

Comparing 2- and 3-dose 9-valent HPV Vaccine Schedules in the U.S.

A Cost-effectiveness Analysis

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Disclaimer

- The findings and conclusions expressed are those of the author and do not necessarily represent the official views of the Centers for Disease Control and Prevention (CDC) or the Department of Health and Human Services (DHHS)

Peer reviewed

- Follows *Guidelines for economic analyses to be presented to the ACIP*

Conflicts of interest statements

- M Brisson, JF Laprise, HW Chesson, LE Markowitz
 - No known conflicts of interest
- M Drolet (past 3 years): Consulted for GSK (Zoster vaccine)

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Introduction

- A 2-dose 9-valent vaccine phase III immunogenicity trial has been completed
- 2 doses of 9-valent in girls and boys 9-14 years old was as immunogenic as 3 doses in women 16-26 years old
 - for types HPV-6/11/16/18/31/33/45/52/58

Study question

From the societal perspective, what is the health and economic impact of switching from a 3- to a 2-dose schedule, in the context of an established 9-valent HPV vaccination program in the U.S.?

- i.e. what is the additional impact of the 3rd dose of 9-valent vaccine vs. 2 doses?

Objective

To evaluate the population-level effectiveness and cost-effectiveness of 3- versus 2-dose 9-valent vaccination in the U.S.

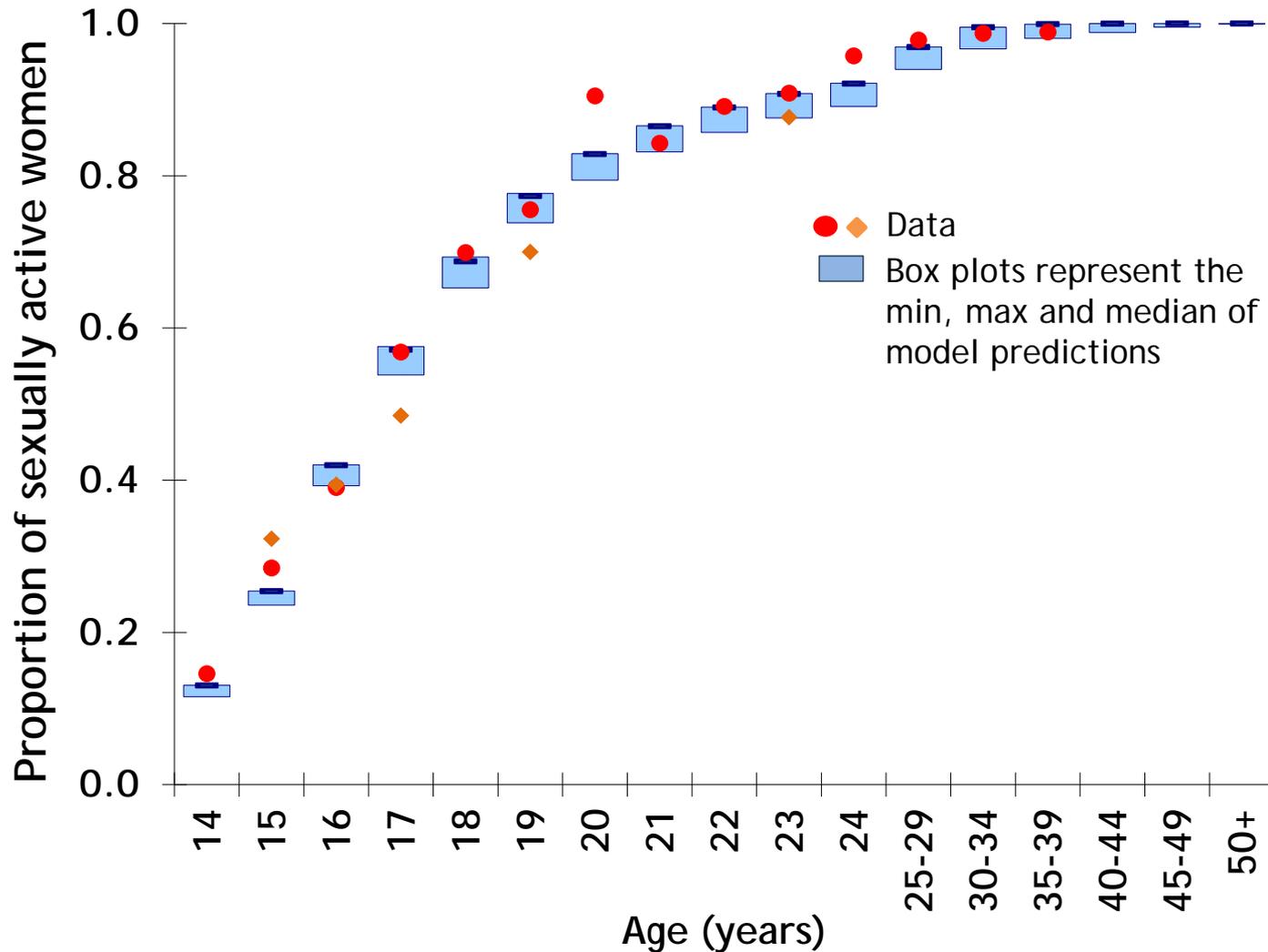
Methods

Model Overview - HPV-ADVISE U.S.

- **Model type:** Individual-based transmission-dynamic model[&]
- **Components:**
 - Demographic
 - Sexual behaviour & HPV transmission
 - Natural history of disease
 - Vaccination
 - Screening & Treatment
 - Economic
- **Population:** Open-Stable, 10 to 100 years of age
- **HPV infections:** 18 genotypes, including 6/11/16/18/31/33/45/52/58
- **Diseases:**
 - Anogenital warts
 - Cervical cancer (SCC & adenocarcinoma)
 - Cancers of the anus, oropharynx, penis, vagina & vulva

