory papillomatosis (RRP), and cervical intraepithelial neoplasia (CIN)<sup>1-3</sup>. Mexico-specific data were used from literature where available; data from other countries were used as proxy where local data was not available. Input data included demographic, behavioral, and epidemiological and screening parameters<sup>6,7</sup>

Figure 1. Simplified schematic diagram of the initial compartments for HPV infection and disease progression



Results

- Over 100 years, switching from a 4vHPV FOV to a 9vHPV FOV or 9vHPV GNV program is estimated to further reduce the incidence of diseases attributed to HPV 6/11/16/18/31/33/45/52/58 in both females and males (**Table 1** and **2**)
- Faster and greater reduction in the incidence of cervical cancer/precursors and non-cervical cancers due to additional protection against HPV 6/11/16/18/31/33/45/52/58 relative to the current strategy
- In 9vHPV GNV scenario, it was seen the greatest cumulative reductions of HPV 6/11/16/18/31/33/45/52/58-attributable diseases compared to 4vHPV FOV at year 100
  - 101,424 avoided cancer cases
  - 97,335 avoided cervical cancer cases and 4,089 head & neck, penile, anal, vaginal, and vulvar cancer cases
  - 5.2 million avoided cases of genital warts (1.5 million cases in females and 3.7 million in males), 1.9 million of CIN 2/3 cases, 5.6 million CIN 1 cases, and 172,325 RRP
  - 42,779 avoided deaths: 34,217 due to cervical cancer and 8,562 due to RRP and head & neck, penile, anal, vaginal, and vulvar cancers

References

1.Secretario de Salud. [https://www.gob.mx/cms/uploads/attachment/file/769721/VPH\\_2022.PDF](https://www.gob.mx/cms/uploads/attachment/file/769721/VPH_2022.PDF). Accessed Oct 16, 2023

2.Dasbach EJ, et al. *Epidemiol Rev.* 2006;28:88-100.

3.Elbashah EH, et al. *Emerg Infect Dis.* 2007;13(1):28-41.

4.Elbashah EH, et al. *Bull Math Biol.* 2008;70(8):2126- 2176.

5.Ortiz AP, et al. *PLoS One.* 2017;12(11):e0184540.

6.IARC - Globocan 2020. Estimated number of deaths in 2020, Mexico, females, all ages (excluding NMSC). [https://gco.iarc.fr/today/online-analysis-table?v=2020&mode=cancer&mode\\_population=continents&population=900&populations=484&key=asr&sex=2&cancer=39&type=1&statistic=5&prevalence=0&population\\_group=0&ages\\_group%5B%5D=0&ages\\_group%5B%5D=17&group\\_cancer=0&include\\_nmssc=0&include\\_nmssc\\_other=1](https://gco.iarc.fr/today/online-analysis-table?v=2020&mode=cancer&mode_population=continents&population=900&populations=484&key=asr&sex=2&cancer=39&type=1&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&group_cancer=0&include_nmssc=0&include_nmssc_other=1). Accessed Nov. 28, 2022.

7.Domenech-Viñolas M, et al. *Salud Publica Mex.*2018;60(6):624-632.

World Health Organization. Immunization Dashboard – Global. <https://immunizationdata.who.int/index.html>. Accessed Oct. 16, 2023.

Results

Table 1. Cumulative incidence reduction per 100,000 inhabitants and additional avoided cases in HPV 6/11/16/18/31/33/45/52/58-attributable disease with 9vHPV relative to 4vHPV over 100 years

