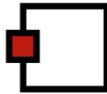


Population-Based Health Impact of Single-Dose HPV Vaccination in the United States

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Objectives

Using two independently-developed mathematical models adapted to the U.S. population:

- To project the **long-term health effects of single-dose HPV vaccination**, taking into account historical HPV vaccination coverage in the U.S. population.
- To explore **key uncertainties of single-dose HPV vaccine efficacy and duration** on the population-level effectiveness.

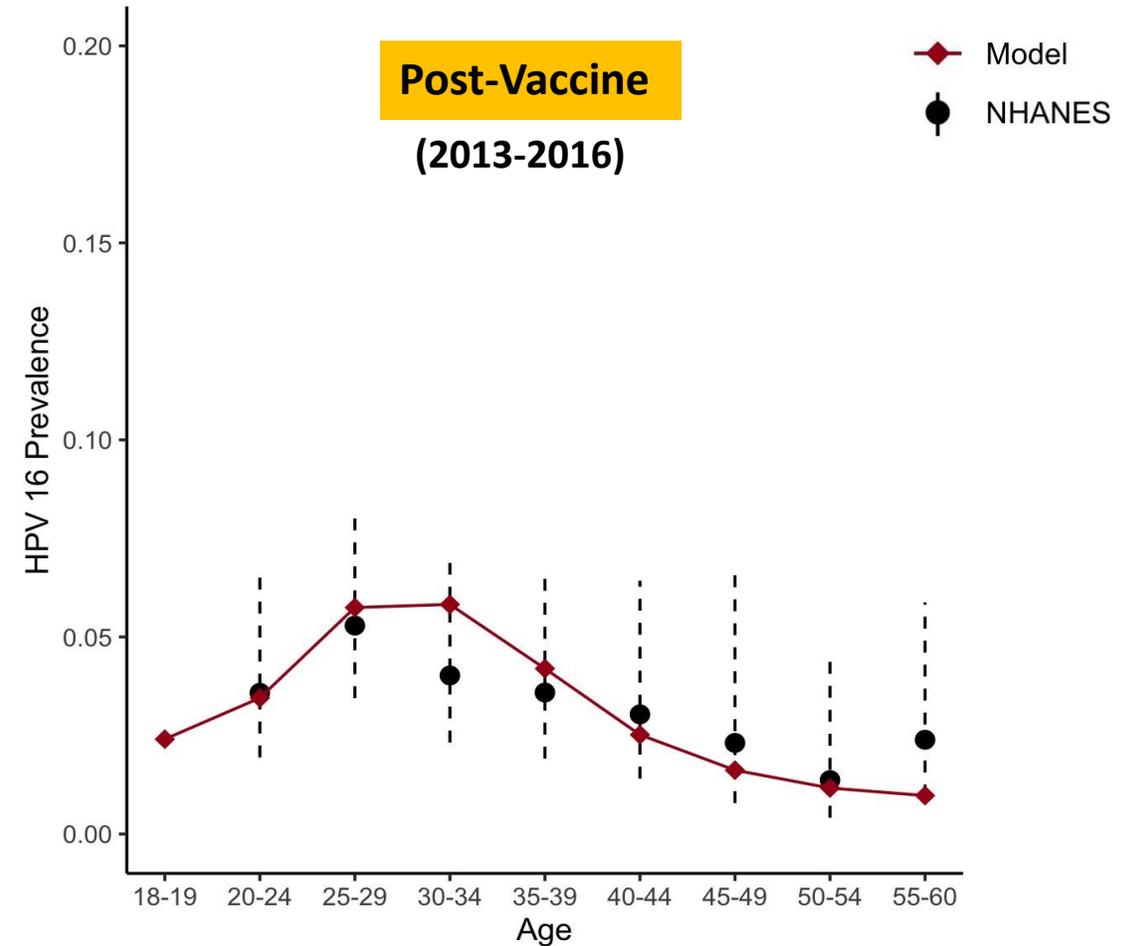
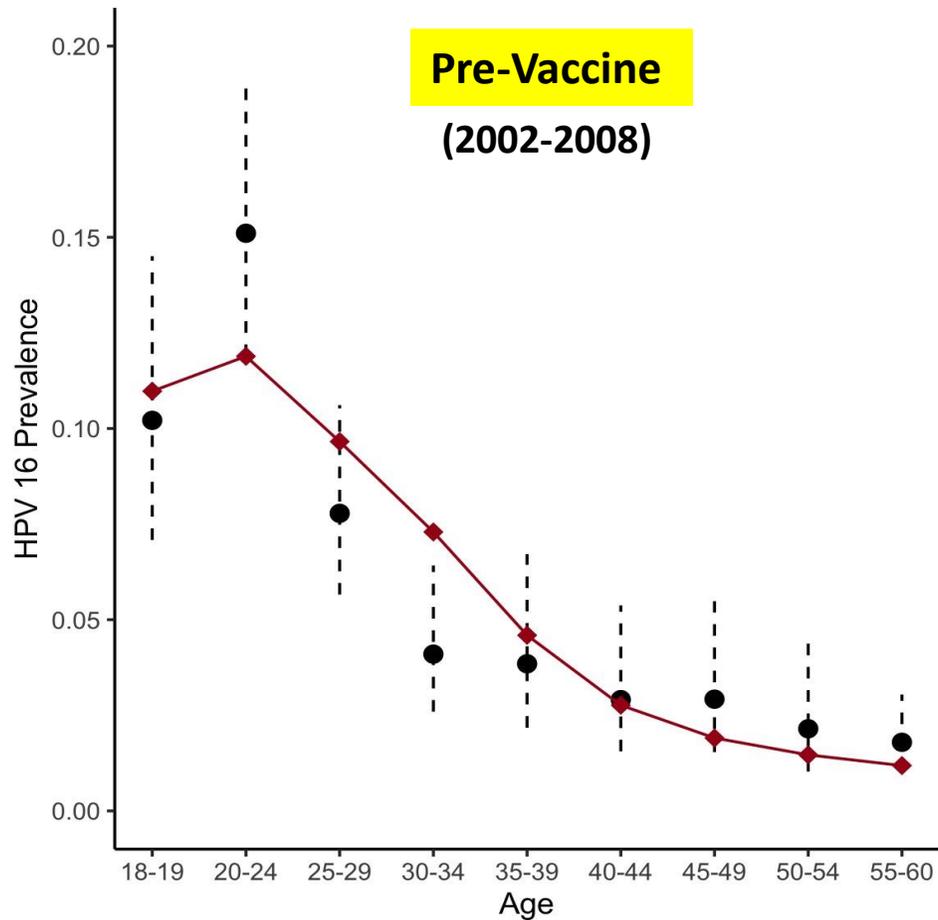
Model Overview

	Harvard ¹⁻²	HPV-ADVISE ³⁻⁵
Model Type	Individual-based sexual transmission model (includes herd immunity)	
Population	Population-based (multi-cohort); females and males by single-year age	
Mixing, Risk Groups	Heterosexual mixing among 4, age-stratified risk groups	

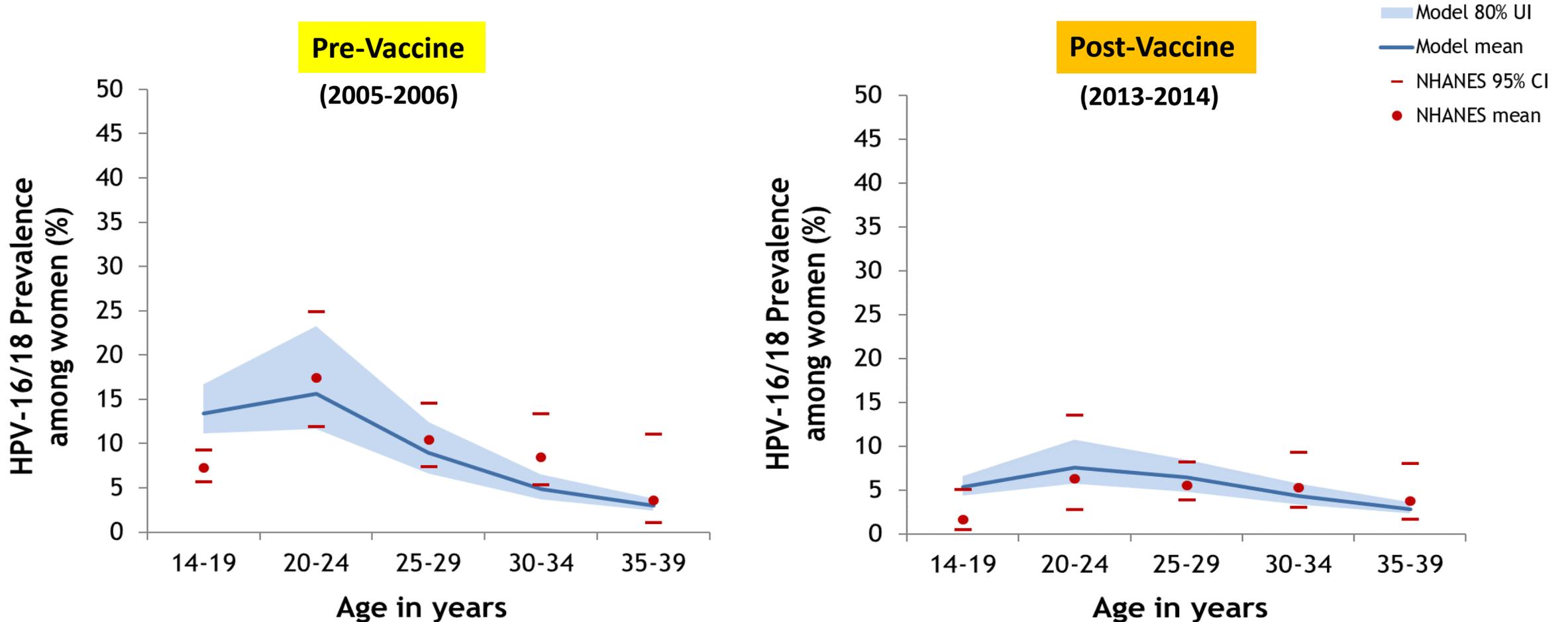
Model Overview

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Mixing, Risk Groups	Heterosexual mixing among 4, age-stratified risk groups	
HPV Genotypes	HPV-16, -18, -31, -33, -45, -52, -58 (modeled separately) + pooled high-risk + pooled low-risk	HPV-16, -18, -31, -33, -45, -52, -58, -6, -11, -35, -39, -51, -56, -59, -66, -68, -73, and -82 (modeled separately)
HPV Transmission	Probability per month of partnership duration (sex and genotype-specific)	Probability per sexual act (sex and genotype-specific)
Health States	No HPV, HPV, CIN2, CIN3, cervical cancer (SCC, by stage), death	No HPV, HPV, CIN1 , CIN2, CIN3, cervical cancer (SCC, by stage), death