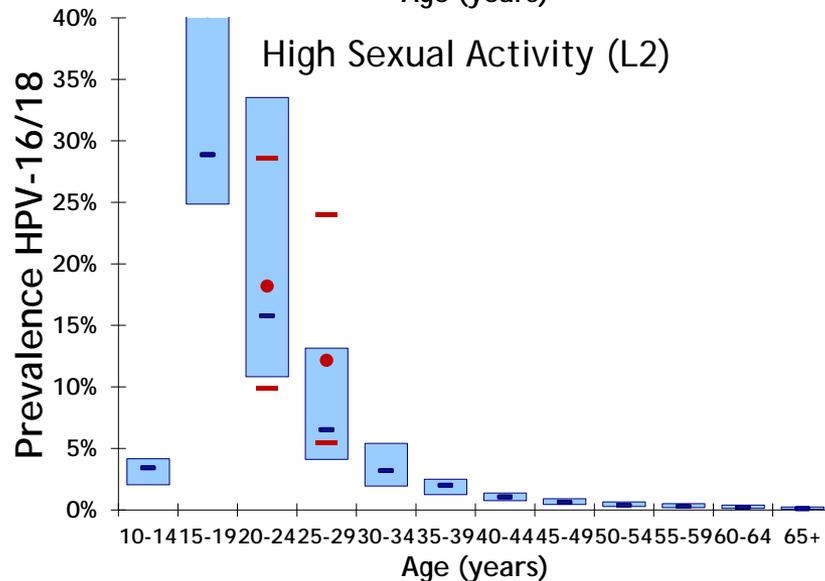
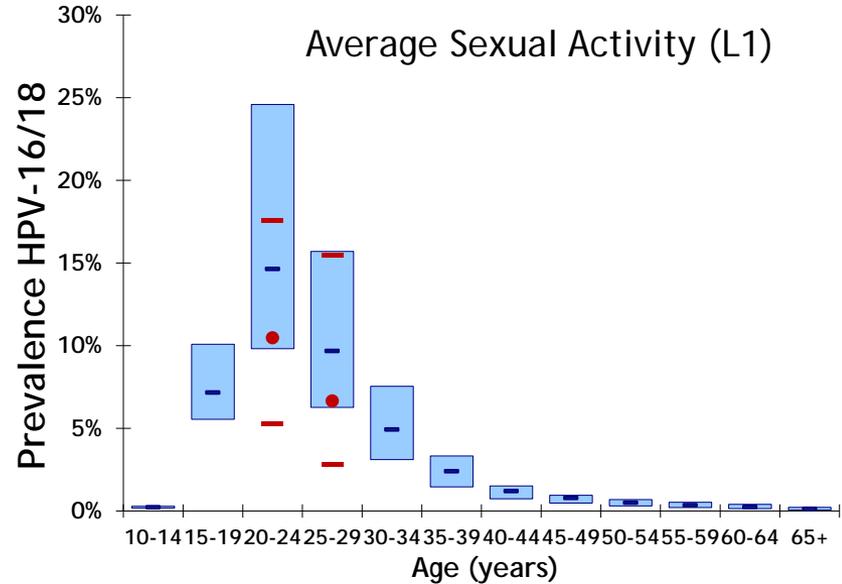
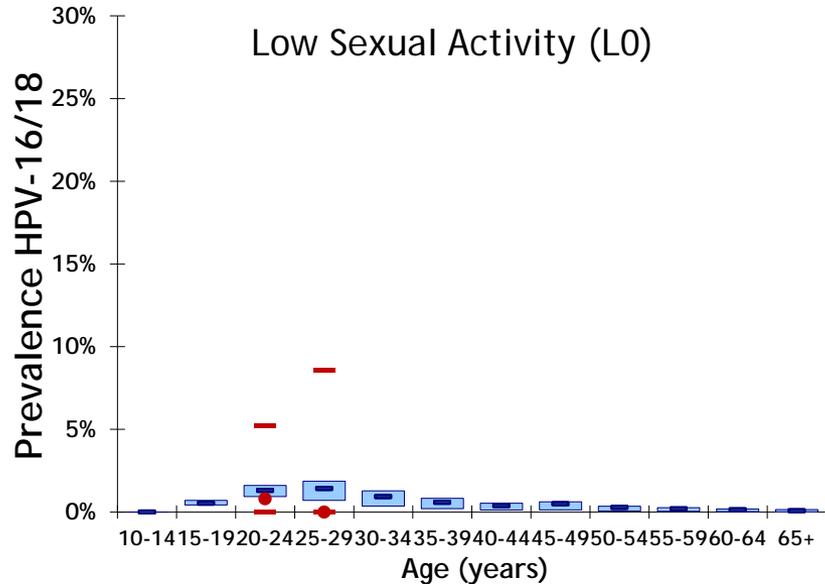
Model Fit - sexual behaviour

Ex: Proportion sexually active women



Model Fit - HPV prevalence in women

Ex: HPV-16/18 prevalence by age and level of sexual activity

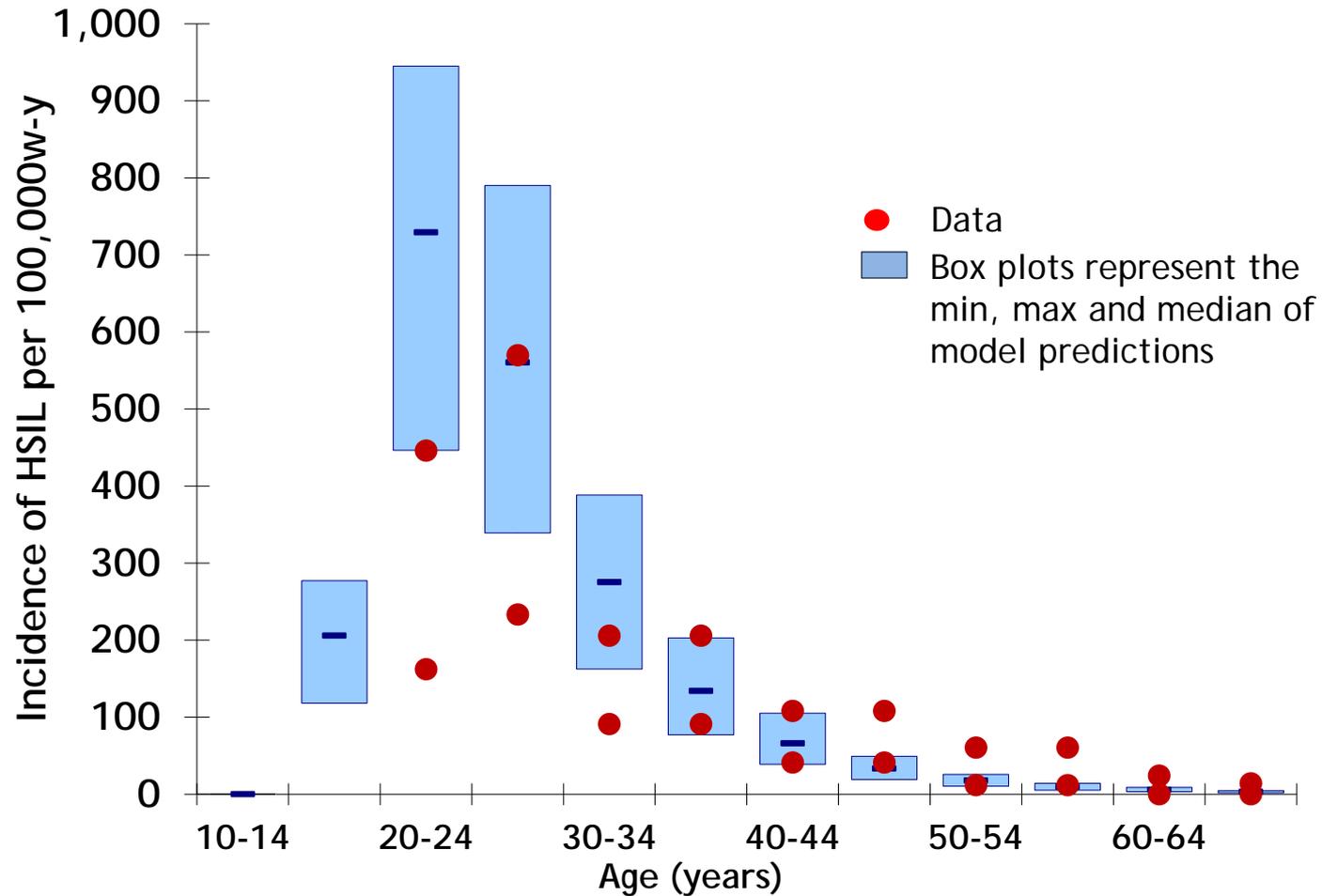


● Data — 95%CI
■ Box plots represent the min, max and median of model predictions

