Economic Evaluation of Vaccination for Prevention of Herpes Zoster and Related Complications

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Conflict of interest statement

Authors have no known conflicts of interest.

Methods: Study questions

- Evaluate the cost-effectiveness of a herpes zoster subunit vaccine (HZ/su) and no vaccination, using healthcare and societal perspectives
- Examine revaccination scenarios with HZ/su
- Compare cost-effectiveness of HZ/su and ZVL

Methods: Interventions

Intervention strategies:

1. Herpes zoster subunit vaccine (HZ/su)
2. Live zoster vaccine (ZVL)
3. No vaccination

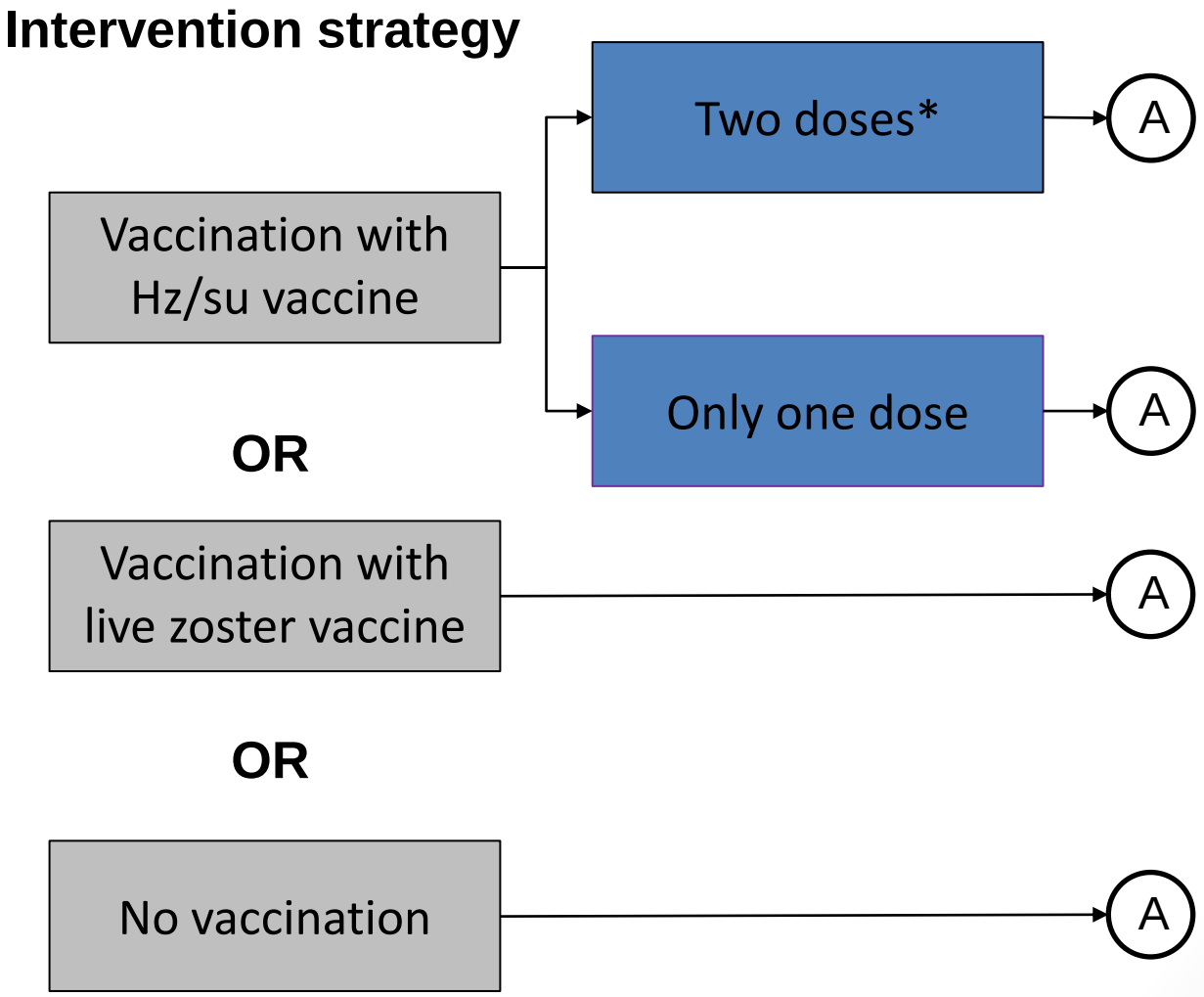
Intervention characteristics:

- 5 age groups: 50-59, 60-69, 70-79, 80-89, 90-99
- Analytic horizon: vaccination age through lifetime
- 100% adherence to 2-dose schedule for HZ/su (base case)