Model Fit to HPV Prevalence: Harvard



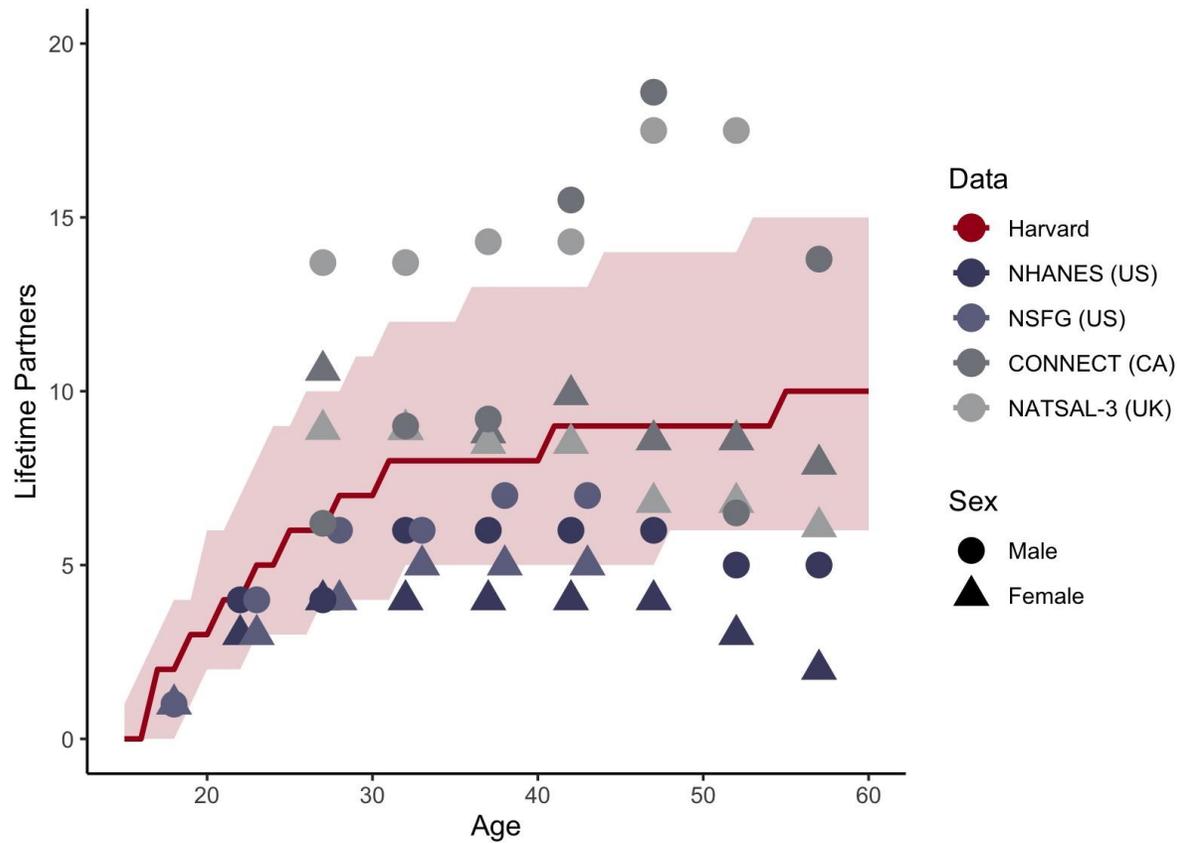
Model Fit to HPV Prevalence: HPV-ADVISE (US)



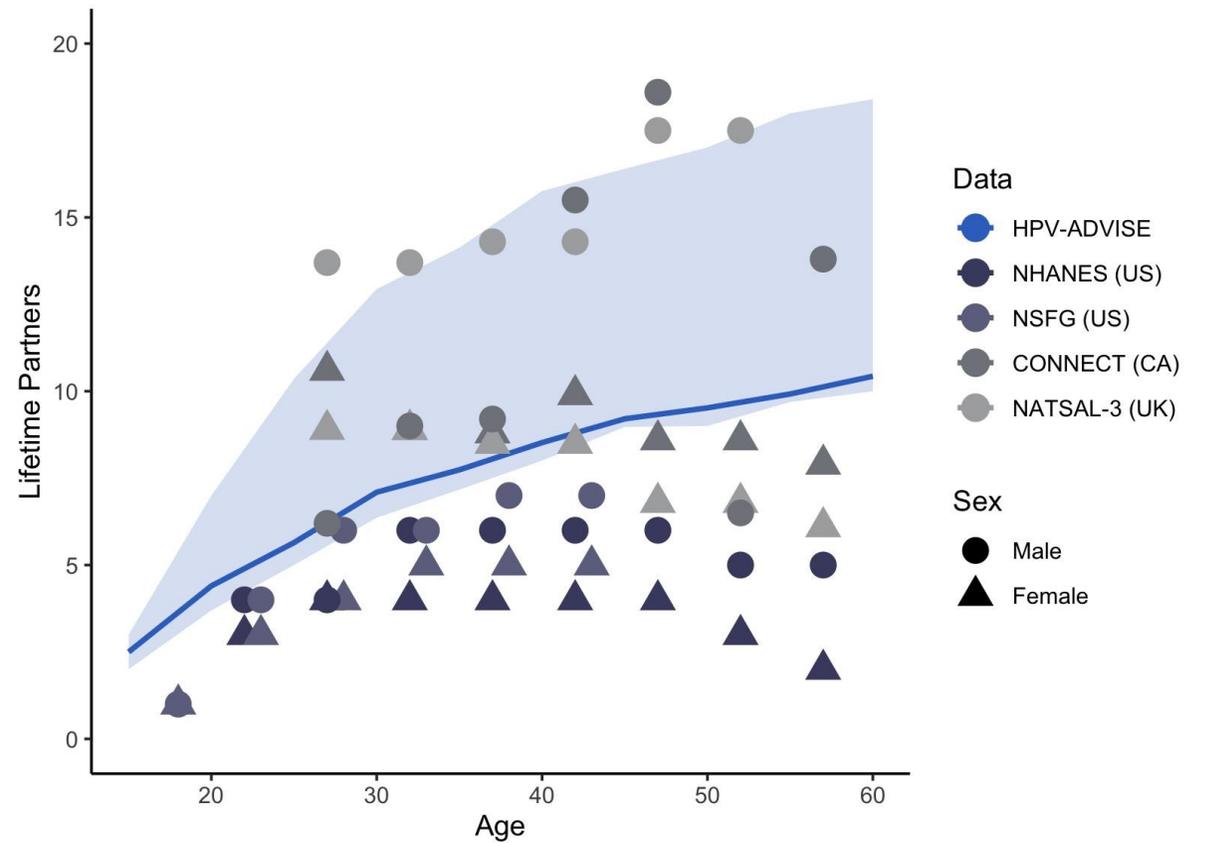
* Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey (NHANES). <http://www.cdc.gov/nchs/nhanes.htm>.

Model Fit to Median Lifetime Partners

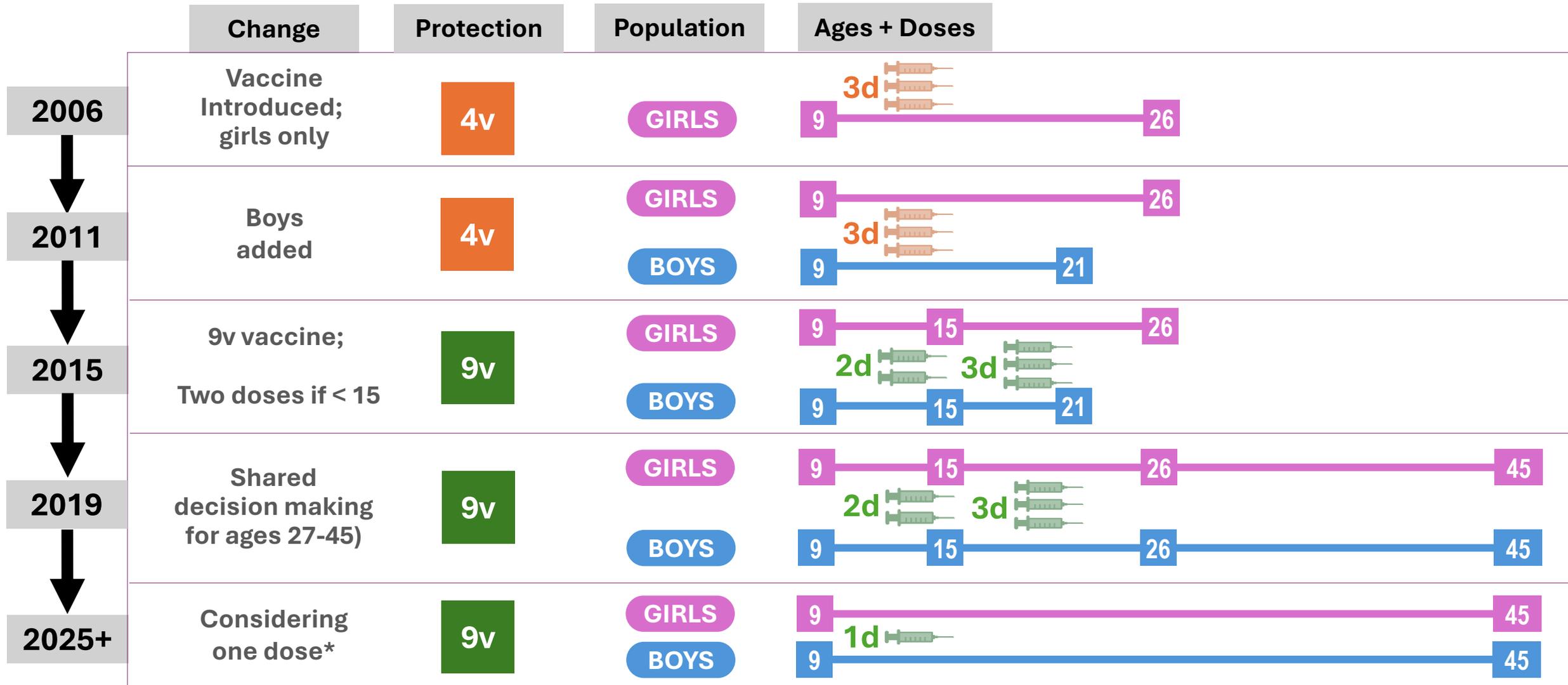
Harvard



HPV-ADVISE



U.S. Vaccination Policy



*1 dose through age 45 years scenario is for illustrative purposes only, to show the maximum possible difference between 1-dose strategies vs. the current strategy.

Vaccine Assumptions & Justifications

1-dose vaccine efficacy (VE)