&: Other examples of model fit in extra slides; Data: NHANES

Model Fit - Screening

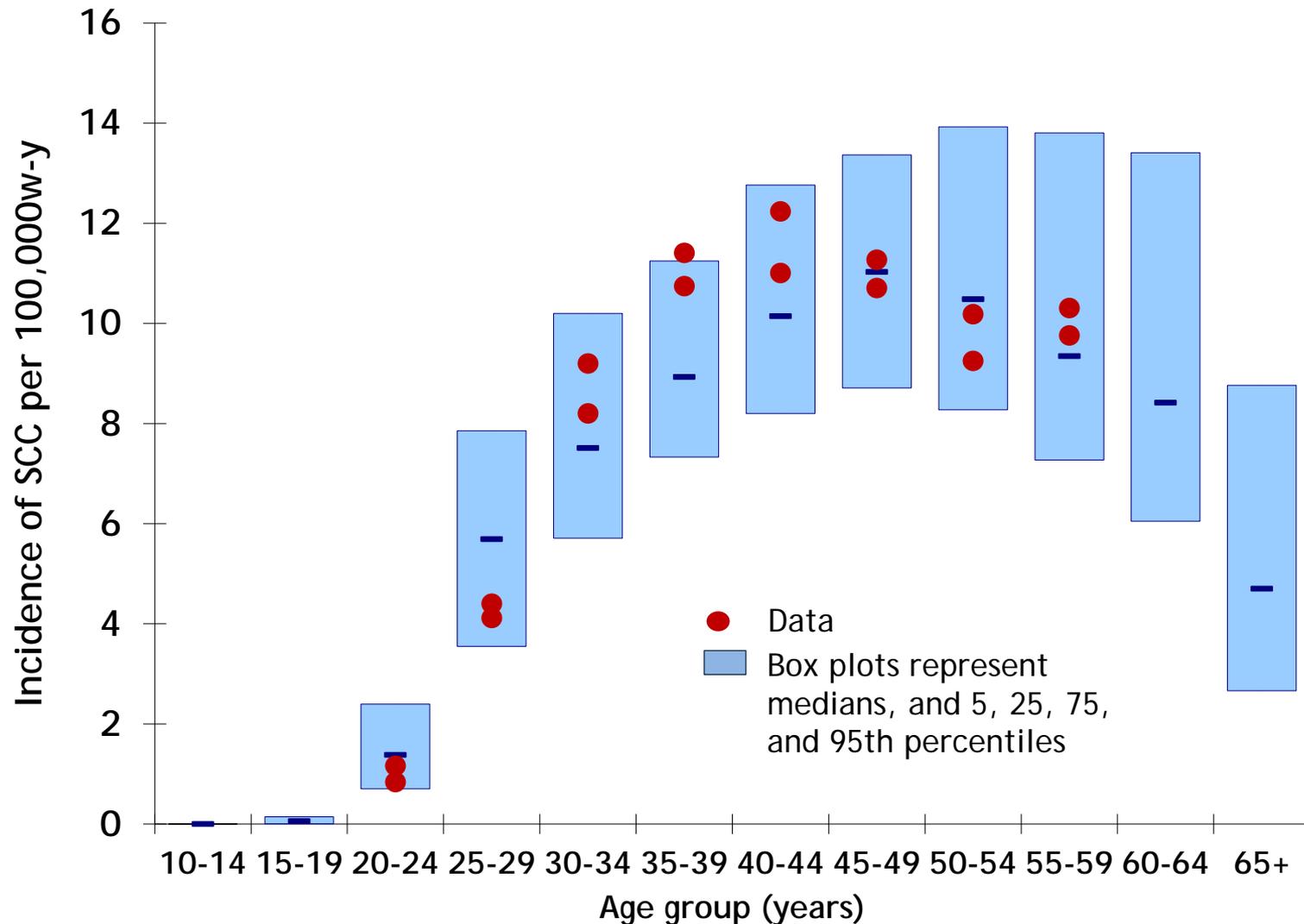
Ex: Incidence of HSIL



&: Other examples of model fit in extra slides; Data: Insinga 2004

Model Fit - Squamous cell carcinoma (SCC)

Ex: Incidence of SCC



&: Other examples of model fit in extra slides; Data: US Cancer Statistics (NPCR/SEER)

Economic analysis

- Perspective: Societal
- Costs: All direct medical costs (\$US 2013)*
- Outcome Measure: Cost per QALY-gained*
- Discounting: 3% for future costs and benefits
- Time Horizon: 100 years
- Vaccine cost per dose[†]: \$158 with administration costs[&]

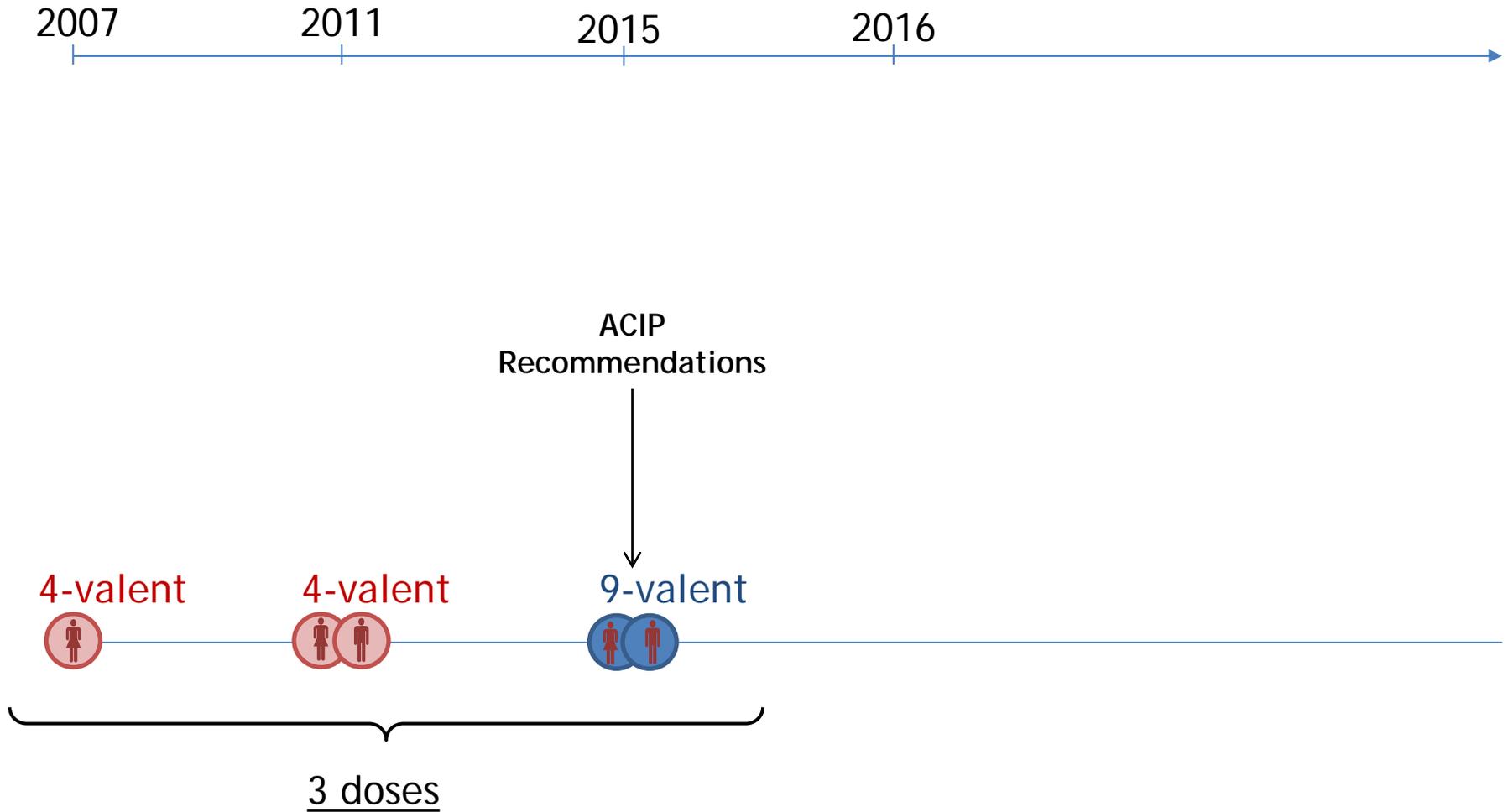
Definition: QALY=quality-adjusted life-year