Methods: Economic model

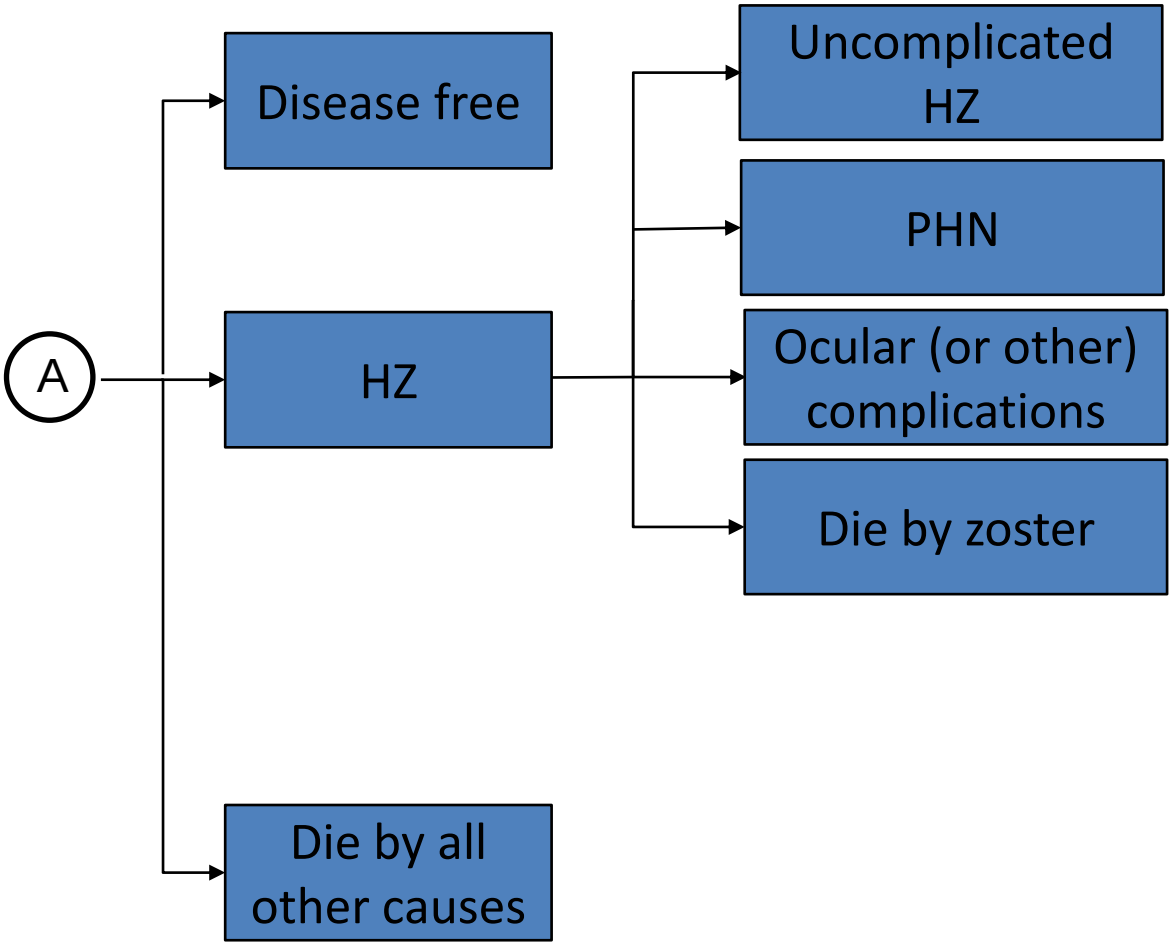
- **Model structure:** state-transition cohort model
- **Primary outcome measure:** incremental cost-effectiveness ratio (ICER)
- **Secondary outcome measures:** Disaggregated costs; disaggregated QALYs; number needed to vaccinate
- **Cycle length:** annual
- **Costing year:** 2016
- **Discount rate:** 3%
- **Model inputs:** published evidence, primary data, expert opinion

Methods: Simulation model



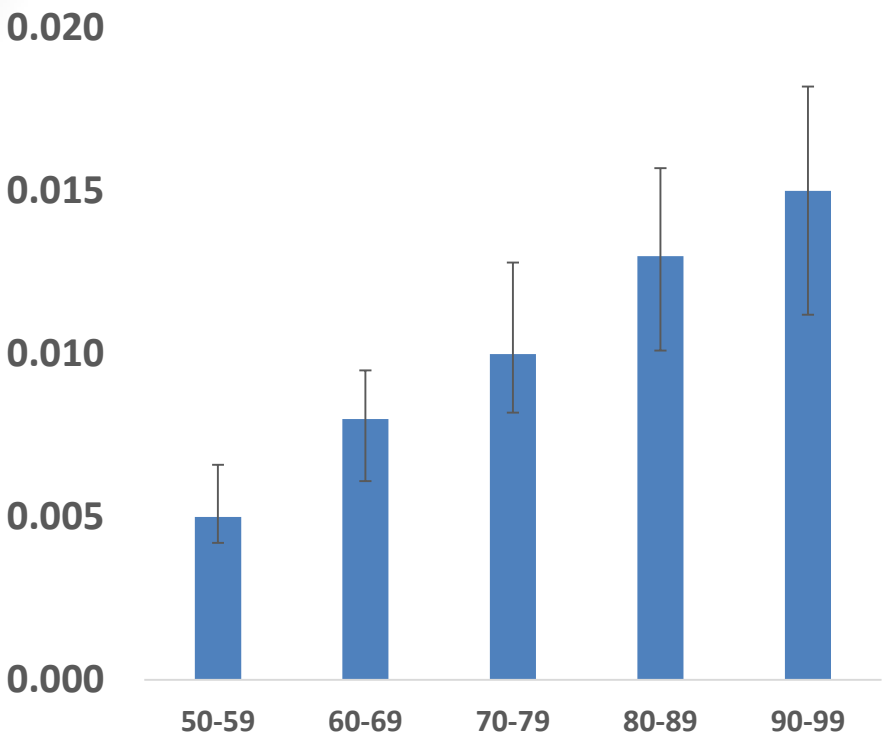
* Base case assumes 100% 2-dose compliance

Methods: Simulation model (2)

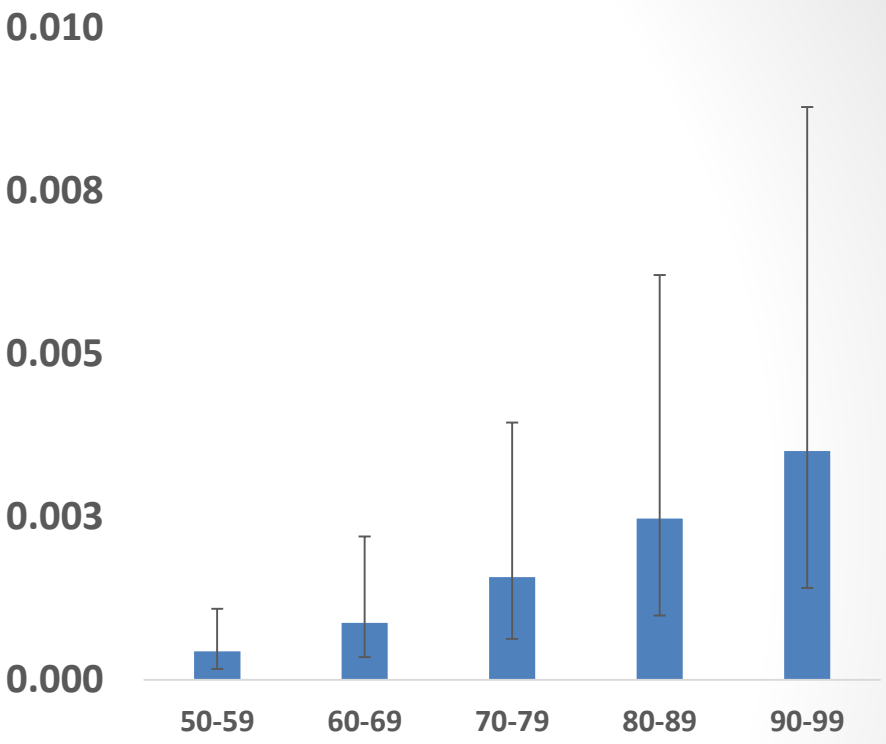


*Simulation model also includes vaccination-related adverse events (injection site reaction, systemic reaction, severe adverse event), recurrent zoster