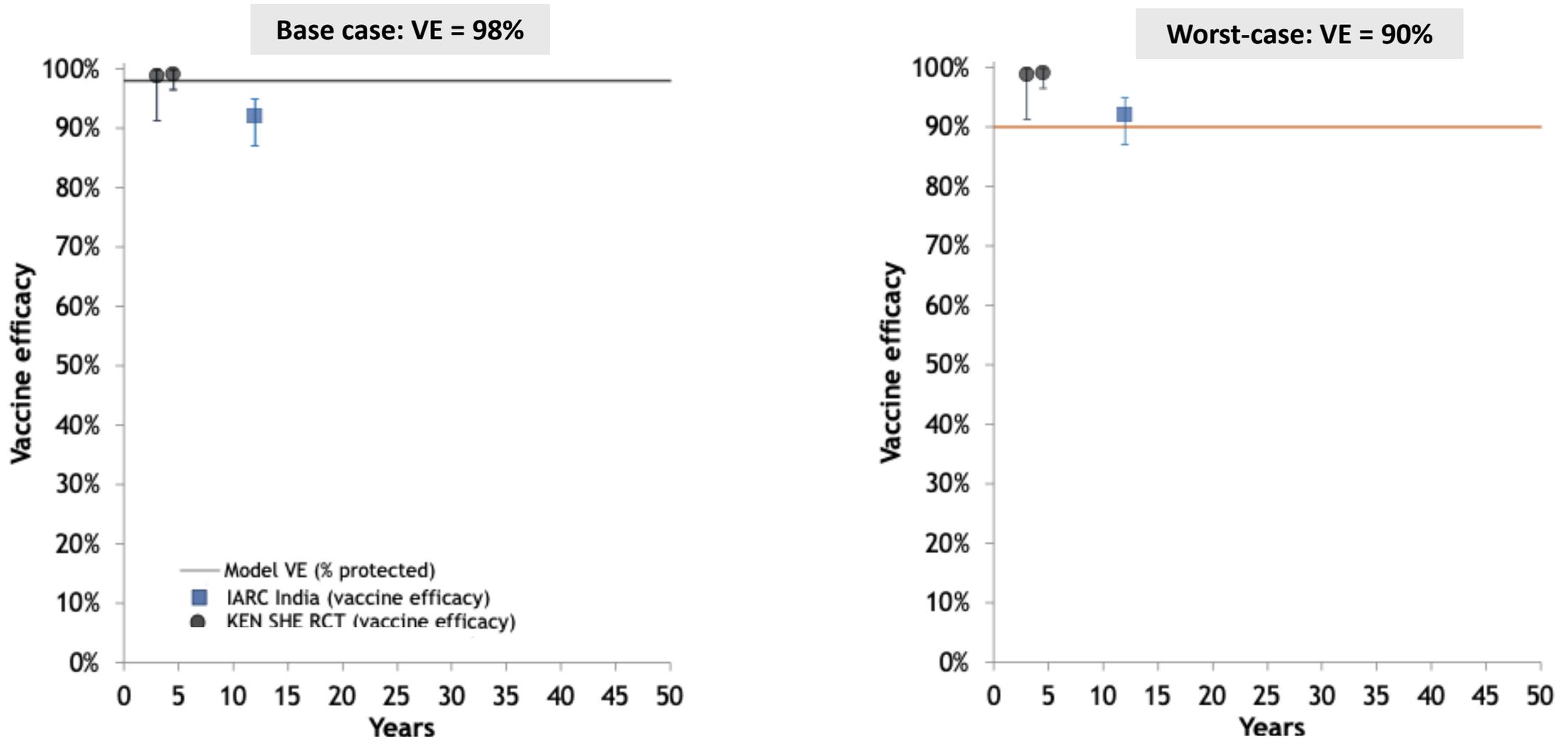
- Empirical data: VE against persistent HPV16/18 infection = 92-99%¹⁻⁴
 - Base-case scenario: VE = 98% (Non-inferior VE, based on the KEN SHE trial³)
 - Worst-case scenario: VE = 90% (Lower bound 95% CI of the KEN SHE trial³)

1-dose vaccine duration (VD)

- Empirical data: Sustained protection 12-16 years (IARC India Study & CVT)^{1,2,5}
 - Base-case scenario: VD = Lifelong
 - Worst-case scenario: VD = average 25 years
 - Normal distribution (Std Dev = 5 years) reflects *stable efficacy followed by steep drop* in protection
 - Implies *waning starts 15 years* after vaccination for some individuals
 - Implies *no protection for 50% of individuals 25 years* after vaccination
 - Implies *no protection for all individuals 35-40 years* after vaccination

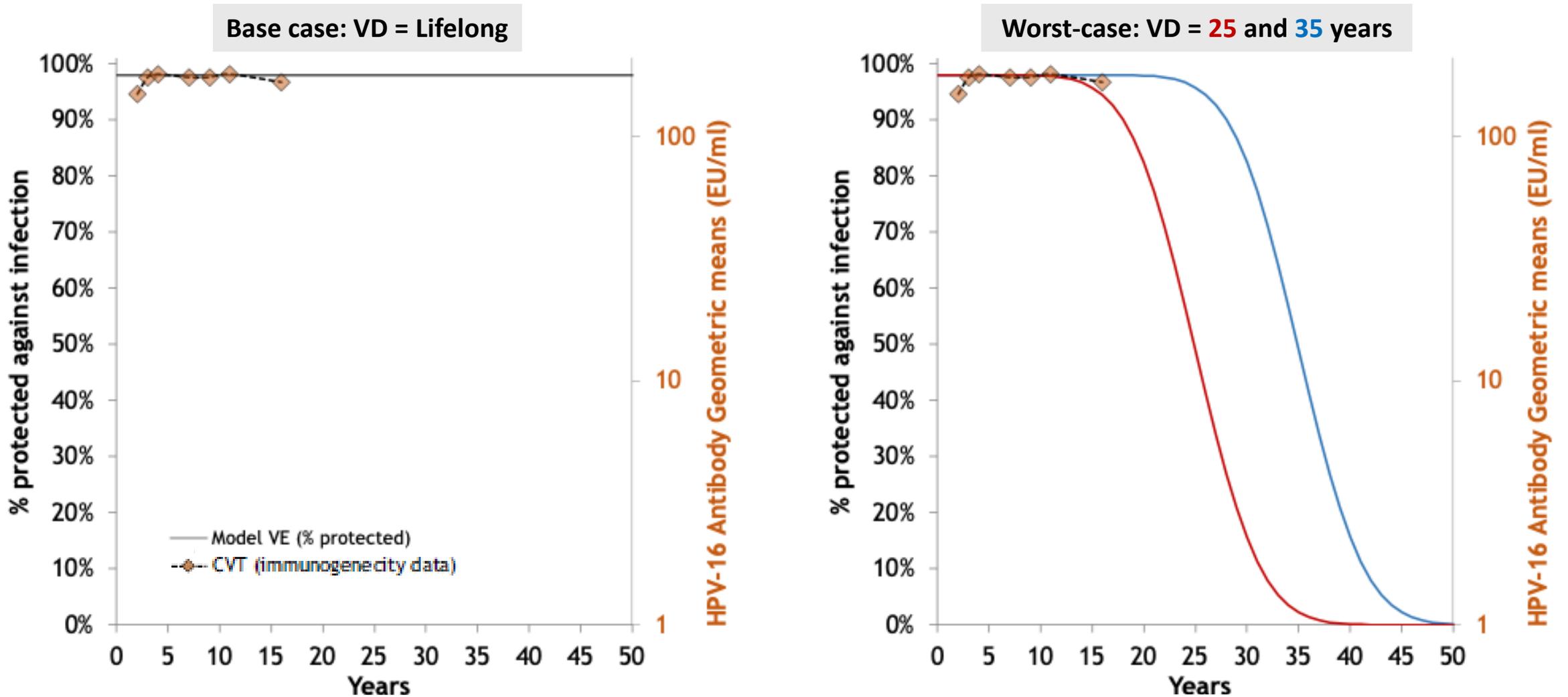
Vaccine Efficacy Assumptions vs Data for Single-Dose

Vaccine efficacy against persistent HPV-16/18 infection, Vaccine duration (VD) = life



Vaccine Duration Assumptions vs Data for Single-Dose

Vaccine efficacy against persistent HPV-16/18 infection, Vaccine efficacy (VE) = 98%

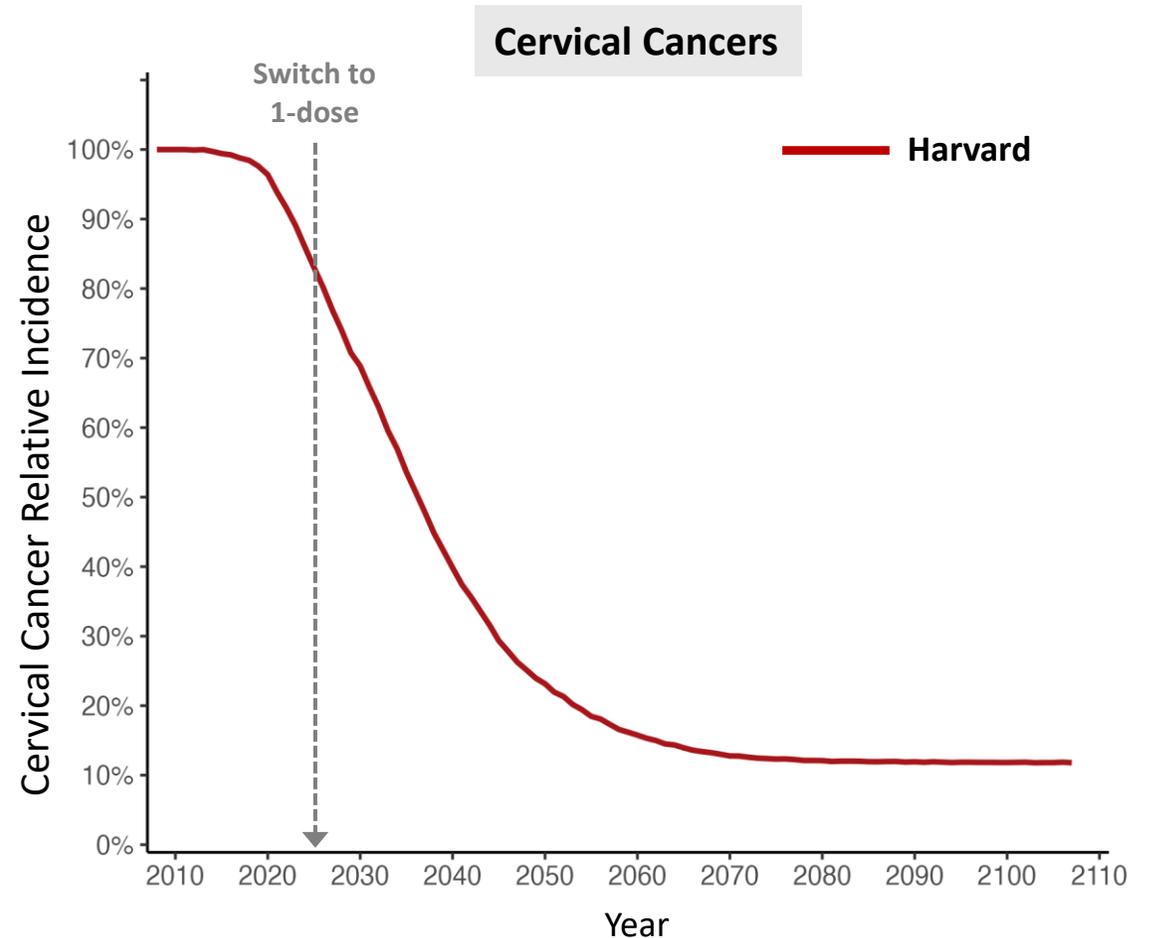
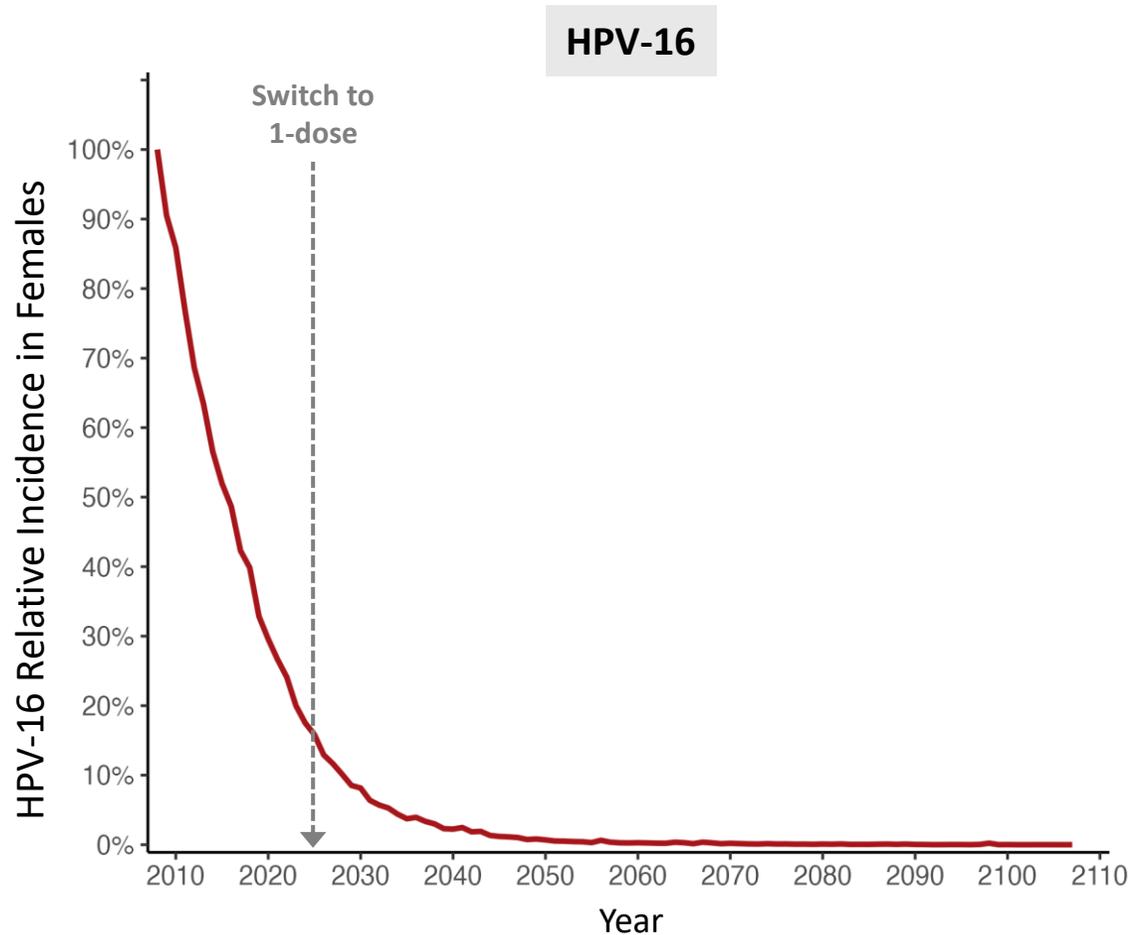