*. Description of parameters and references available in extra slides

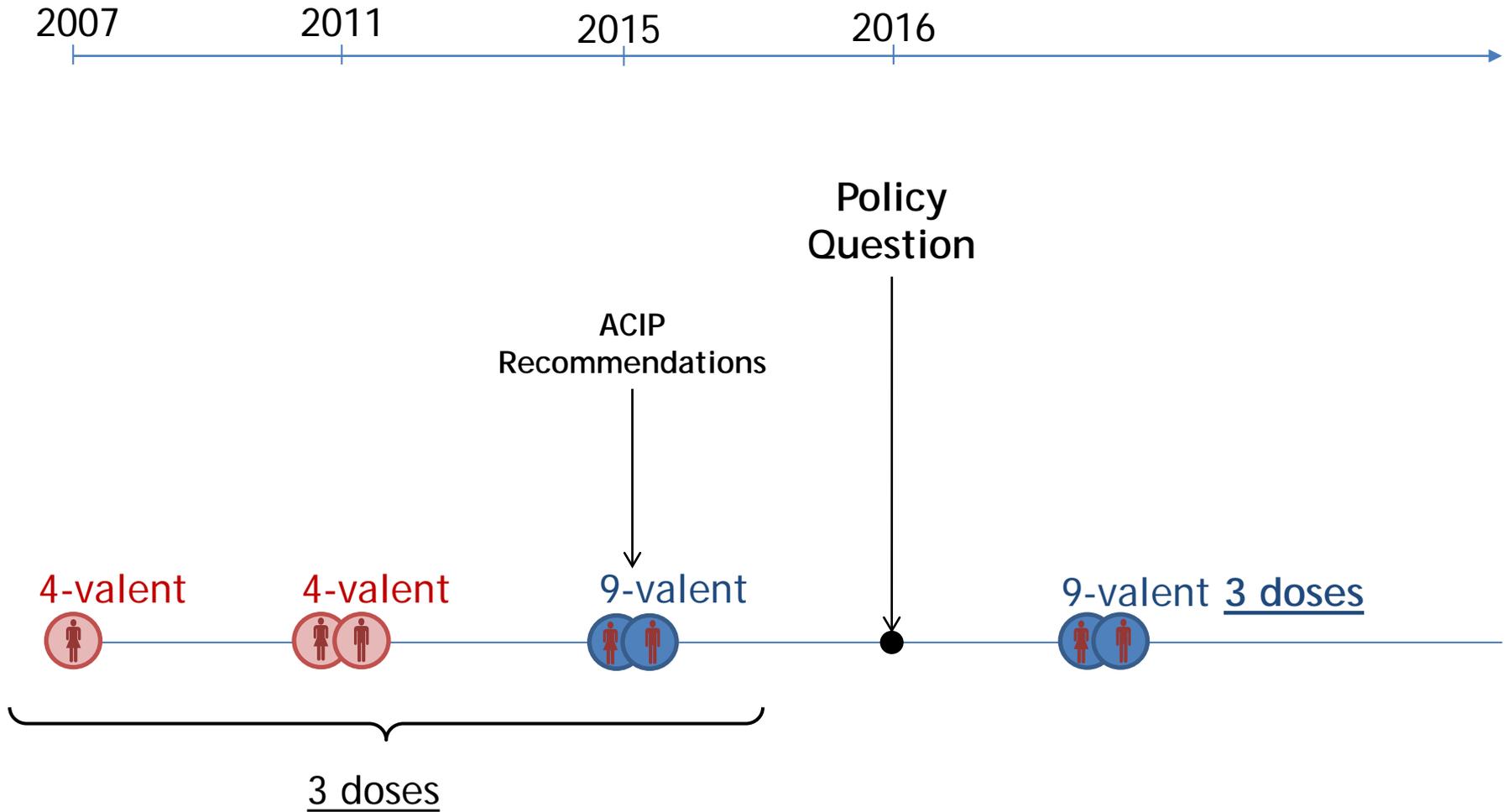
&. All vaccine prices in this presentation include the administration costs. We assume equal vaccine cost per dose for 2- and 3-dose schedule.

†: Cost from Merck presentation at the 29th International Papillomavirus Conference, 2014

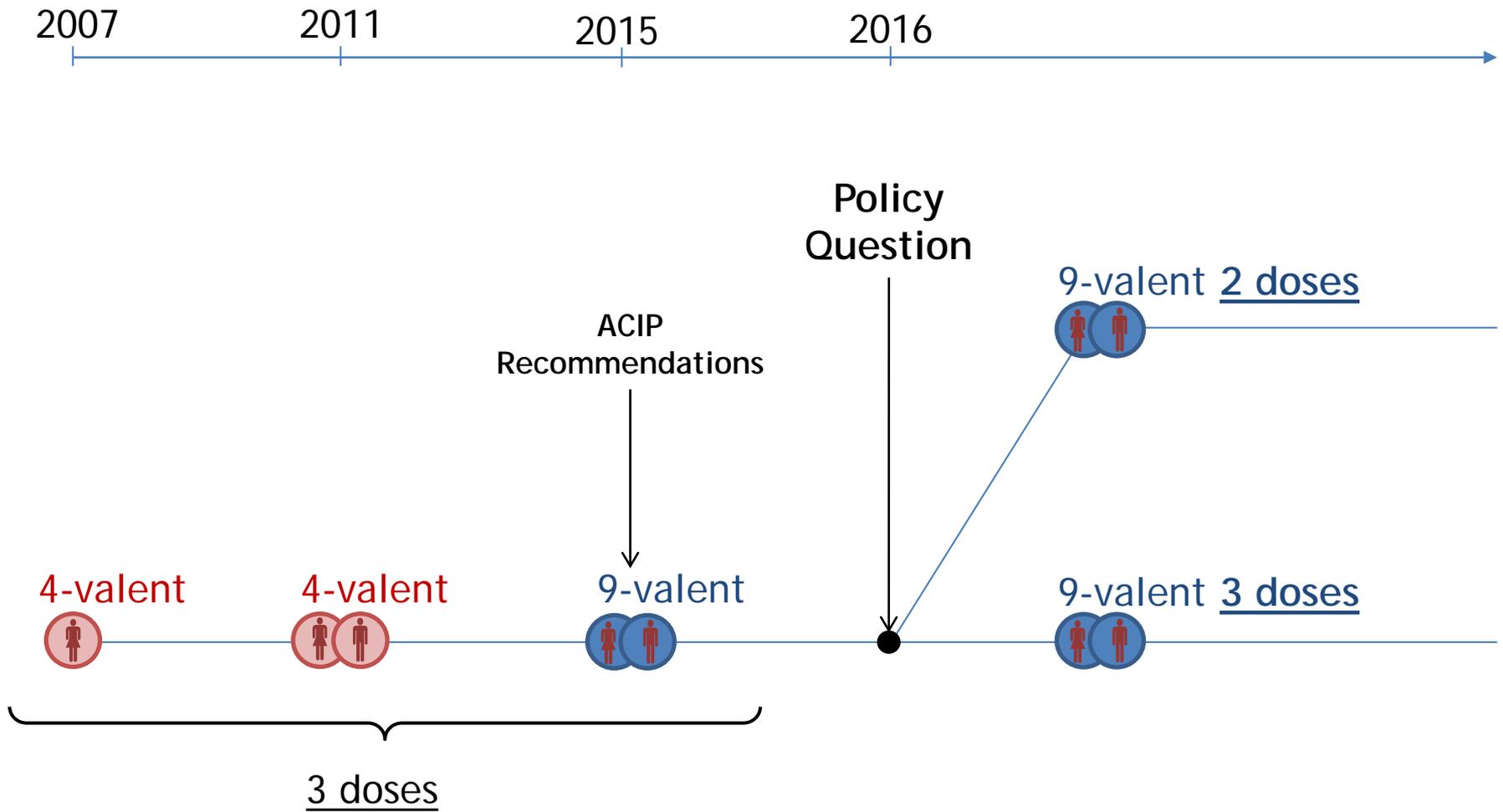
Intervention HPV vaccination in the U.S.