Methods: Epidemiology



HZ Incidence by Age

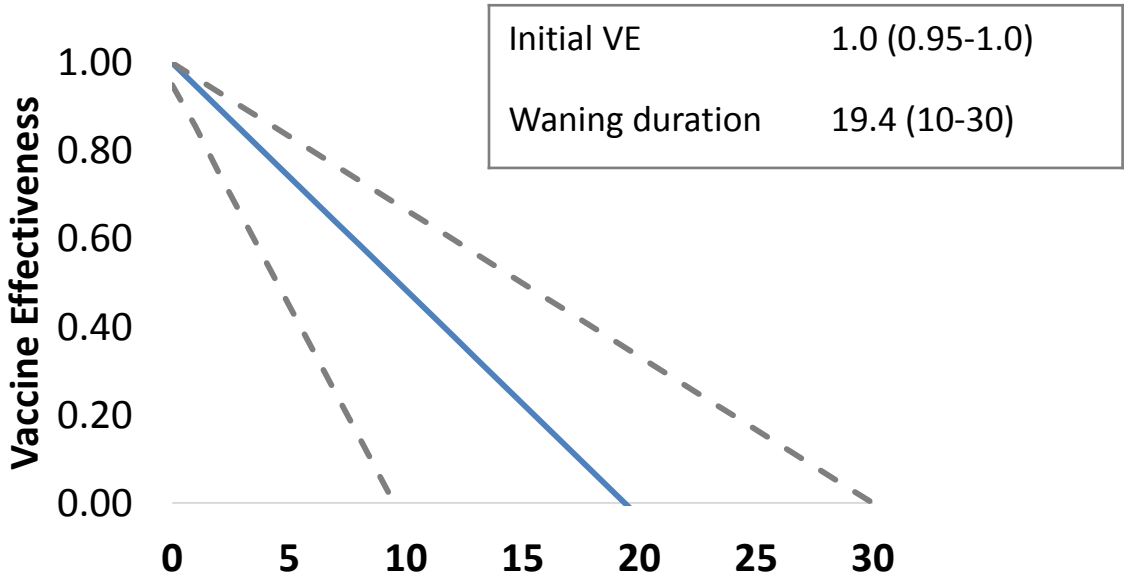


PHN Incidence by Age

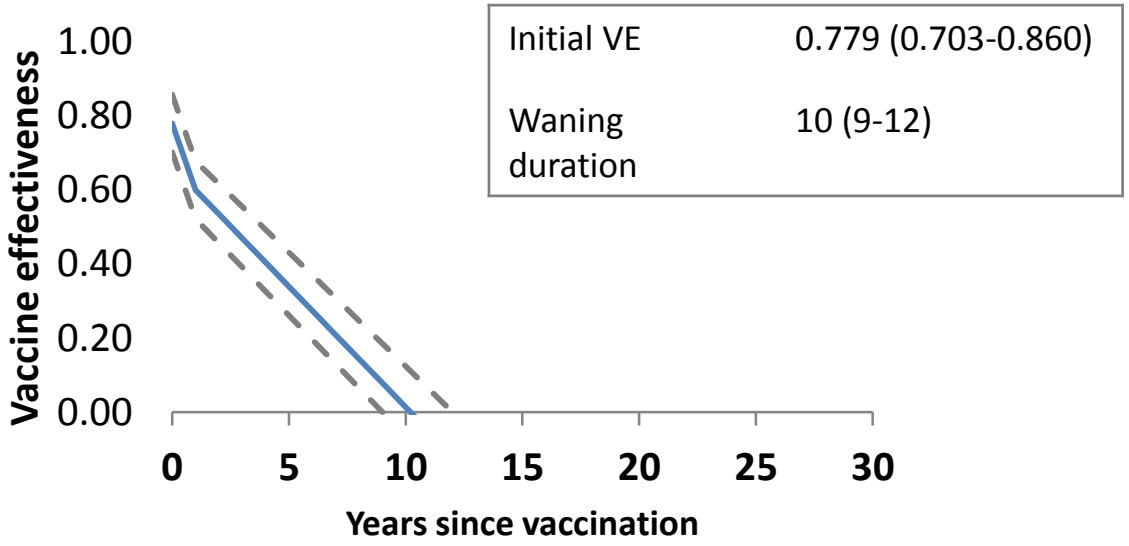
Sources:
HZ Incidence- Leung et al 2011, Insigna et al 2005, Donahue et al 1995, Harvey et al. 2016 (unpublished report)
PHN Incidence- Hope-Simpson 1975, Cerbian-Cuenca et al 2011, Helgason et al 2000, Yawn et al 2007, Gautheir et al 2009, Stein et al 2009, Gialloreti et al 2010, Harvey et al. 2016 (unpublished report)

Vaccine Effectiveness, 60-69 years

HZ/su



ZVL



Methods: Vaccine Effectiveness, HZ/su

Variable	Base value	Range	Source
Initial Year, 2 doses			
Age 50-69	1.00	0.95-1	Cunningham et al 2016, Lal et al 2015
Age 70+	0.97	0.92-1	
Initial Year, 1 dose			
Age 50-69	0.90	0.85-0.95	Unpublished post hoc analysis by GSK from ZOE 50/70
Age 70+	0.69	0.64-0.74	
Waning duration, 2 doses (yrs)			
Age 50-69	19.4	10-30	Cunningham et al 2016, Assumption
Age 70+	18.8	10-30	
Waning duration, 1 dose (yrs)			
Age 50-69	11.0	1-17.5	Assumption
Age 70+	4.0	1-13.4	

Methods: Vaccine Effectiveness, ZVL

Variable	Base value	Range	Source
Initial year			
Age 50	0.781	0.703-0.860	Morrison et al 2015, Oxman et al 2005, Schmader et al 2012, Rohan 2005
Age 60	0.779	0.701-0.857	
Age 70	0.659	0.593-0.725	
Age 80	0.385	0.346-0.423	
Waning duration (yrs)			
Age 50	12	10-15	
Age 60	10	9-12	
Age 70	7	6-8	
Age 80	4	3-5	

*Model assumes additional protection against PHN; protection varies by age

Methods: Additional Inputs

- Direct medical costs
- Productivity losses
- QALY losses
- Vaccination-related costs
- Adverse event costs and QALY losses

Methods: Analysis Plan

- Incremental cost-effectiveness ratio (ICER):