RESULTS

**What is the impact of switching to 1-dose
vaccination in the United States?**

Results: Switching to 1-Dose - Non-inferior 1-Dose

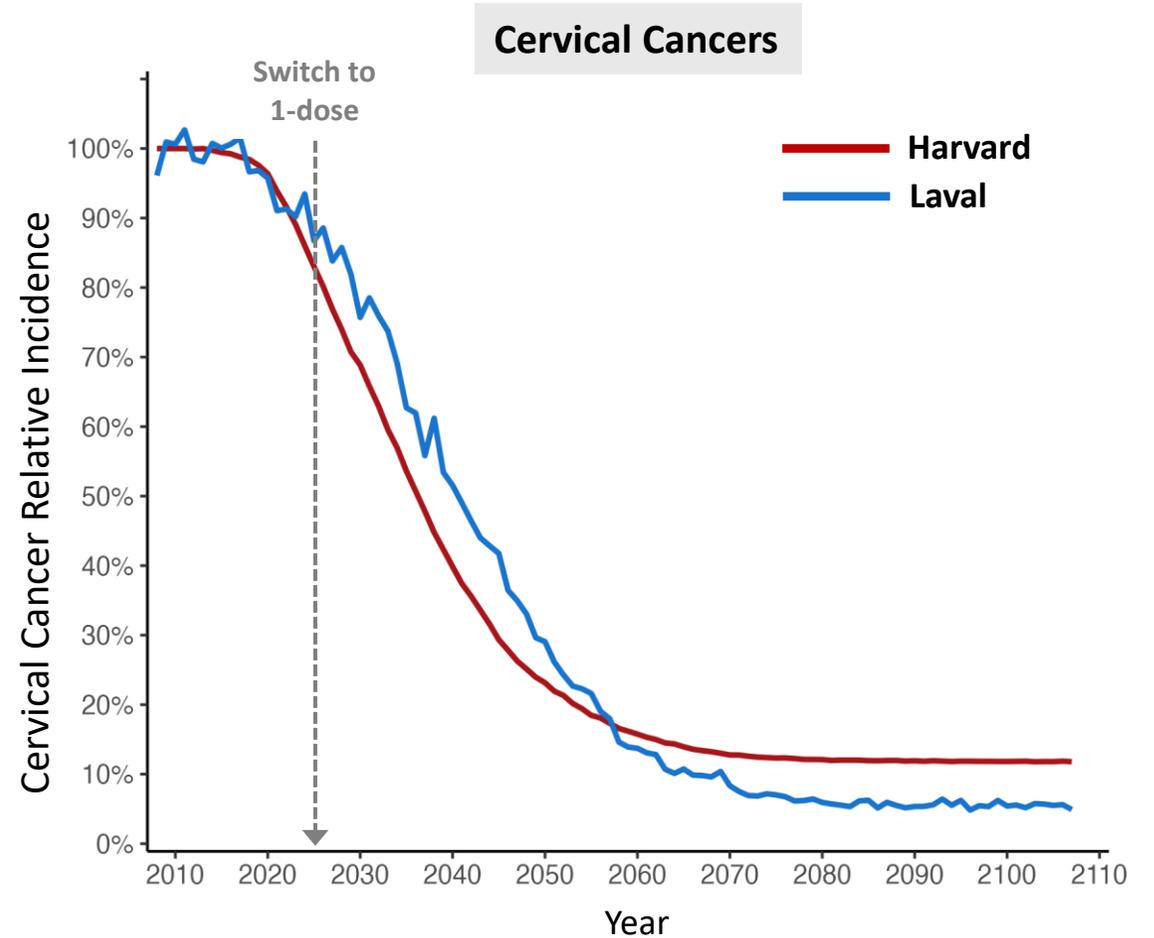
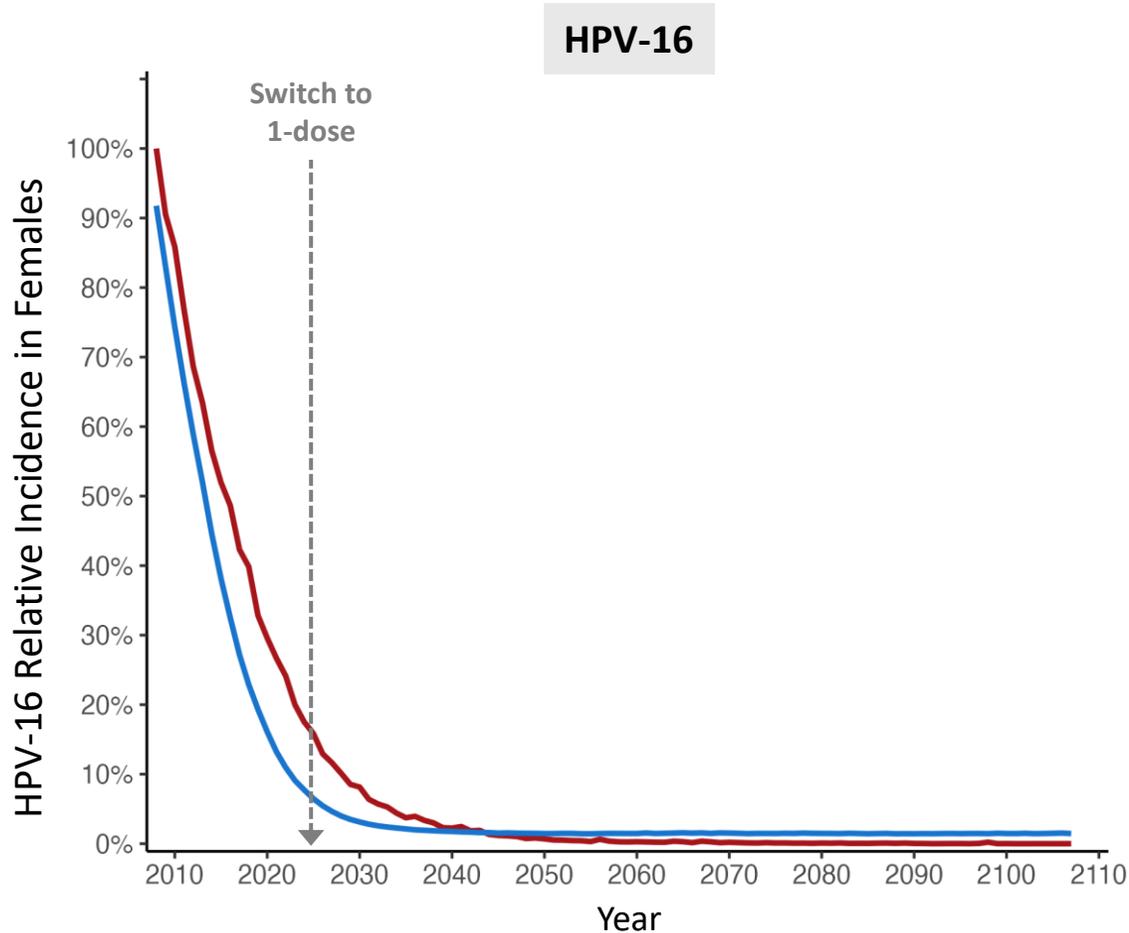
Gender-neutral 9-valent vacc, 2-Dose VE=98%, 2-Dose VD=Life, U.S. coverage



Relative incidence calculated against no vaccination.