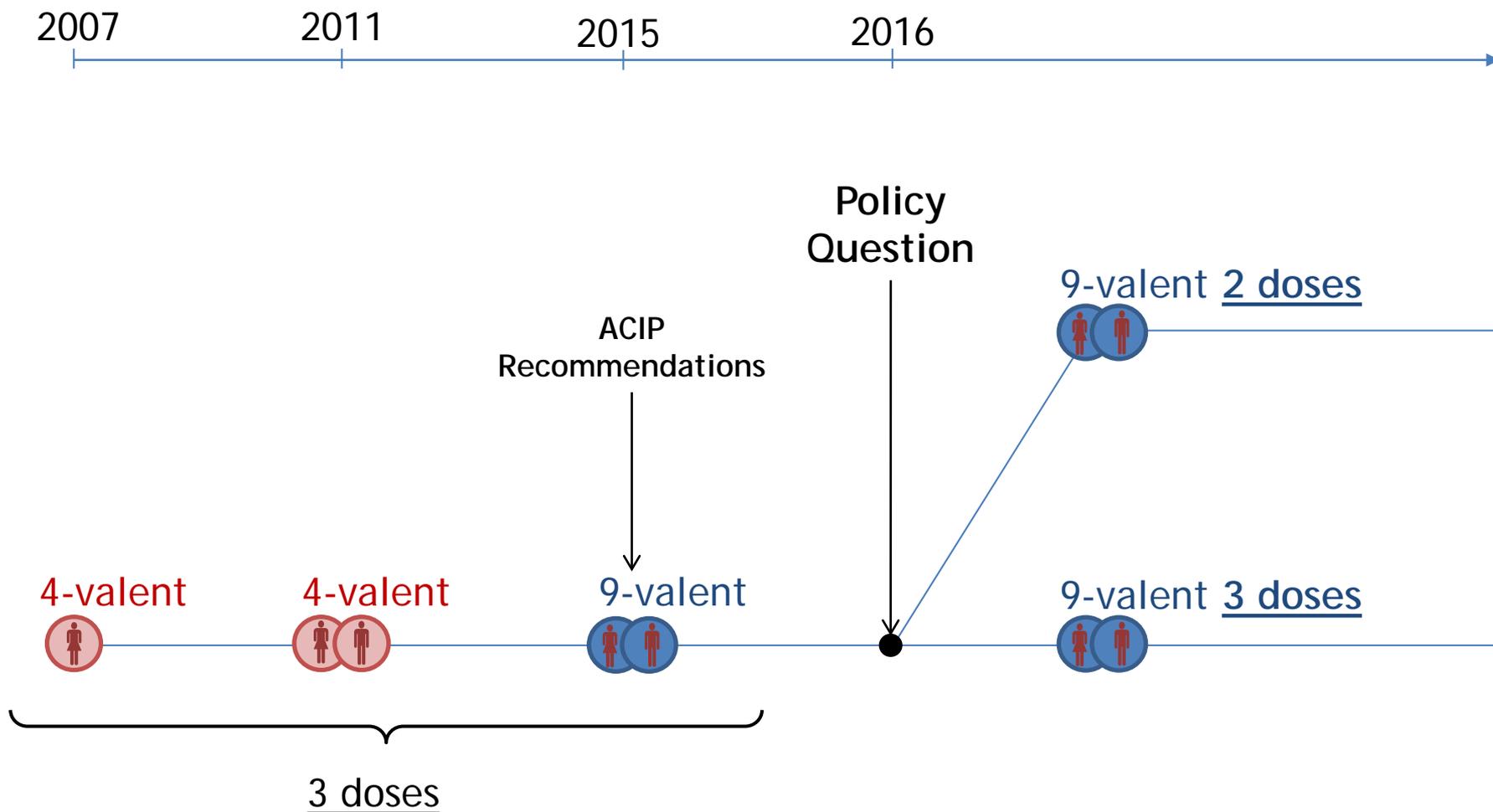
Intervention HPV vaccination in the U.S.



Intervention HPV vaccination in the U.S.



Intervention HPV vaccination in the U.S.



- Vaccination coverage:**
- Used age-specific uptake rates: Annual % vaccinated among those who had not previously completed their schedule
 - 2007-14: Observed uptake rates (U.S. National Immunization Survey)
 - 2015+: Assumed uptake rates constant at 2014 levels

Vaccine characteristics

	Scenarios	
Schedule	3-dose	2-dose
Duration	Life	Life, 30, 25, 20, 15 yrs
Efficacy ^[1]	95%	95%, 85%
Vaccination coverage	Observed	Observed, 5-15 percentage point increase ^{&}

We know that:

- If efficacy and duration are similar, 2 doses will be cost saving compared with 3 doses

Therefore:

- We examined the potential impact if 2 doses provided lower efficacy or shorter duration of protection

REF: [1] Joura *NEJM* 2015; we assume that vaccine efficacy is the same in boys and girls