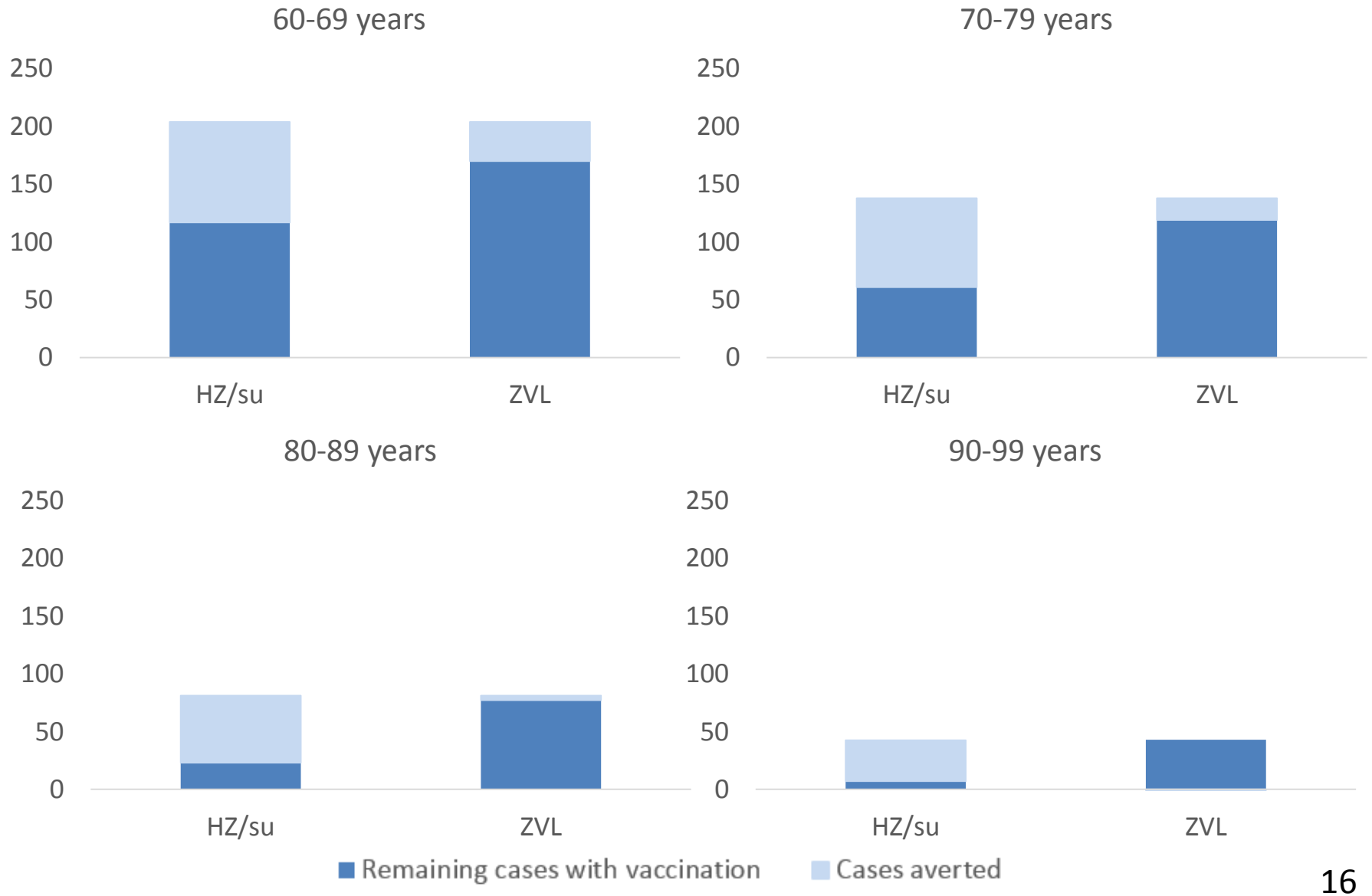
$$\frac{\text{Costs}_{\text{Vaccination}} - \text{Costs}_{\text{No Vaccination}}}{\text{QALYs}_{\text{Vaccination}} - \text{QALYs}_{\text{No Vaccination}}}$$

- Healthcare sector and societal perspectives
- Sensitivity analyses:
  - Probabilistic sensitivity analysis
  - Univariate and multi-way sensitivity analyses
  - Scenario analyses:
    - Revaccination with HZ/su following vaccination with ZVL
    - Preferential recommendation

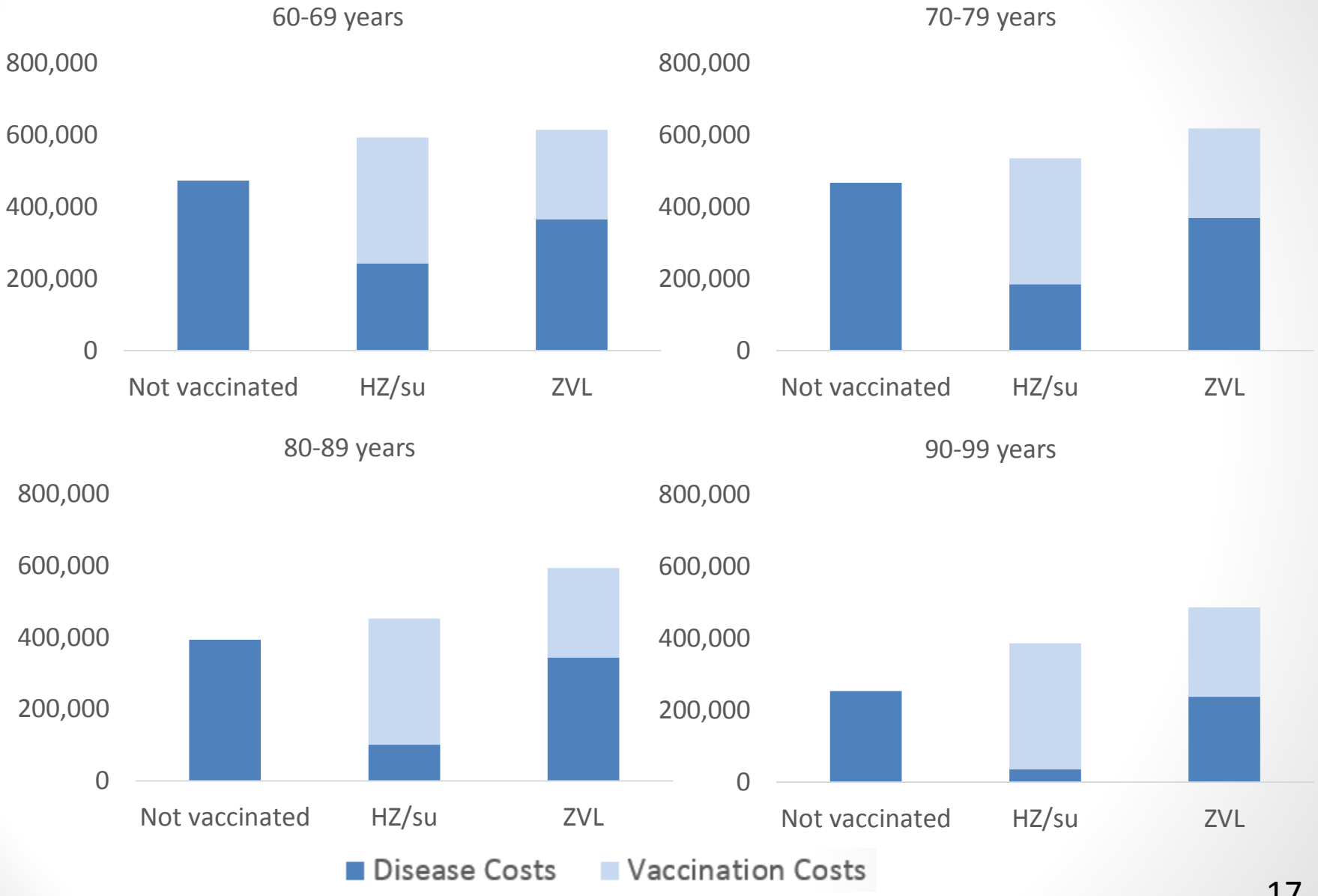
Results: Projected Cases (per 1000)