Results: Switching to 1-Dose - Non-inferior 1-Dose

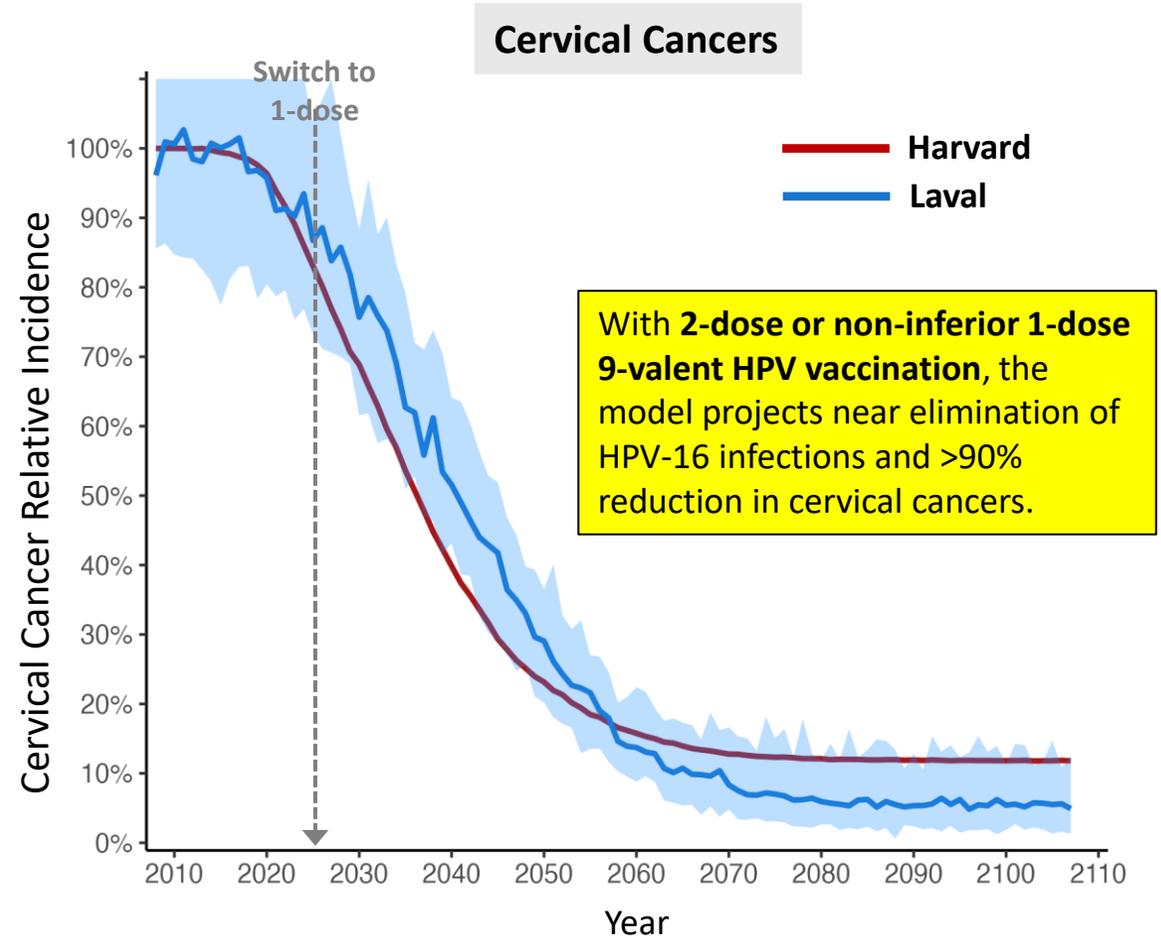
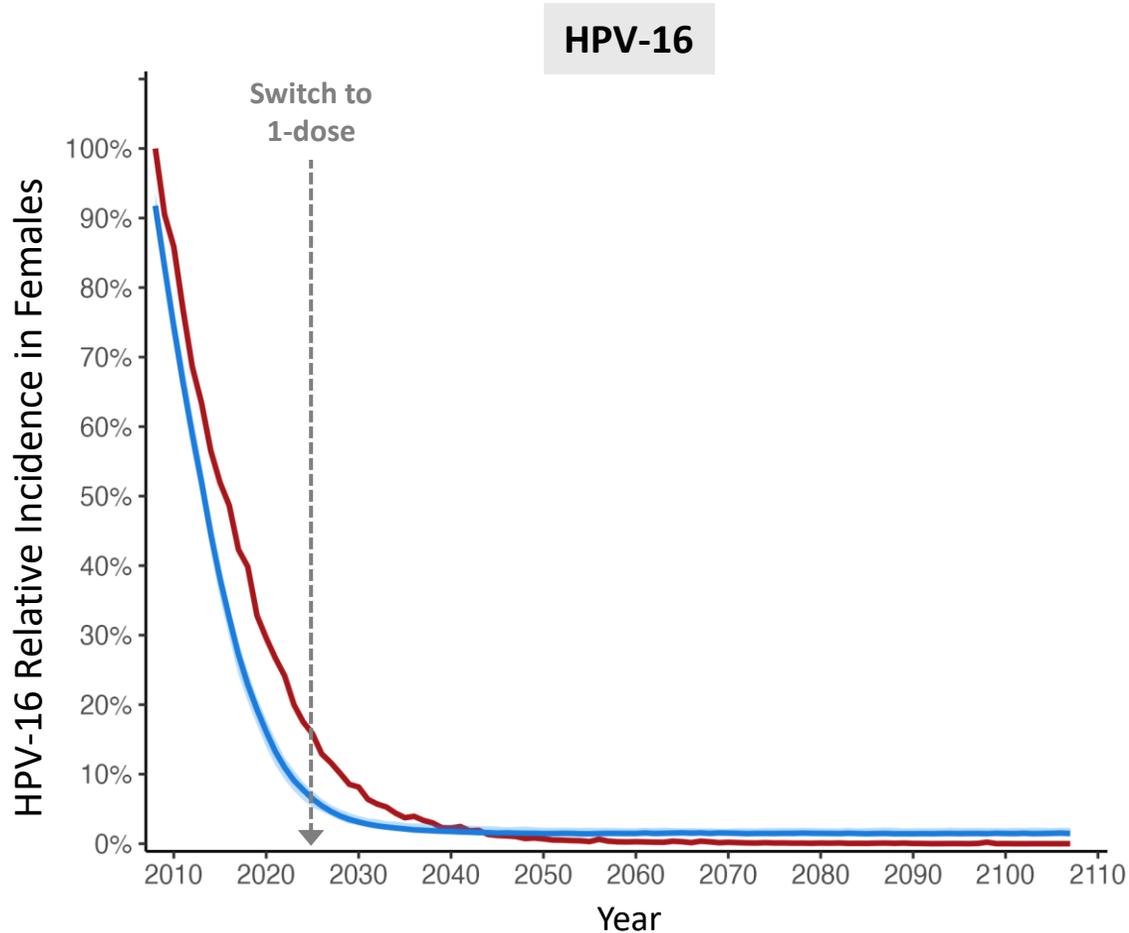
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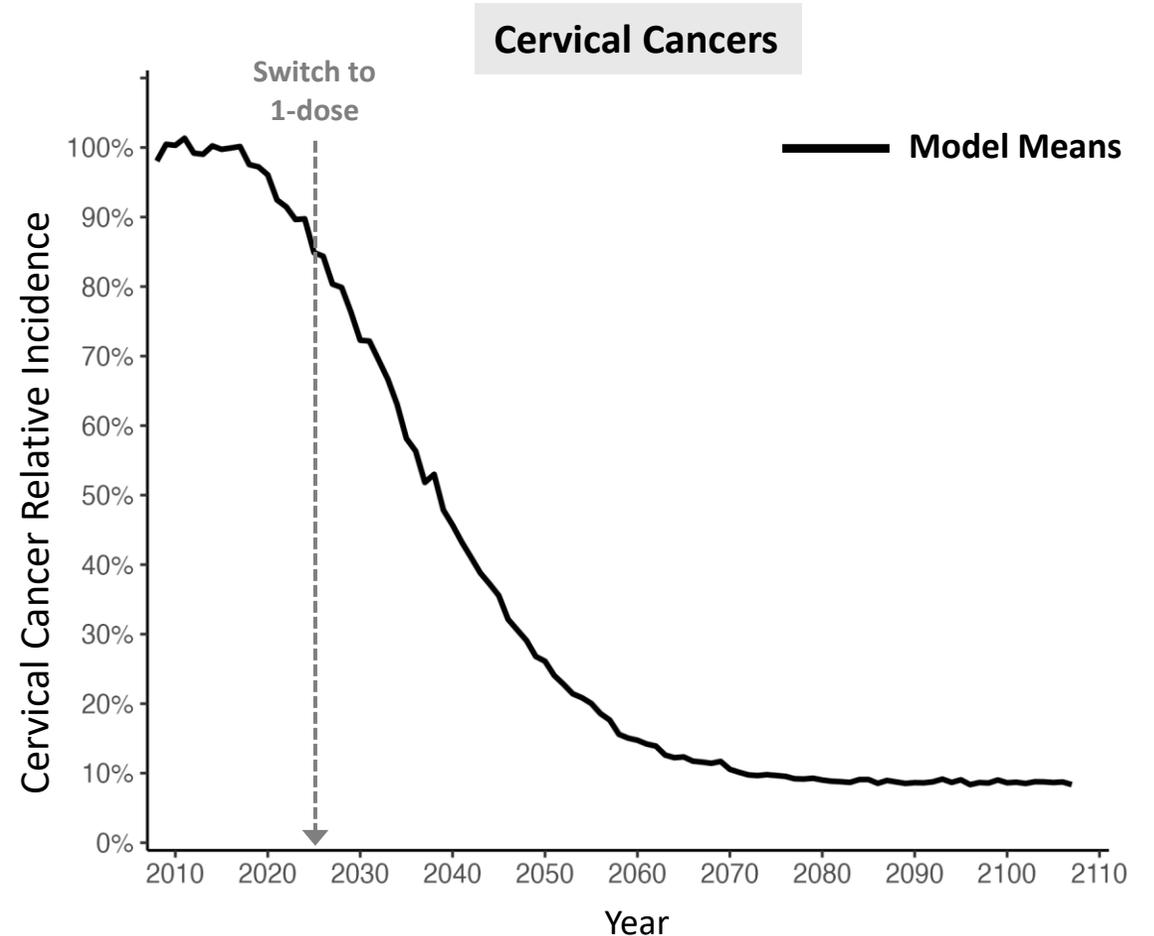
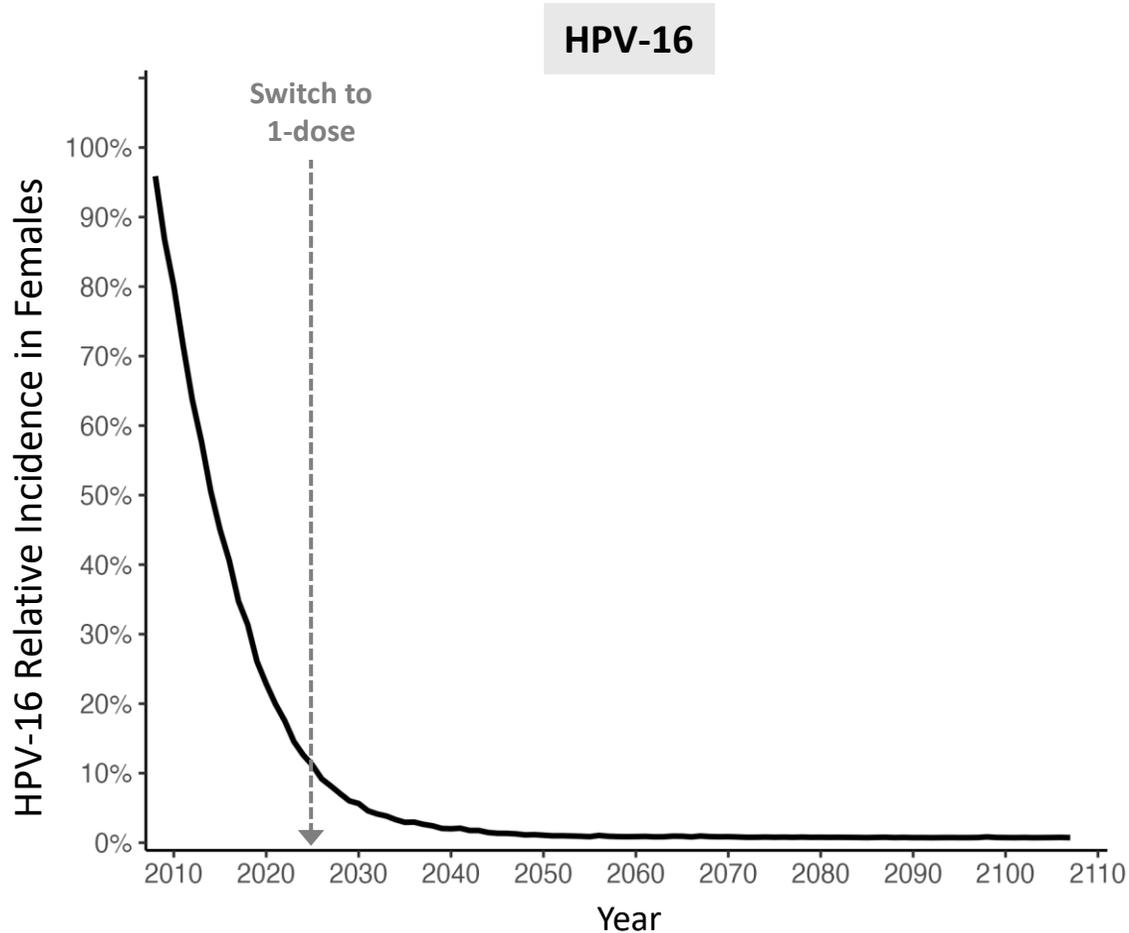
Gender-neutral 9-valent vacc, 2-Dose VE=98%, 2-Dose VD=Life, U.S. coverage



Relative incidence calculated against no vaccination.