&: Absolute increase in coverage

Results: Effectiveness

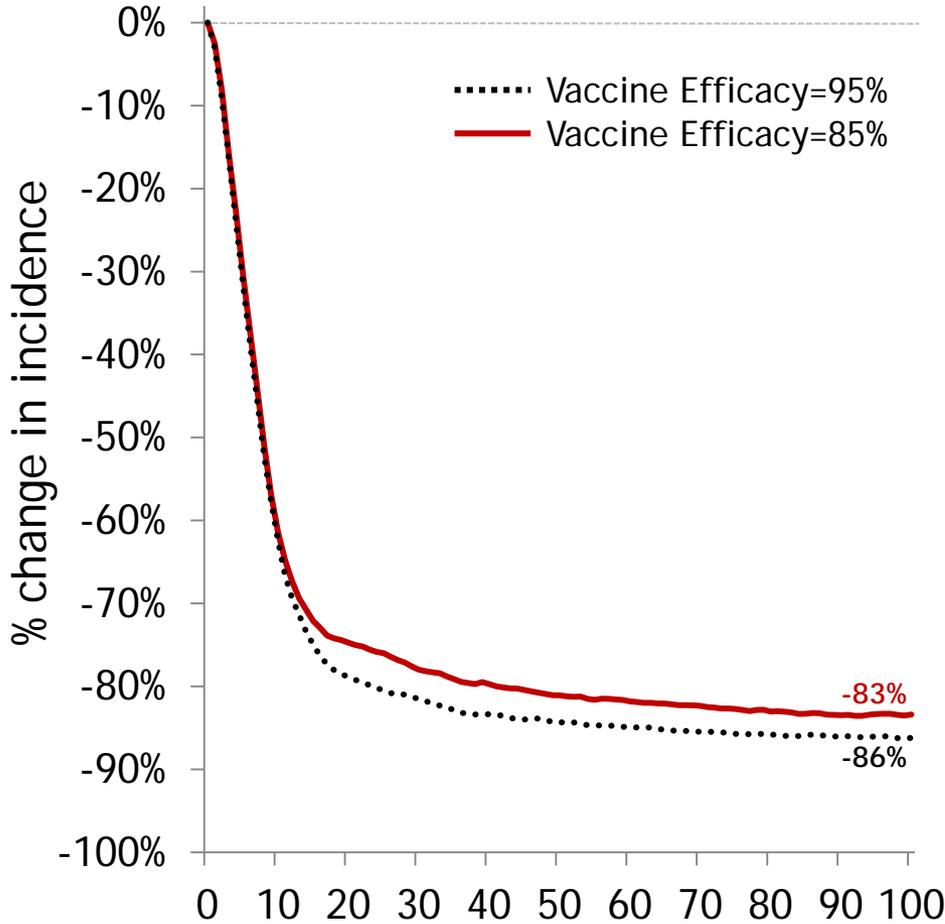
Key question:

What vaccine characteristics are most important when considering reducing doses?