	No vaccine	Vaccinated-HZ/su	Vaccinated-ZVL
Herpes zoster			
50-59 years	265	186	231
60-69 years	204	117	170
70-79 years	138	61	119
80-89 years	81	23	77
90-99 years	42	7	42
Postherpetic neuralgia (PHN)			
50-59 years	32	27	29
60-69 years	31	21	25
70-79 years	27	13	20
80-89 years	21	6	17
90-99 years	14	2	12

Projected HZ cases and cases averted (per cohort of 1000)



Results: Costs (societal, per 1000)

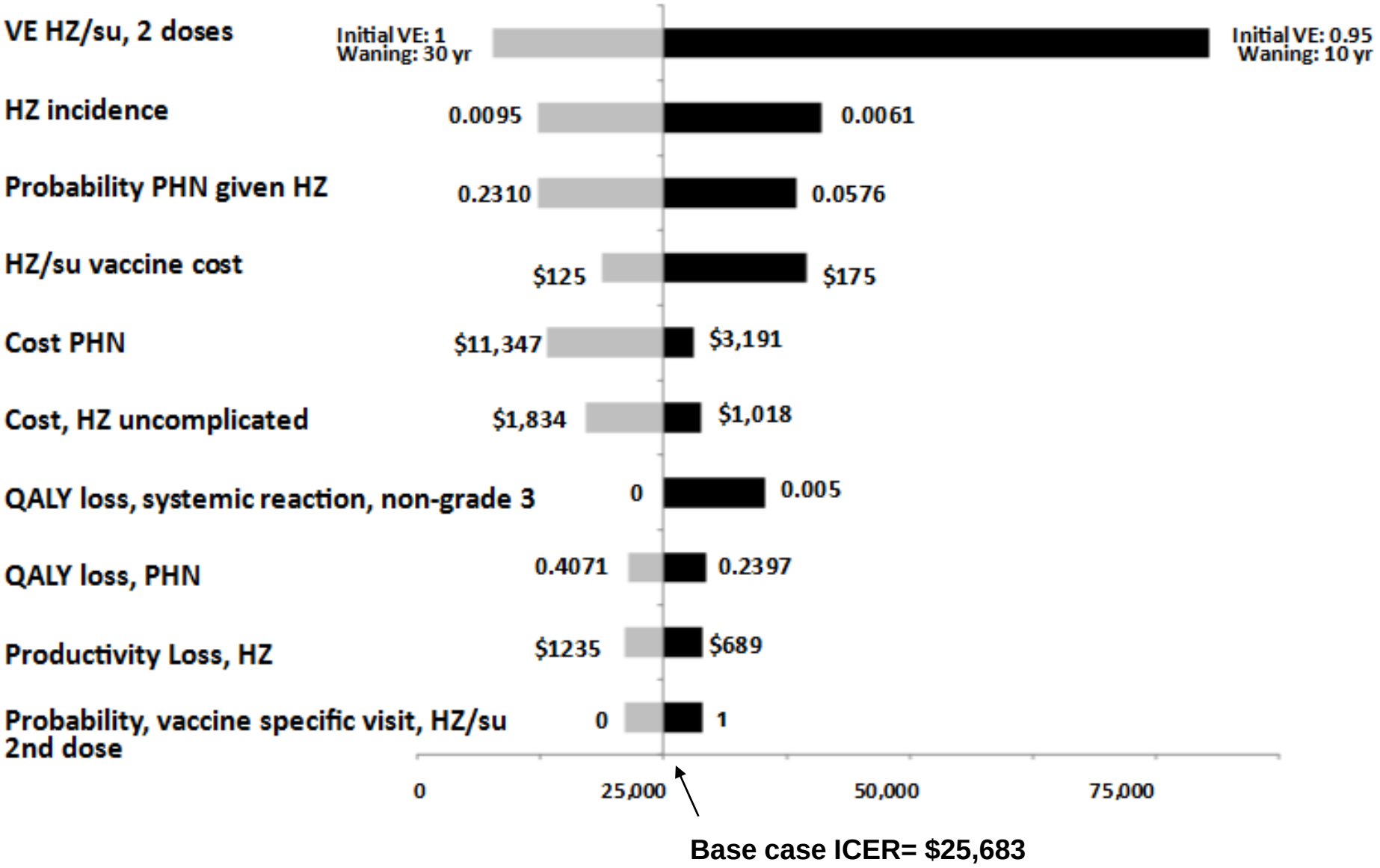


Results: Base Case Analysis, HZ/su vs No Vaccination

Age	Societal Perspective $/QALY
50-59 y	$46,824
60-69 y	$25,683
70-79 y	$11,561
80-89 y	$9,739
90-99 y	$27,310
50+ y	$30,797