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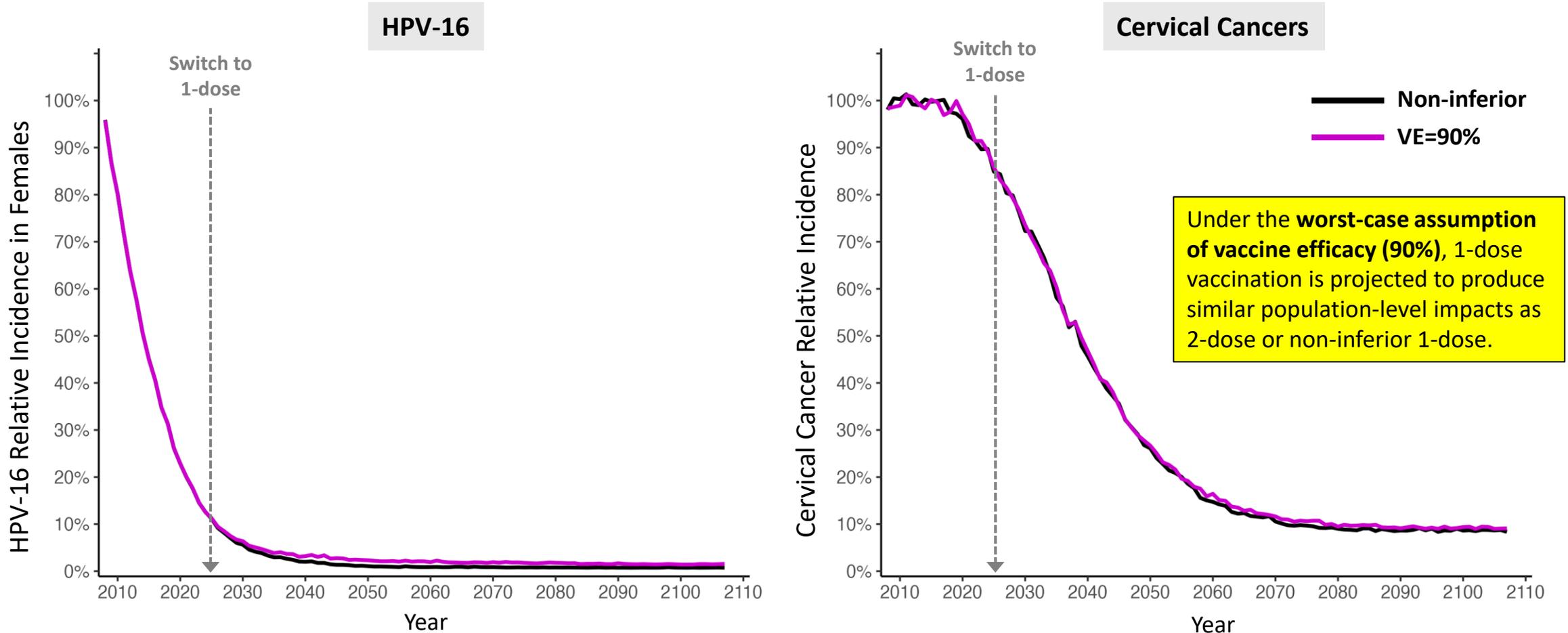
Gender-neutral 9-valent vacc, 2-Dose VE=98%, 2-Dose VD=Life, U.S. coverage



Relative incidence calculated against no vaccination; lines represent the mean model projections from the Harvard and HPV-ADVISE US models.

Results: Switching to 1-Dose - Lower 1-Dose VE (90%)

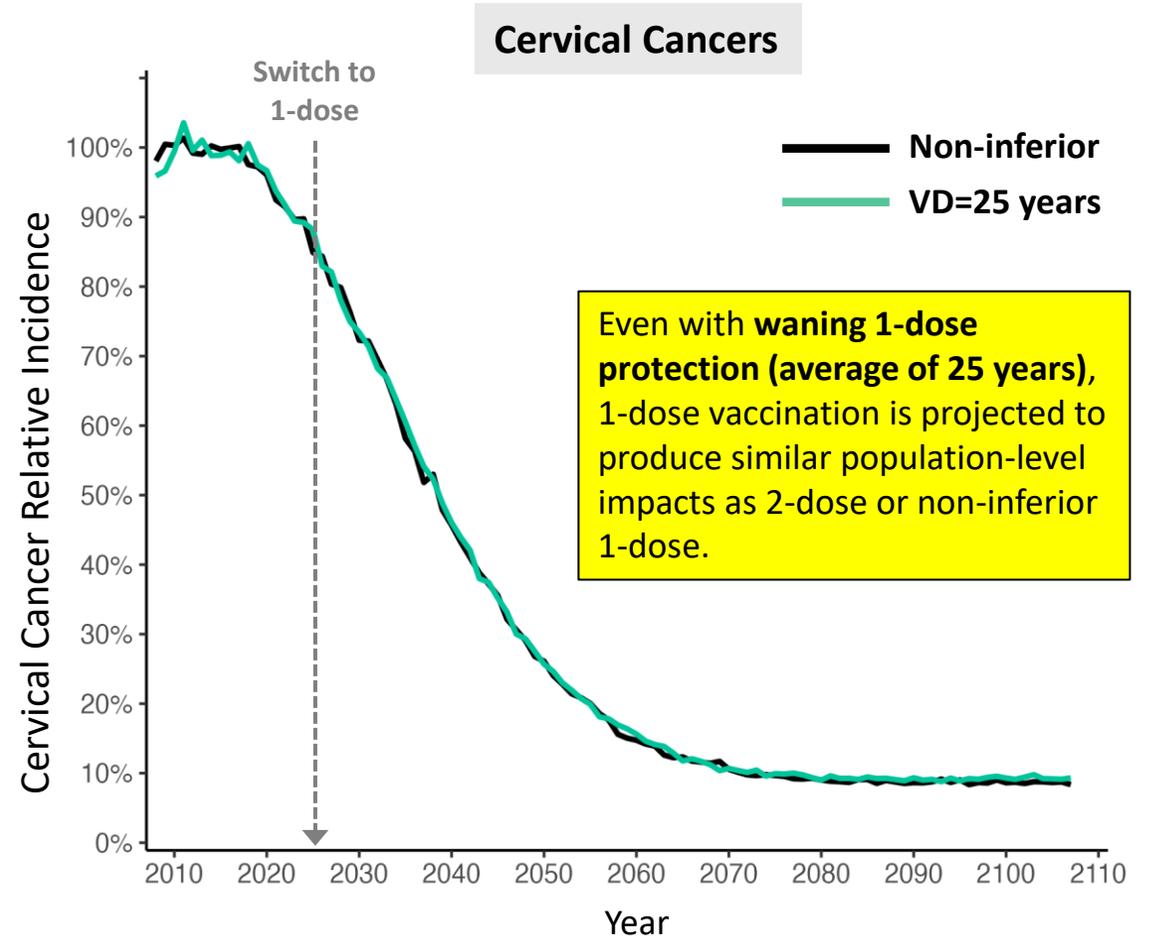
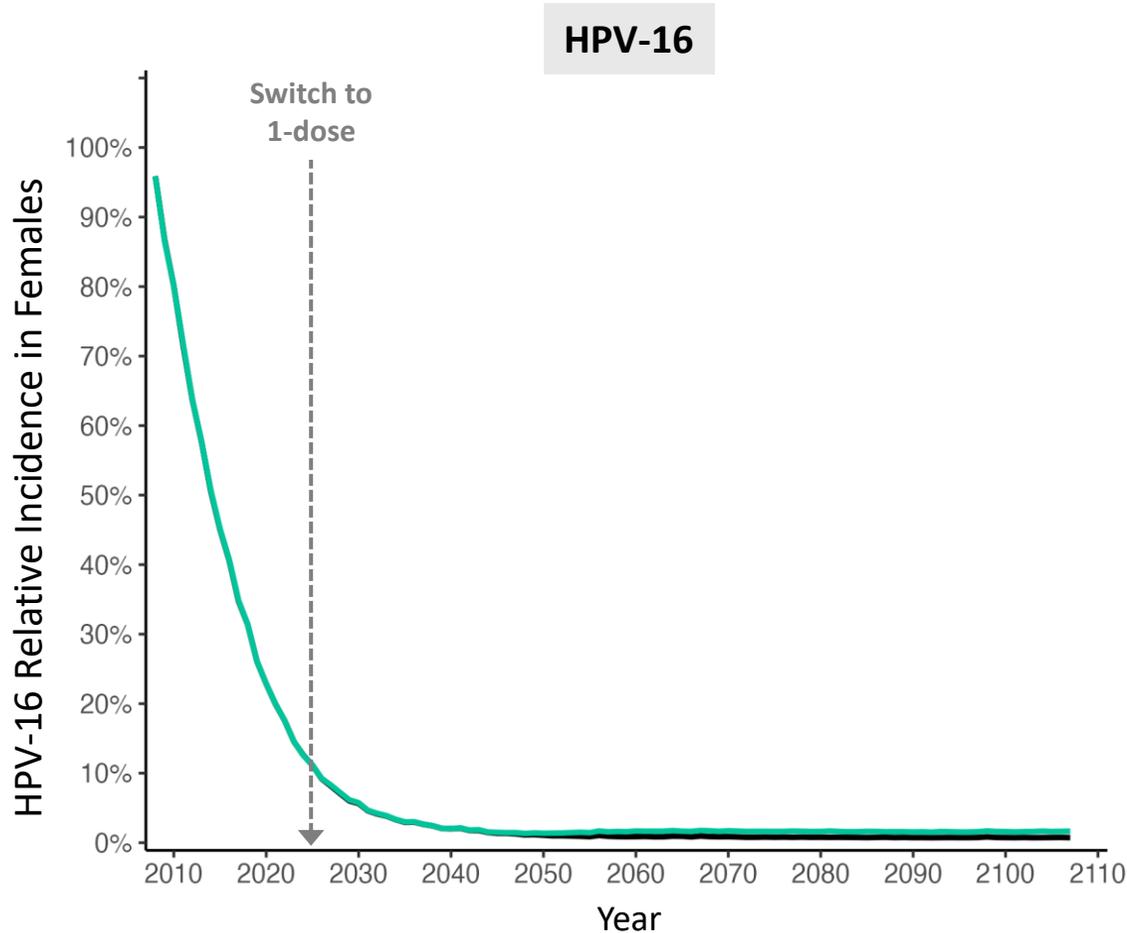
Gender-neutral 9-valent vacc, 2-Dose VE=98%, 2-Dose VD=Life, U.S. coverage



Relative incidence calculated against no vaccination; lines represent the mean model projections from the Harvard and HPV-ADVISE US models.