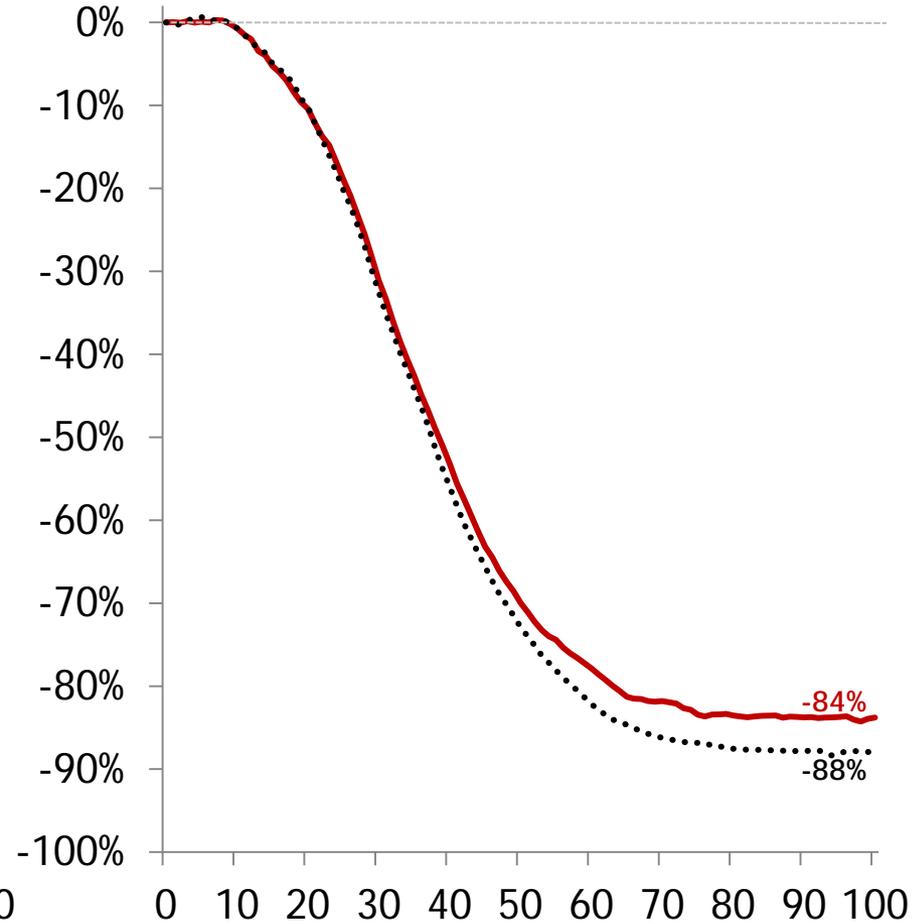
Effectiveness Impact of efficacy

Vaccine duration=Lifelong

Anogenital Warts



Cervical Cancer

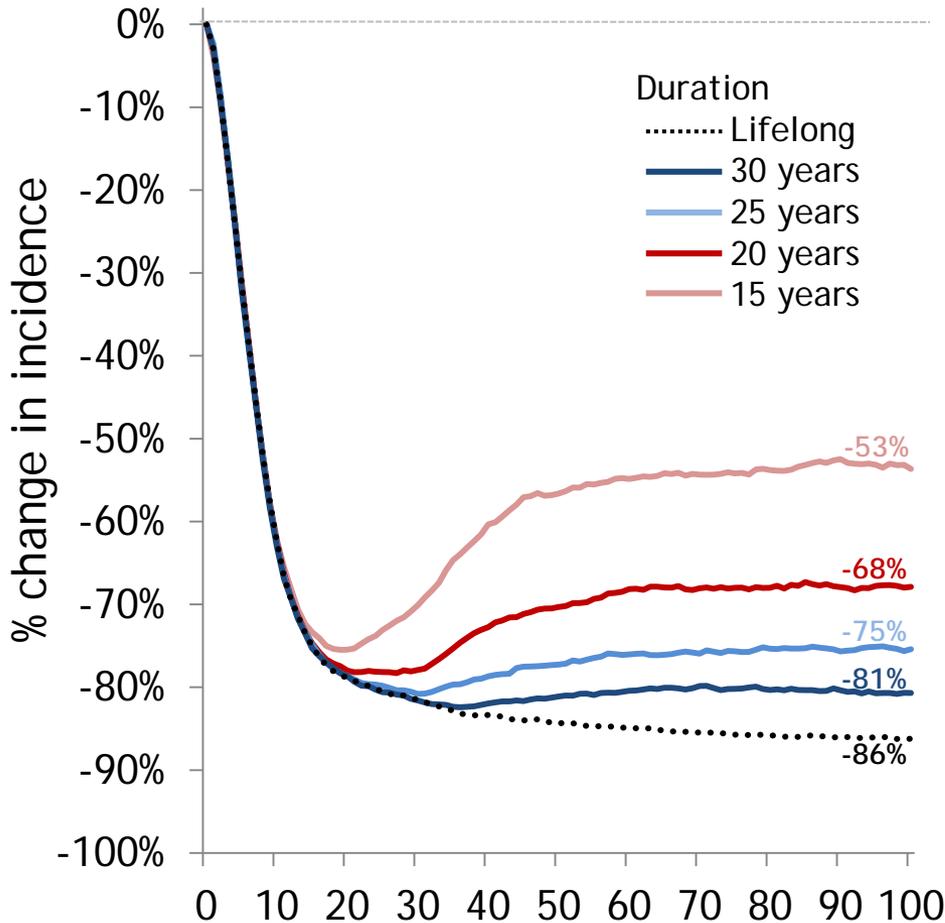


Years since start of vaccination

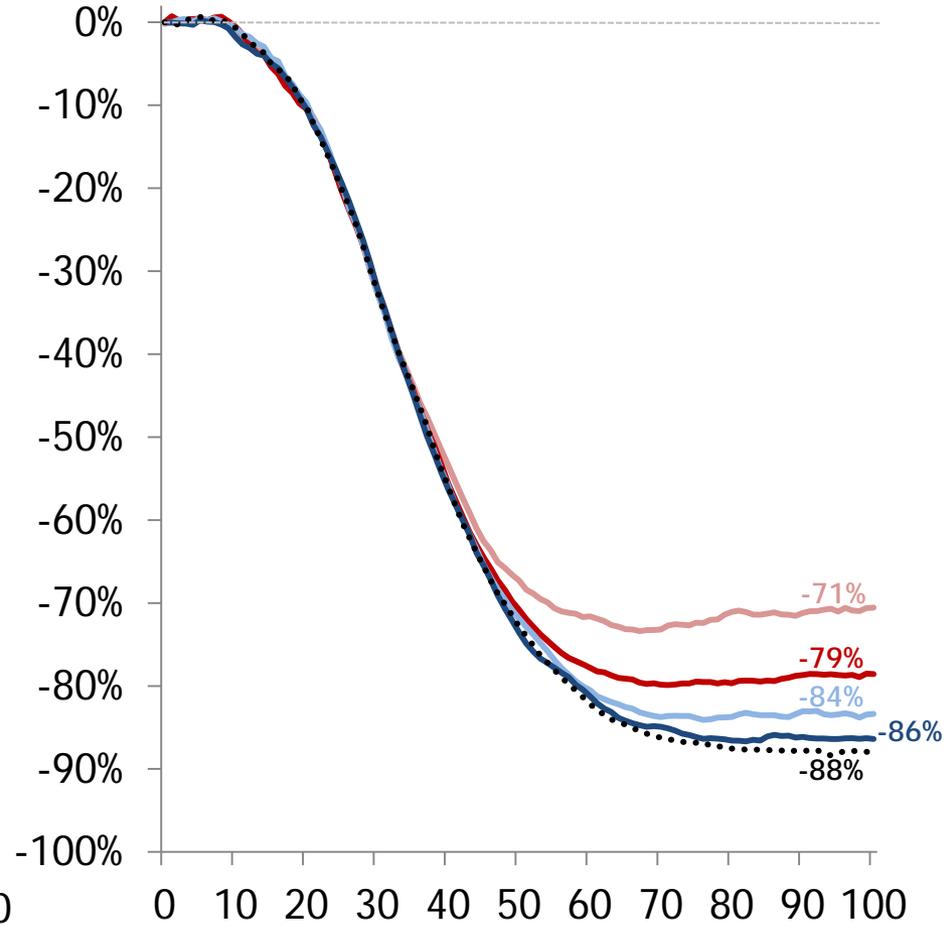
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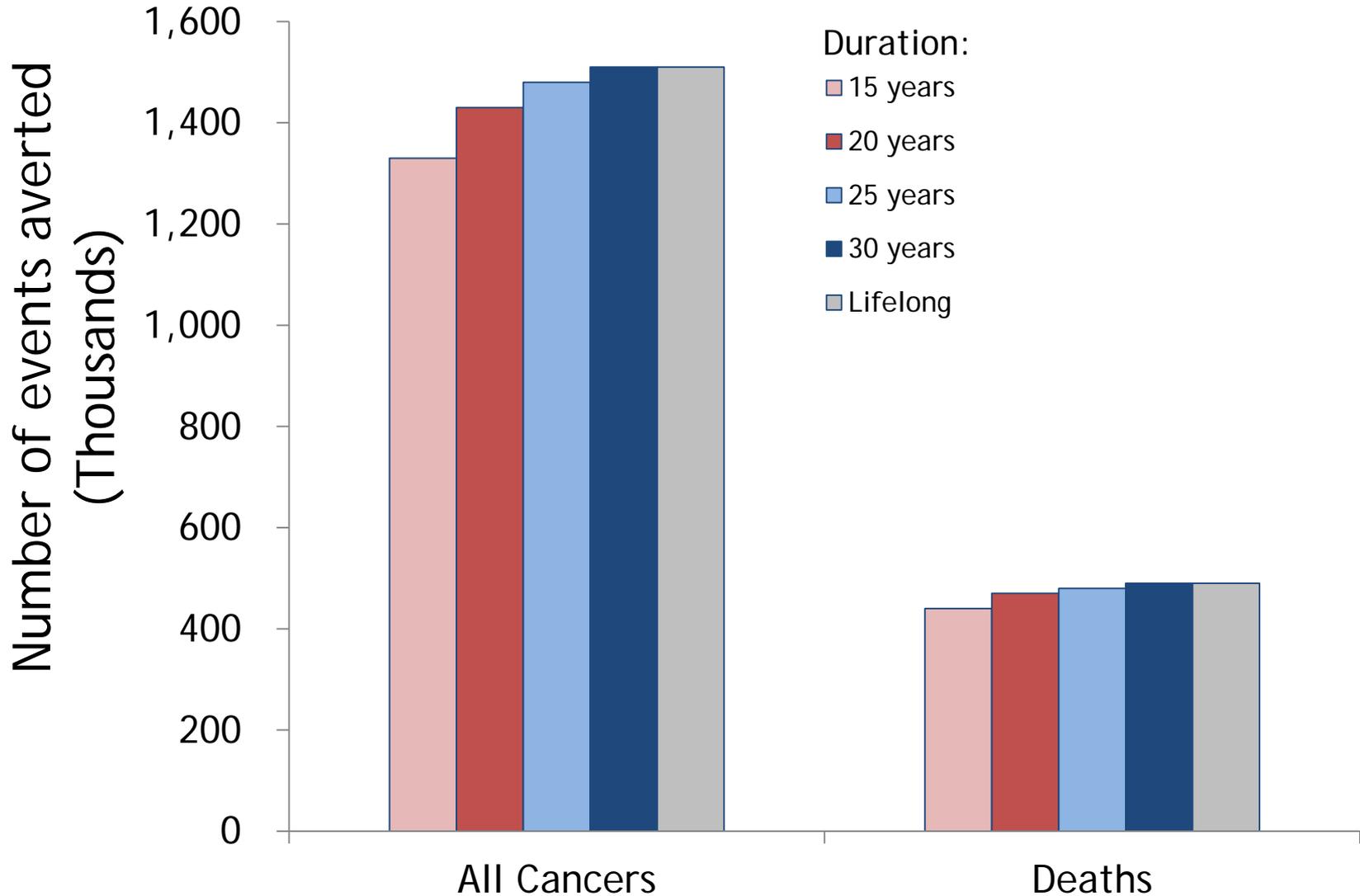