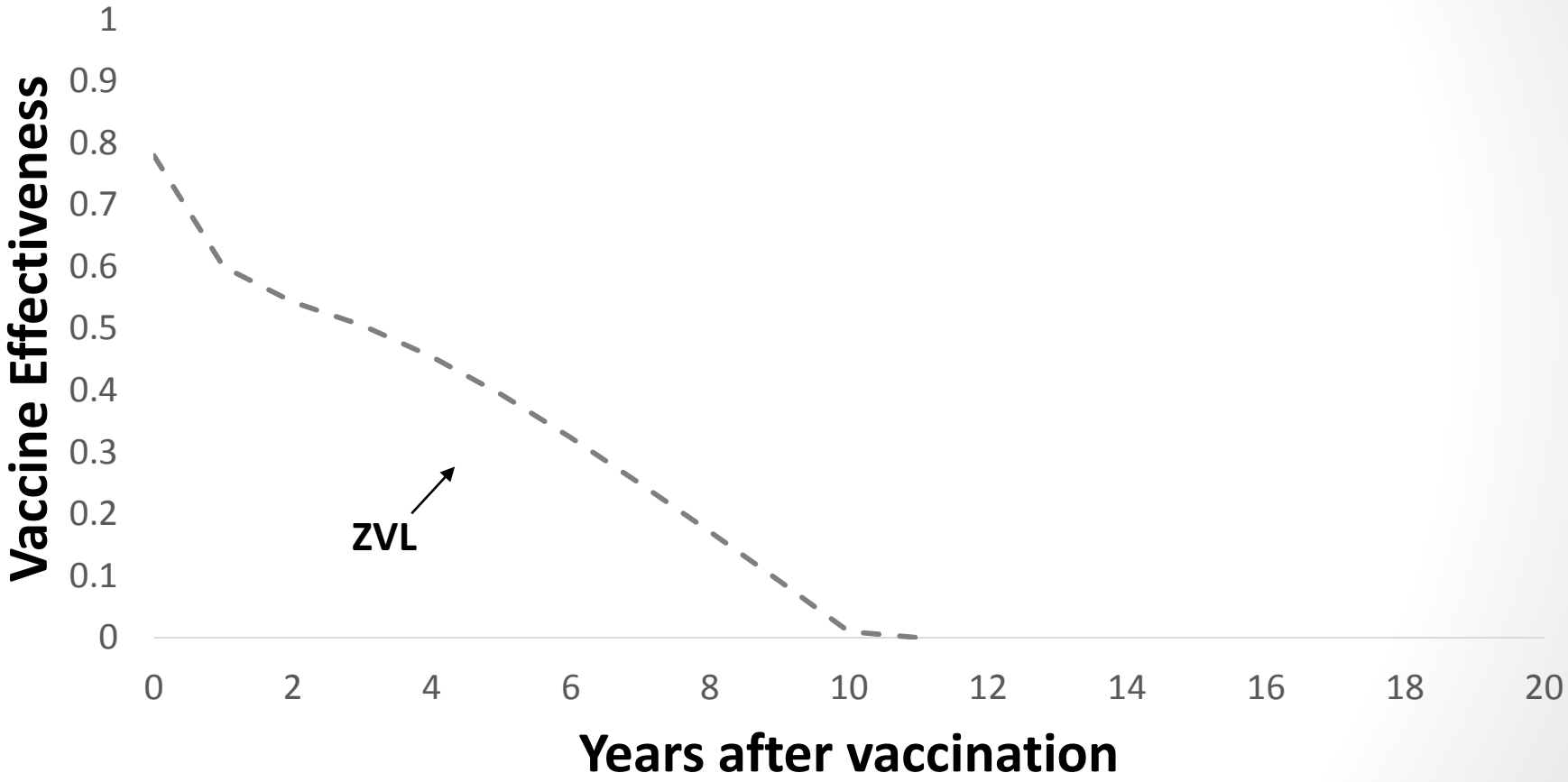
Sensitivity Analyses

One-way Sensitivity Analyses (60-69y)



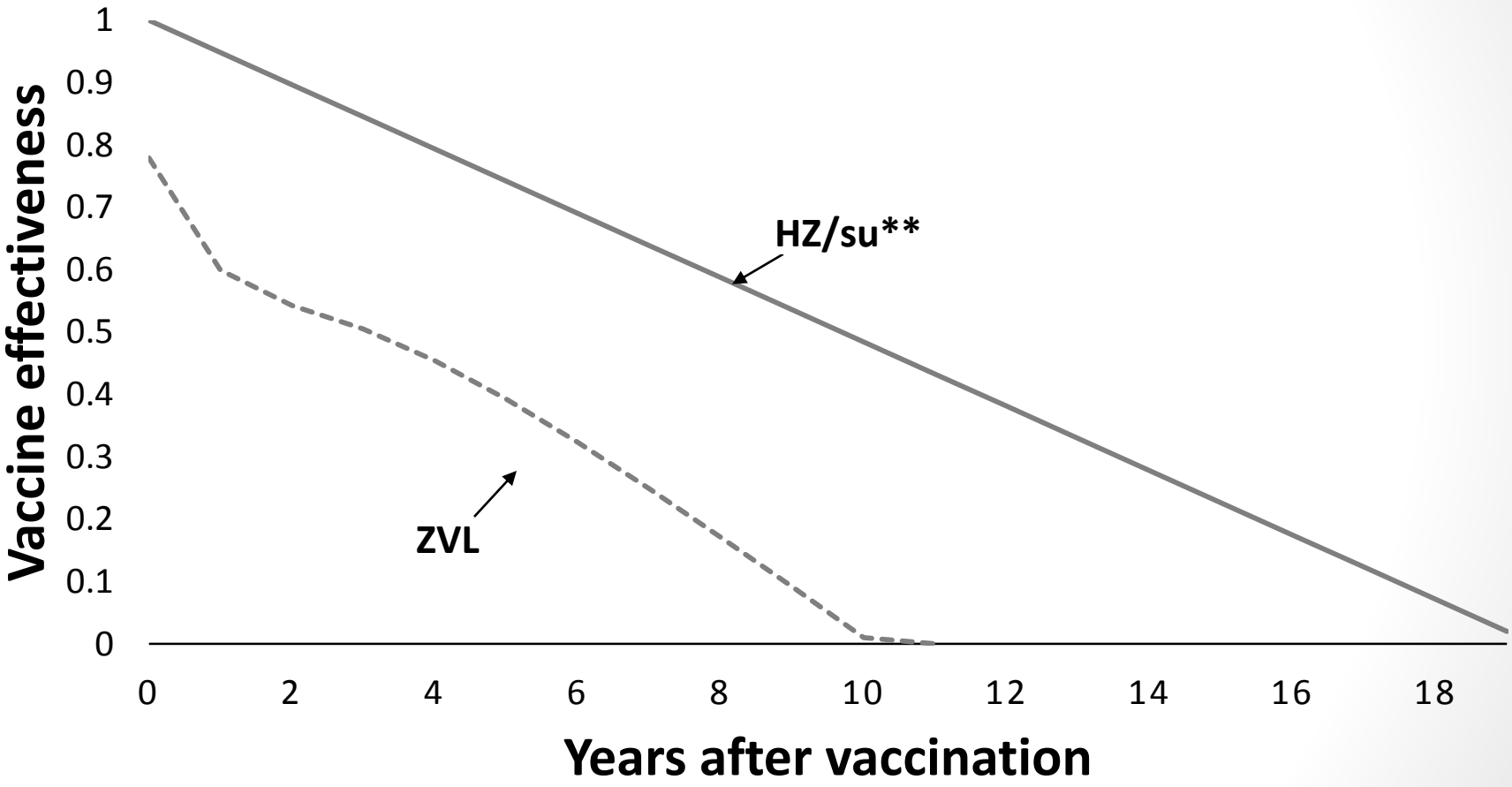
Scenario Analyses: Revaccination

Revaccination – 8wks [Immediately*]
VE Assumptions (60-69y)