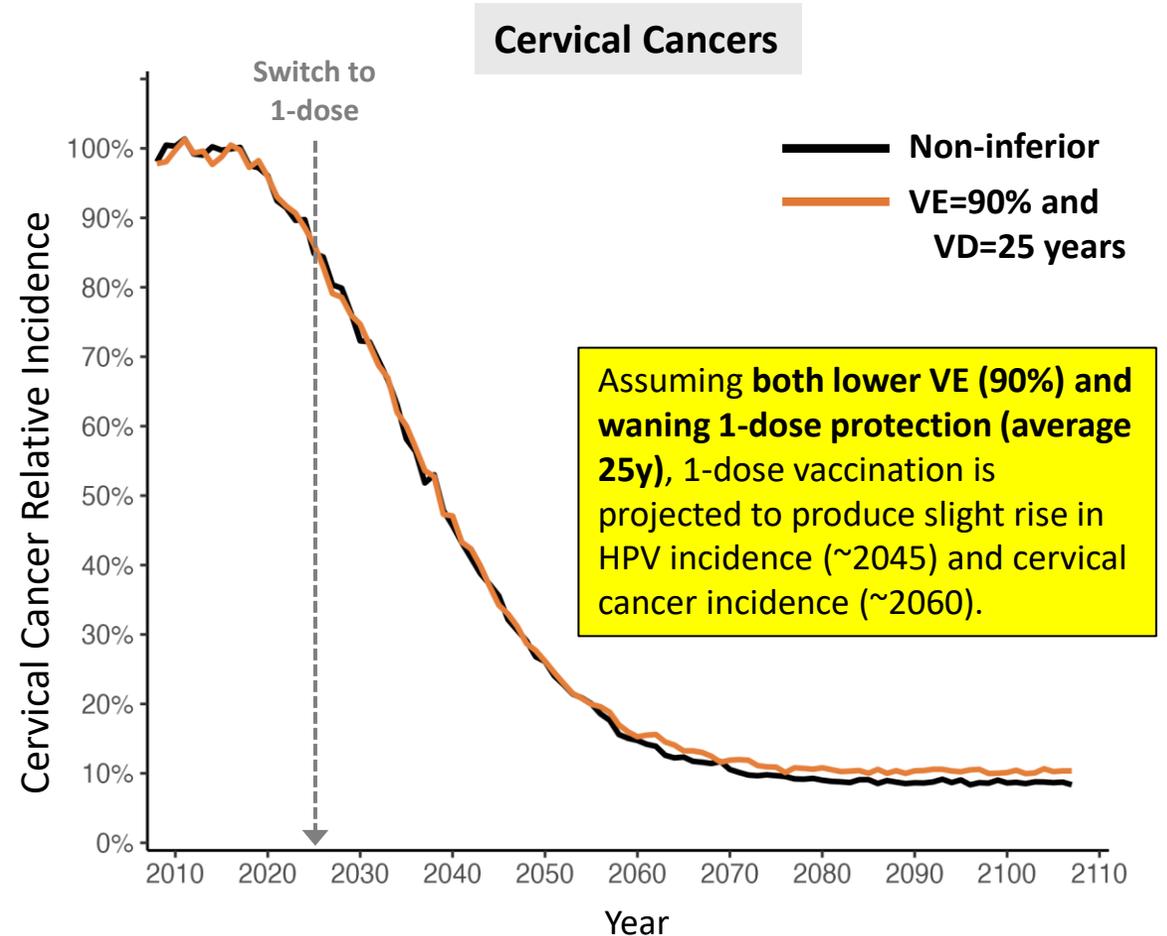
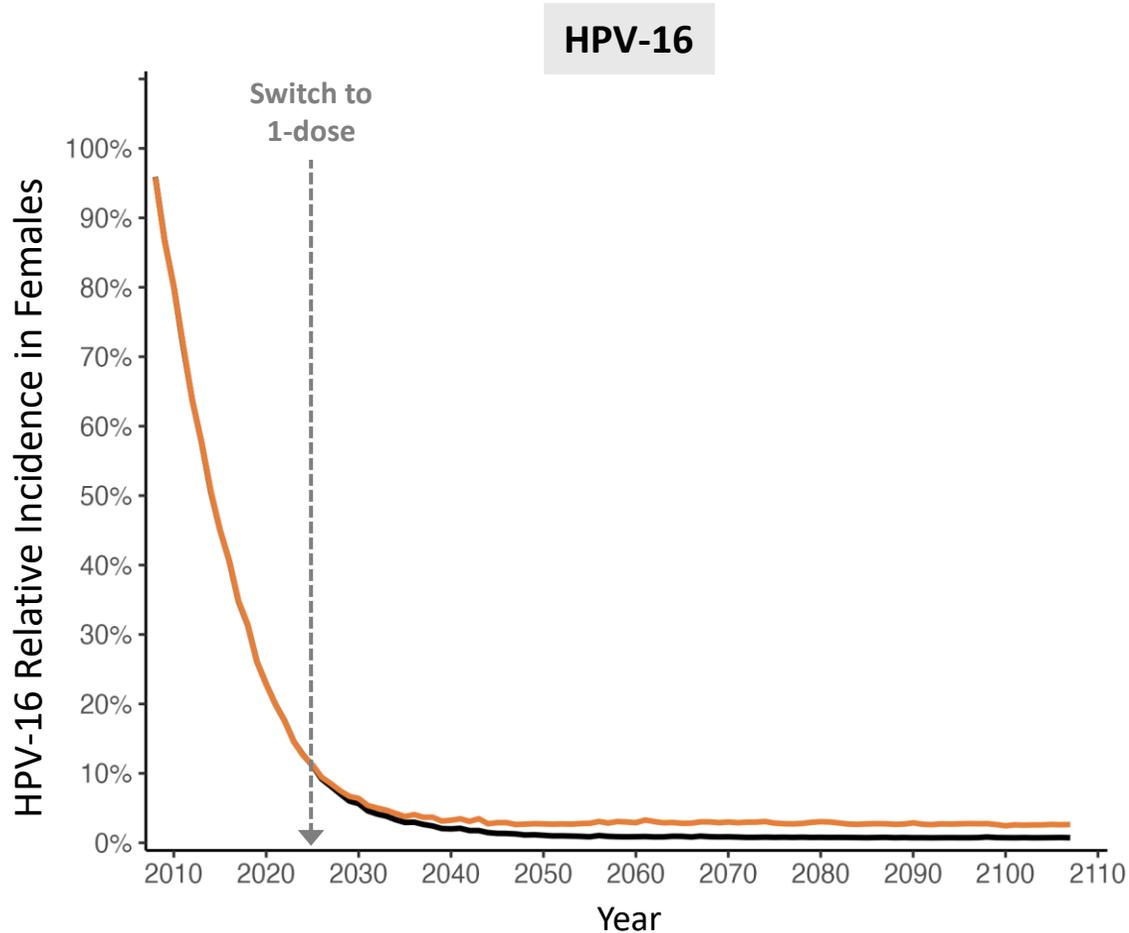
Results: Switching to 1-Dose - Waning 1-Dose VD (25 years)

Gender-neutral 9-valent vacc, 2-Dose VE=98%, 2-Dose VD=Life, U.S. coverage



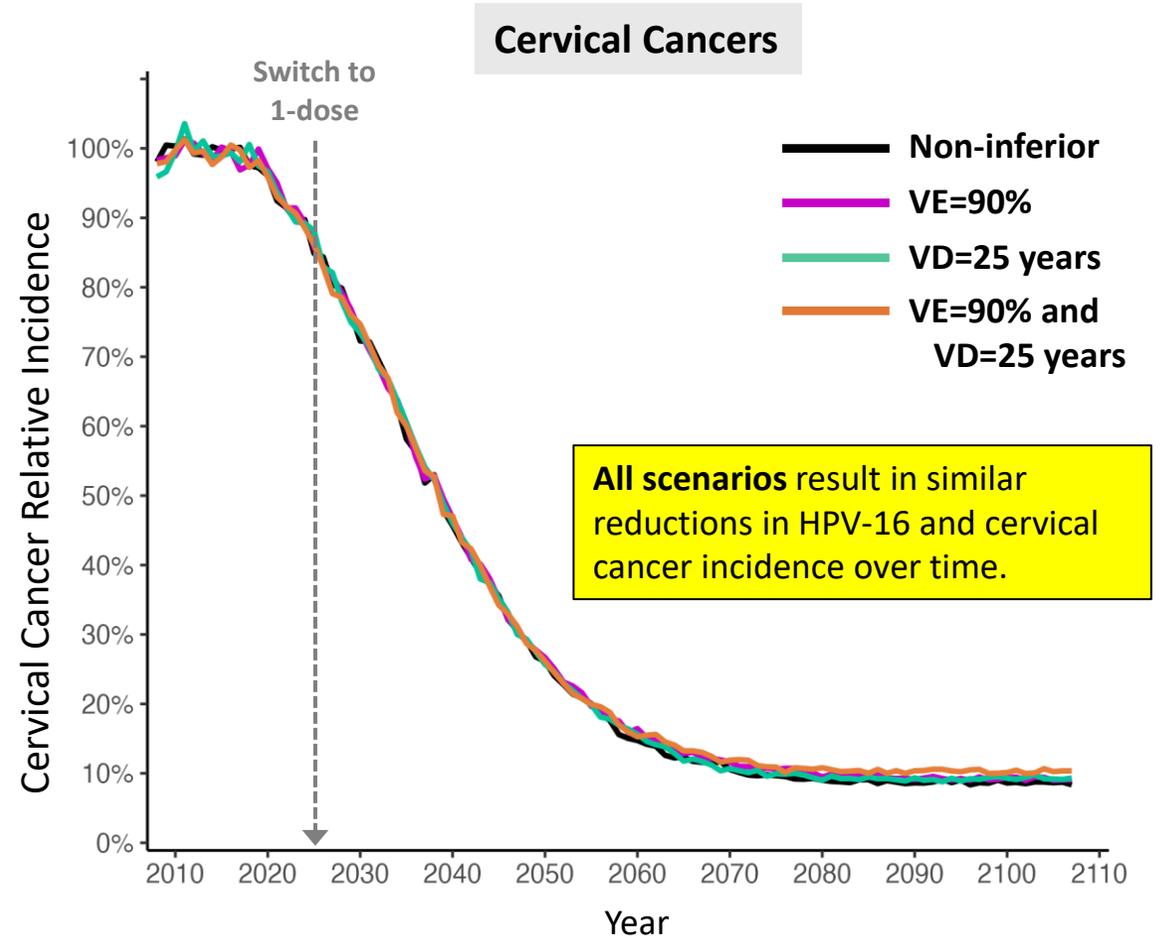
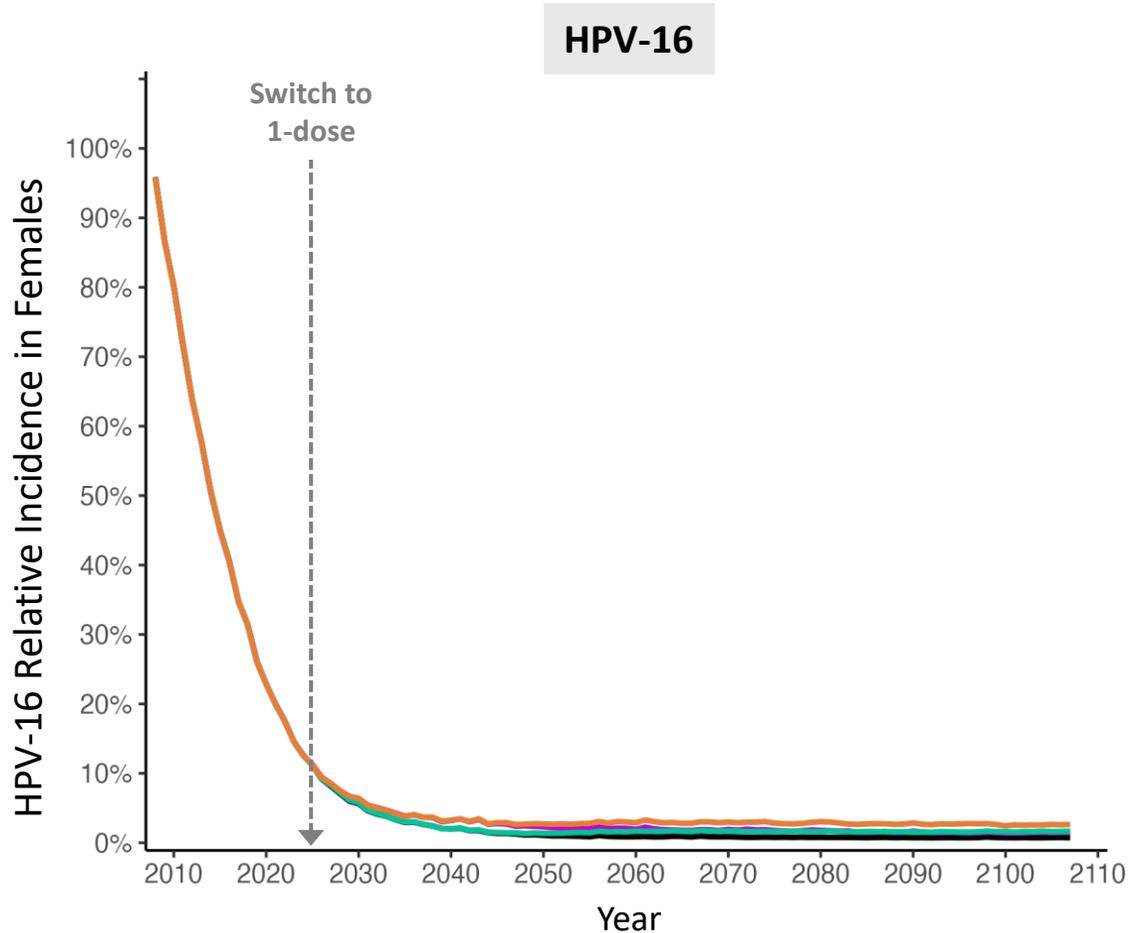
Results: Switching to 1-Dose - Lower VE (90%) & Wane (25y)