Years since start of vaccination

Health Outcomes Prevented over 100 years

Impact of duration

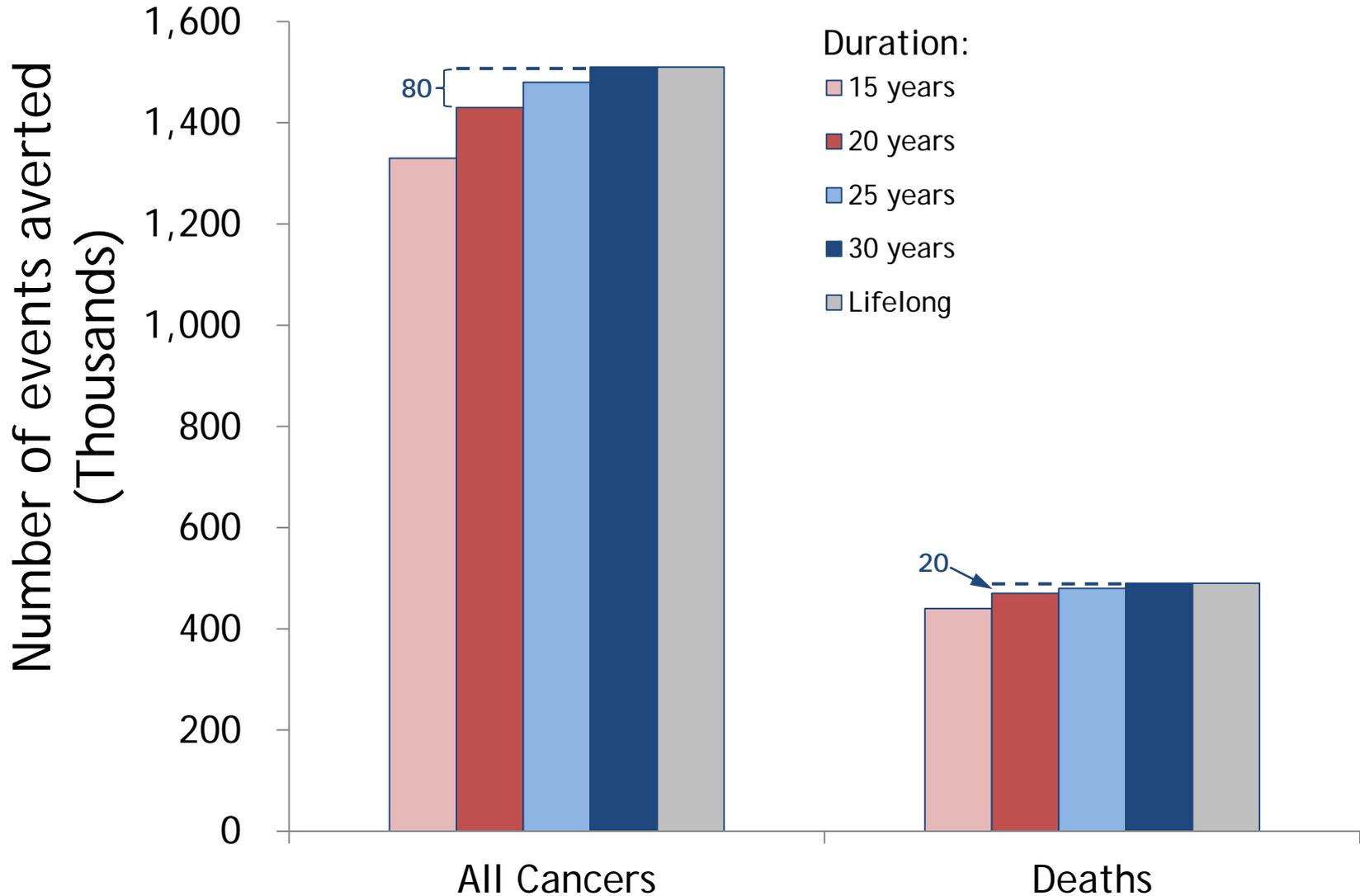
Vaccine Efficacy=95%, Population=300 million, Undiscounted



Health Outcomes Prevented over 100 years

Impact of duration

Vaccine Efficacy=95%, Population=300 million, Undiscounted



Results: Cost-Effectiveness

Key question:

What is the cost-effectiveness of 2-dose and 3-dose vaccination for different assumptions of duration of protection?

Cost-effectiveness

Impact of duration

Vaccine Efficacy=95%; 3-dose Duration=Lifelong; Pop=300 million; Horizon=100 years

	Change in costs (\$ million)	Change in QALY- gained (1,000 QALY)	ICER (\$/QALY-gained)	
			Mean	[80%UI]
<u>2 doses (vs. No vaccination)</u>				
2-dose duration Lifelong	(5,786)	2,209	CS	[CS; 500]
30 years	(5,764)	2,218	CS	[CS; 400]
25 years	(5,157)	2,189	CS	[CS; 700]
20 years	(3,830)	2,134	CS	[CS; 1,500]
15 years	(1,195)	2,018	CS	[CS; 2,600]
<u>3rd dose (vs. 2 doses)</u>				
2-dose duration Lifelong	10,671	0	Dominated	Dominated
30 years	10,355	5	>1million	[209,300; Dominated]
25 years	9,787	32	303,700	[97,800; Dominated]
20 years	8,718	73	118,700	[57,000; 307,500]
15 years	6,463	171	37,700	[19,100; 70,000]

Definitions: 80%UI=10th and 90th percentiles of 50 parameter sets run 20 times each; CS=Cost-saving

Cost-effectiveness

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Results: Sensitivity Analysis Influential Variables

Univariate Sensitivity Analysis

Incremental Cost-effectiveness (\$/QALY-gained)

3-dose Duration=Lifelong; U.S. Vaccination coverage

2-dose duration	2-dose (vs. No vacc.)		3rd dose (vs. 2 doses)	
	Lifelong	20 years	Lifelong	20 years
Reference scenario ^{&}	CS	CS	Dominated	118,700
Vaccination coverage				
5 pp increase	CS	CS	Dominated	Dominated
15 pp increase	CS	CS	Dominated	Dominated
2-dose Efficacy=85%	CS	n/a	144,800	n/a
Screening Program Cotesting	CS	CS	Dominated	96,500
Economic Parameters				
Min Disease Burden	CS	CS	Dominated	141,700
Max Disease Burden	CS	CS	Dominated	53,000
Min Healthcare costs	4,800	5,800	Dominated	122,600
Max Healthcare costs	CS	CS	Dominated	109,200
Time Horizon=30yrs	9,100	9,400	Dominated	Dominated

[&]. Reference scenario: Vaccine Efficacy=95%; Max(Min): All parameters set to their max(min) values.

Predictions: Mean of 50 parameter sets run 20 times each.

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Discussion

Main limitations

- Duration of 2-dose and 3-dose 9-valent vaccine efficacy and future vaccination coverage remain unknown:
 - Varied duration of protection and vaccination coverage
 - Duration of protection and coverage assumptions have an important impact on conclusions
- Screening may change in the coming years:
 - Modeled both cytology-based screening and HPV co-testing
 - Screening method does not impact conclusions

Comparison of results with other studies

- First effectiveness and cost-effectiveness analysis of 2- vs. 3-dose vaccination with the 9-valent vaccine (in the U.S. or elsewhere)
- Conclusions are consistent with 4-valent effectiveness and cost-effectiveness analyses in Canada and the U.K.^[1,2] :
 - 2 doses must protect for more than 20 years for the 3rd dose to be cost-*ineffective*

Summary

Summary

- The incremental health benefits and cost-effectiveness of a 3rd dose of HPV vaccine depend on relative duration of efficacy provided by 2 vs. 3 doses
- **2-dose vaccination** is predicted to reduce HPV-burden of disease substantially and is cost saving if 2-dose protection > 20 years
- **3-dose vaccination** is predicted to have a high cost per QALY gained (greater than \$118,000) compared to 2-dose vaccination, except when 2-dose protection is < 20 years
- **2-dose vaccination** will provide similar population-level health benefits to **3-dose vaccination**:
 - Unless 2 doses provide shorter duration of vaccine protection AND 2-dose schedules do not enable higher vaccination coverage