* Immediate revaccination with HZ/su simulated as proxy for 8-week interval

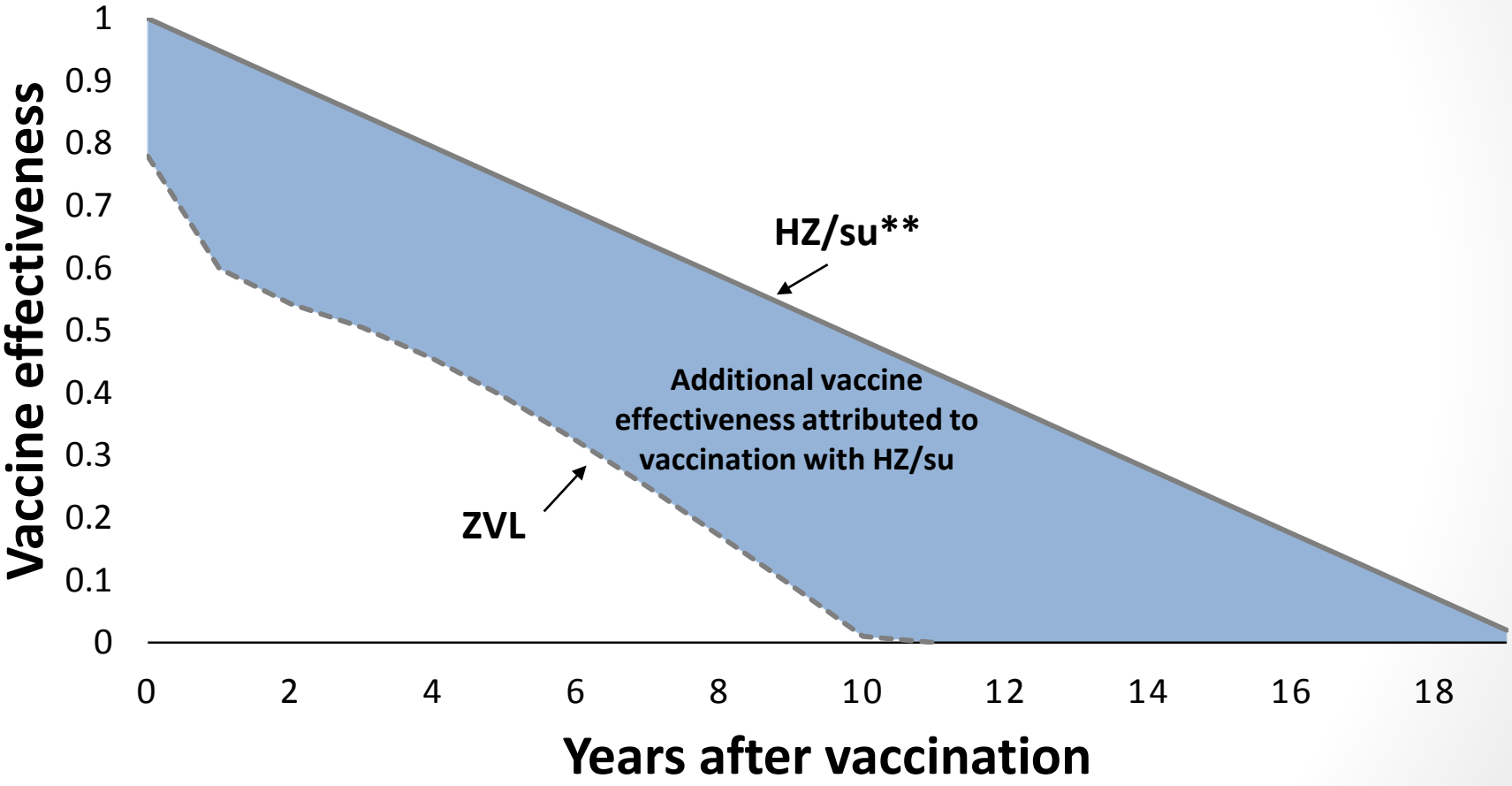
Revaccination – 8wks [Immediately*]
VE Assumptions (60-69y)