Gender-neutral 9-valent vacc, 2-Dose VE=98%, 2-Dose VD=Life, U.S. coverage



Results: Switching to 1-Dose – Summary

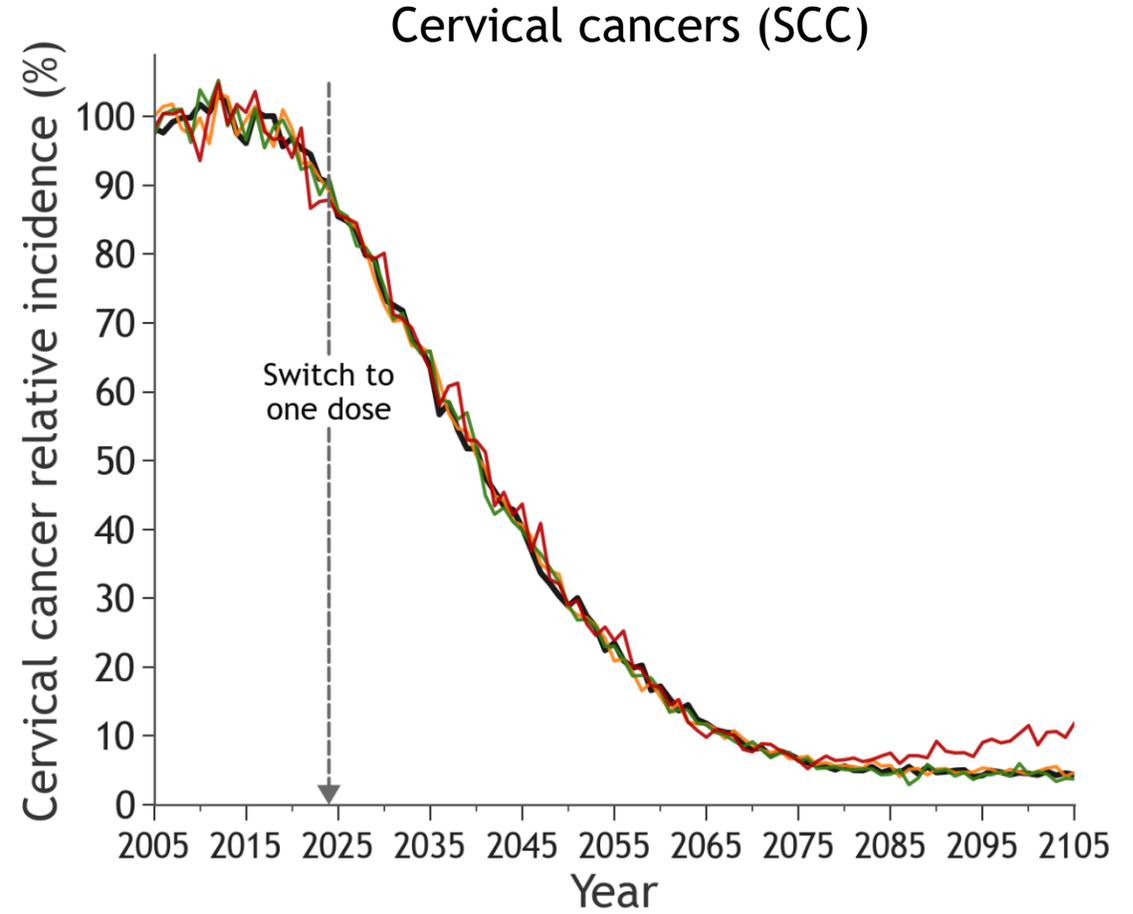
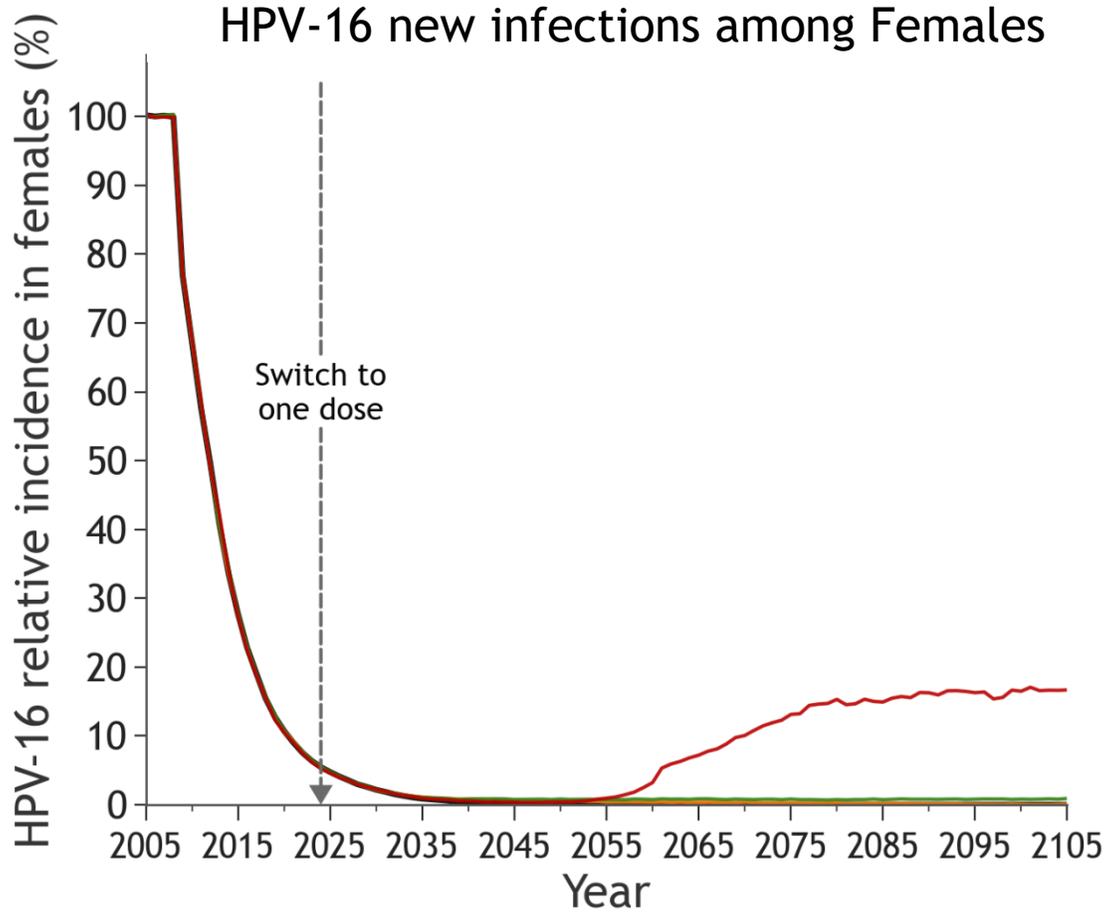
Gender-neutral 9-valent vacc, 2-Dose VE=98%, 2-Dose VD=Life, U.S. coverage



**How do these findings compare against
previously published results?**

Results **Impact of switching to 1 dose - 1-dose VD=25 years**

Gender-neutral 9-valent vaccination, 2-dose VE=98%, 2-dose VD=Life, VC=85%



Non-inferior one dose or status quo with two doses	One dose pessimistic VE	One dose pessimistic VD
— VE=98%, VD=life	— VE=90%	— VD=25 years
	— Girls: VE=98%, Boys: VE=70%	

Brisson JNCI, 2024; the lines are the median result of model projections using 100 parameter sets (50 from HPV-ADVISE US and 50 from HPV-ADVISE Canada); Relative incidence calculated as % incidence vs no vaccination; HPV infection results excludes reactivation or deposition of HPV infections.

Other Scenarios Explored in Prior Analyses

- What is the impact of 1-dose vaccine efficacy for males?
 - In a pessimistic scenario of lower 1-dose vaccine efficacy (70%) for males only, HPV-ADVISE showed a similar population-level impact as non-inferior 1-dose for all individuals.
 - Herd effects would mitigate a lower vaccine efficacy for males if gender-neutral vaccination coverage is high and vaccine efficacy for females is high and long lasting.
- What is the impact of 1-dose vaccination on non-cervical HPV-related cancers ?
 - More work is required to better understand the natural history of these cancers and the potential impact of 1-dose vaccination on their epidemiology.
 - Prior analyses suggest more limited/delayed rebound for other HPV-related cancers for all pessimistic 1-dose scenarios given slower progression from infection to cancer.¹
- Can mitigation strategies offset potential rebounds in infection and cancer?
 - Both models have shown that if ongoing trial data were to signal waning (i.e., in the next 10 years), switching back to a 2-dose regimen would mitigate any rebounds in HPV-16 and cervical cancer.¹⁻³
 - Mitigation strategies could be population-level and would not require revaccinating those who received 1 dose to be successful.

Conclusions: 1-Dose HPV Vaccination in the U.S.

- Switching to 1-dose HPV vaccination is projected to have similar reductions in HPV and cervical cancer incidence as continuing with 2 doses in the U.S.
- Under the pessimistic assumptions of vaccine efficacy (90%) and vaccine duration (25 years), a switch to 1-dose vaccination is projected to have limited rebound in HPV infection and cervical cancer incidence.
 - Switching to 1-dose vaccination would occur when HPV prevalence is low due to high 2-dose vaccination coverage in the U.S.
 - Individuals would be protected during their peak ages of sexual activity, providing direct protection and herd effects to unprotected adults.
- Continued monitoring of 1-dose protection over time is required to rapidly detect any potential signs of waning protection and introduce mitigation strategies, if needed.
 - Under pessimistic assumptions of 1-dose duration of protection, switching back to 2-dose vaccination is projected to mitigate losses in cervical cancer prevention.

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