| HPV-attributable disease                                | 9vHPV FOV     |                                             | 9vHPV GNV     |                                             |
|---------------------------------------------------------|---------------|---------------------------------------------|---------------|---------------------------------------------|
|                                                         | Cases avoided | Cumulative incidence reduction <sup>a</sup> | Cases avoided | Cumulative incidence reduction <sup>a</sup> |
| <b>Cervical</b>                                         |               |                                             |               |                                             |
| Cancer                                                  | 97,000        | 21.6                                        | 97,335        | 21.7                                        |
| CIN 1                                                   | 4,222,330     | 64.6                                        | 4,224,614     | 64.7                                        |
| CIN 2/3                                                 | 1,942,439     | 55.8                                        | 1,943,180     | 55.8                                        |
| <b>Vaginal</b>                                          |               |                                             |               |                                             |
| Cancer                                                  | 569           | 8.6                                         | 575           | 8.7                                         |
| VAIN 1                                                  | 126           | 22.6                                        | 127           | 22.7                                        |
| VAIN 2/3                                                | 560           | 18.5                                        | 564           | 18.6                                        |
| <b>Vulvar</b>                                           |               |                                             |               |                                             |
| Cancer                                                  | 467           | 9.1                                         | 474           | 9.2                                         |
| <b>Genital warts and CIN 1 attributable to HPV 6/11</b> |               |                                             |               |                                             |
| Genital warts (female)                                  | 0             | 0.0                                         | 1,453,017     | 9.6                                         |
| Genital warts (male)                                    | 0             | 0.0                                         | 3,738,999     | 18.7                                        |
| CIN 1                                                   | 0             | 0.0                                         | 1,364,299     | 12.3                                        |
| <b>Anal</b>                                             |               |                                             |               |                                             |
| Cancer (female)                                         | 683           | 7.1                                         | 739           | 7.7                                         |
| Cancer (male)                                           | 352           | 4.4                                         | 633           | 7.9                                         |
| <b>Head &amp; neck</b>                                  |               |                                             |               |                                             |
| Cancer (female)                                         | 193           | 2.0                                         | 235           | 2.4                                         |
| Cancer (male)                                           | 248           | 1.4                                         | 719           | 4.0                                         |
| <b>Penile cancer</b>                                    |               |                                             |               |                                             |
| Cancer                                                  | 649           | 9.4                                         | 714           | 10.4                                        |
| <b>RRP</b>                                              |               |                                             |               |                                             |
| RRP (female)                                            | 0             | 0.0                                         | 19,217        | 10.0                                        |
| RRP (male)                                              | 0             | 0.0                                         | 153,108       | 18.0                                        |

<sup>a</sup>Per 100,000 inhabitants. 9vHPV FOV, 9-valent human papillomavirus vaccine female only-vaccination; GNV, gender-neutral vaccination; CIN, cervical intraepithelial neoplasia; VAIN, vaginal intraepithelial neoplasia; RRP, recurrent respiratory papillomatosis.

Table 2. Mortality reduction per 100,000 inhabitants and additional deaths avoided with 9vHPV relative to 4vHPV over 100 years

| HPV-attributable disease    | 9vHPV FOV      |                                  | 9vHPV GNV      |                                  |
|-----------------------------|----------------|----------------------------------|----------------|----------------------------------|
|                             | Deaths avoided | Mortality reduction <sup>a</sup> | Deaths avoided | Mortality reduction <sup>a</sup> |
| Cervical                    | 34,132         | 14.7                             | 34,217         | 14.7                             |
| Vaginal                     | 172            | 7.1                              | 174            | 7.2                              |
| Vulvar                      | 137            | 7.8                              | 140            | 7.9                              |
| Anal cancer (female)        | 169            | 6.7                              | 184            | 7.2                              |
| Anal cancer (male)          | 86             | 4.1                              | 156            | 7.5                              |
| Head & neck cancer (female) | 85             | 1.7                              | 104            | 2.1                              |
| Head & neck cancer (male)   | 128            | 1.2                              | 379            | 3.6                              |
| Penile cancer               | 176            | 8.2                              | 195            | 9.1                              |
| RRP (female)                | 0              | 0.0                              | 823            | 8.7                              |
| RRP (male)                  | 0              | 0.0                              | 6,407          | 16.3                             |

<sup>a</sup>Per 100,000 inhabitants. 9vHPV FOV, 9-valent human papillomavirus vaccine female only-vaccination; GNV, gender-neutral vaccination; CIN, cervical intraepithelial neoplasia; VAIN, vaginal intraepithelial neoplasia; RRP, recurrent respiratory papillomatosis.

Limitations

This model has several limitations that should be considered when interpreting the results:

- First, it assumes a high and sustained VCR over 100 years
- Second, the model relies on the use of Pap smear as the standard cervical cancer screening method throughout the entire 100-year period
- Lastly, the model uses proxy inputs when specific data for Mexico was unavailable, such as sexual activity information and local HPV-attributable fraction for laryngeal cancer

Conclusions

- Under the model assumptions, switching from 4vHPV FOV to 9vHPV FOV or GNV is projected to significantly reduce the incidence of HPV 6/11/16/18/31/33/45/52/58- attributable diseases in both females and males
- The greatest cumulative reductions in HPV 6/11/16/18/31/33/45/52/58-attributable diseases are observed in the 9vHPV GNV scenario compared to the 4vHPV FOV at year 100
- The results of this modeling study underscore the potential long-term benefits of transitioning to more comprehensive HPV vaccination programs, including additional coverage for males and for five additional oncogenic genotypes, in terms of HPV disease prevention, cancer burden reduction, and a positive impact on public health in both genders