* Immediate revaccination with HZ/su simulated as proxy for 8-week interval

**2- dose efficacy

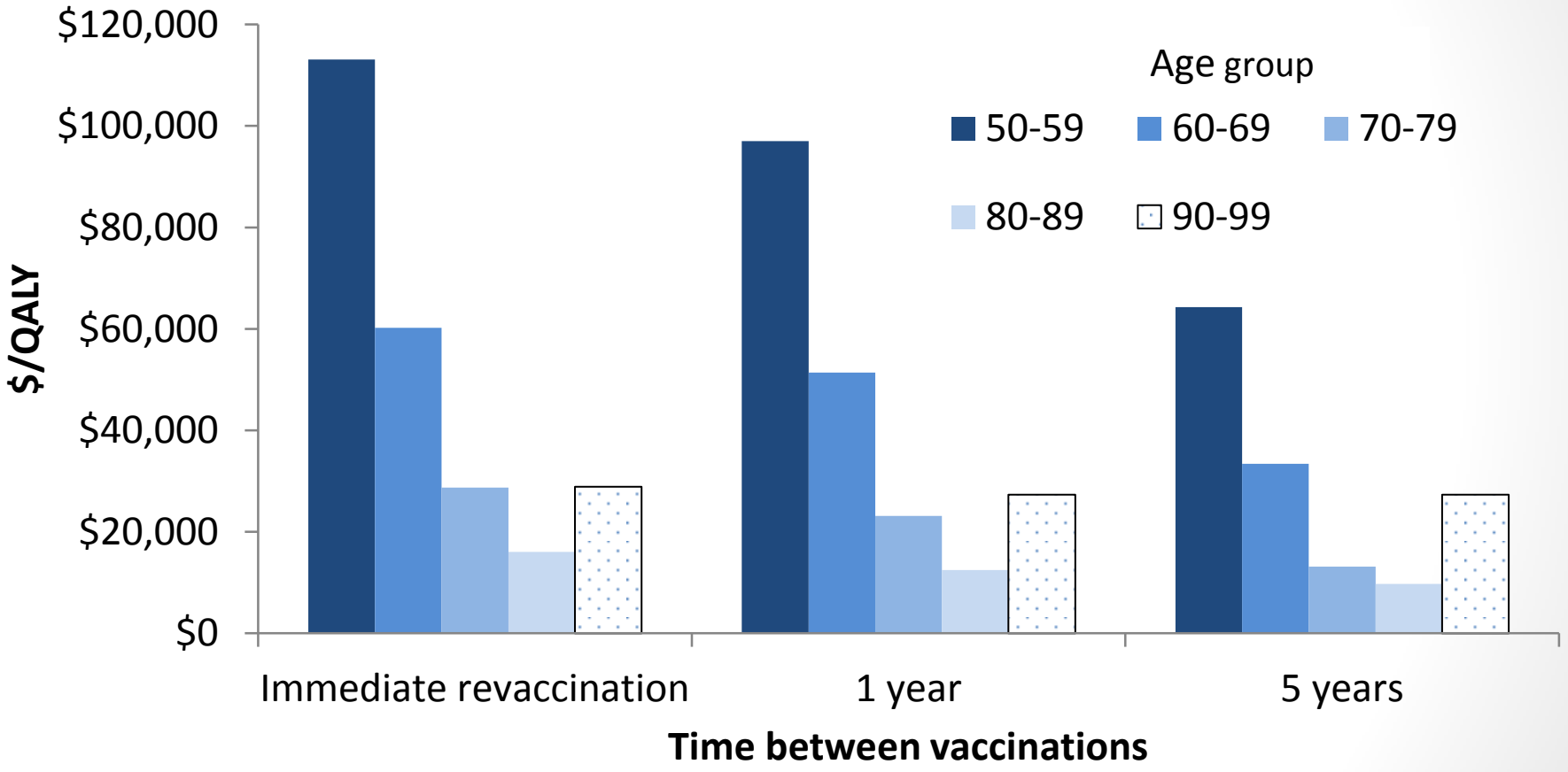
Revaccination – 8wks [Immediately*] VE Assumptions (60-69y)



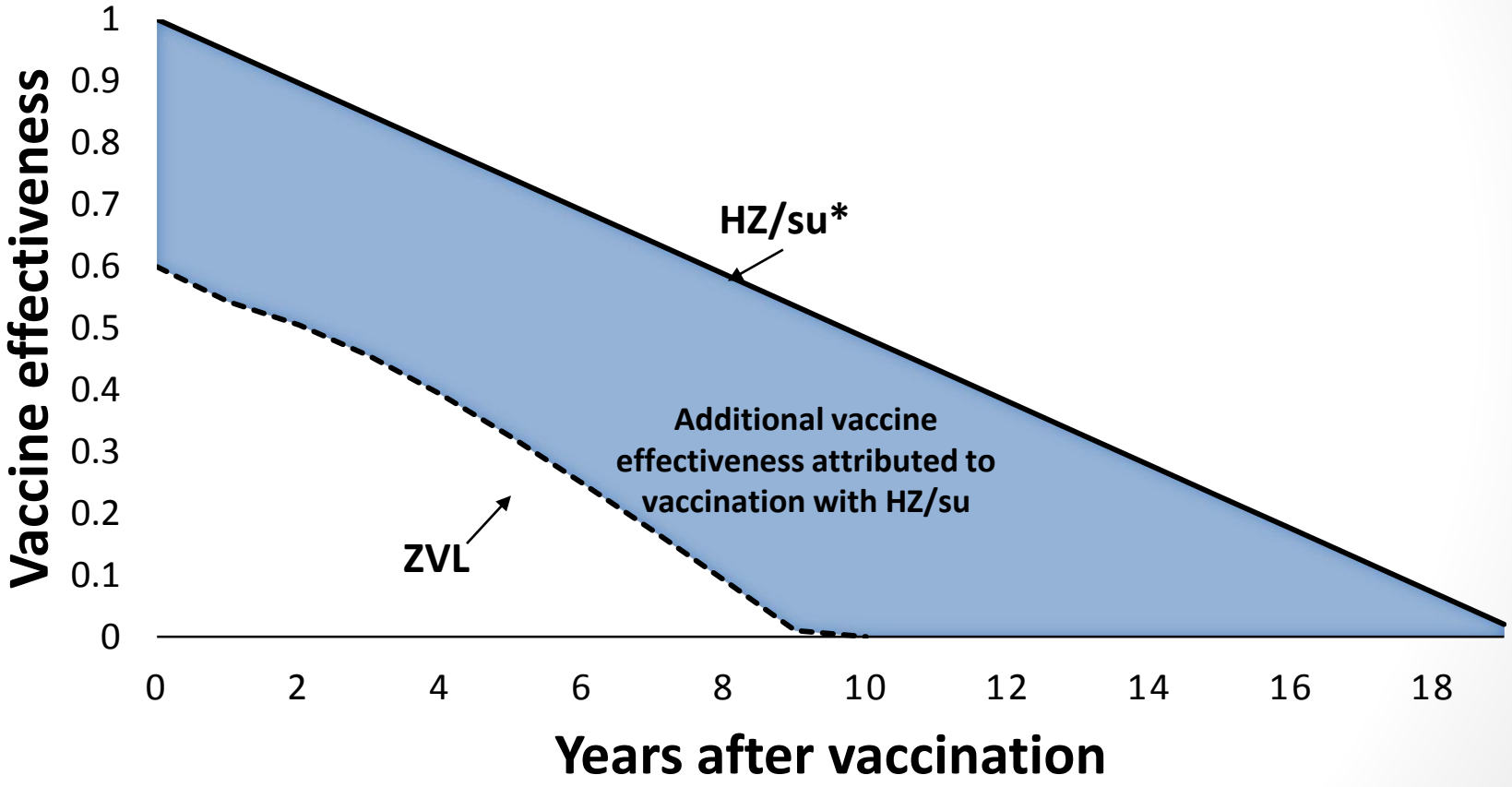
* Immediate revaccination with HZ/su simulated as proxy for 8-week interval

**2-dose efficacy

Results:
Revaccination Scenario Analysis

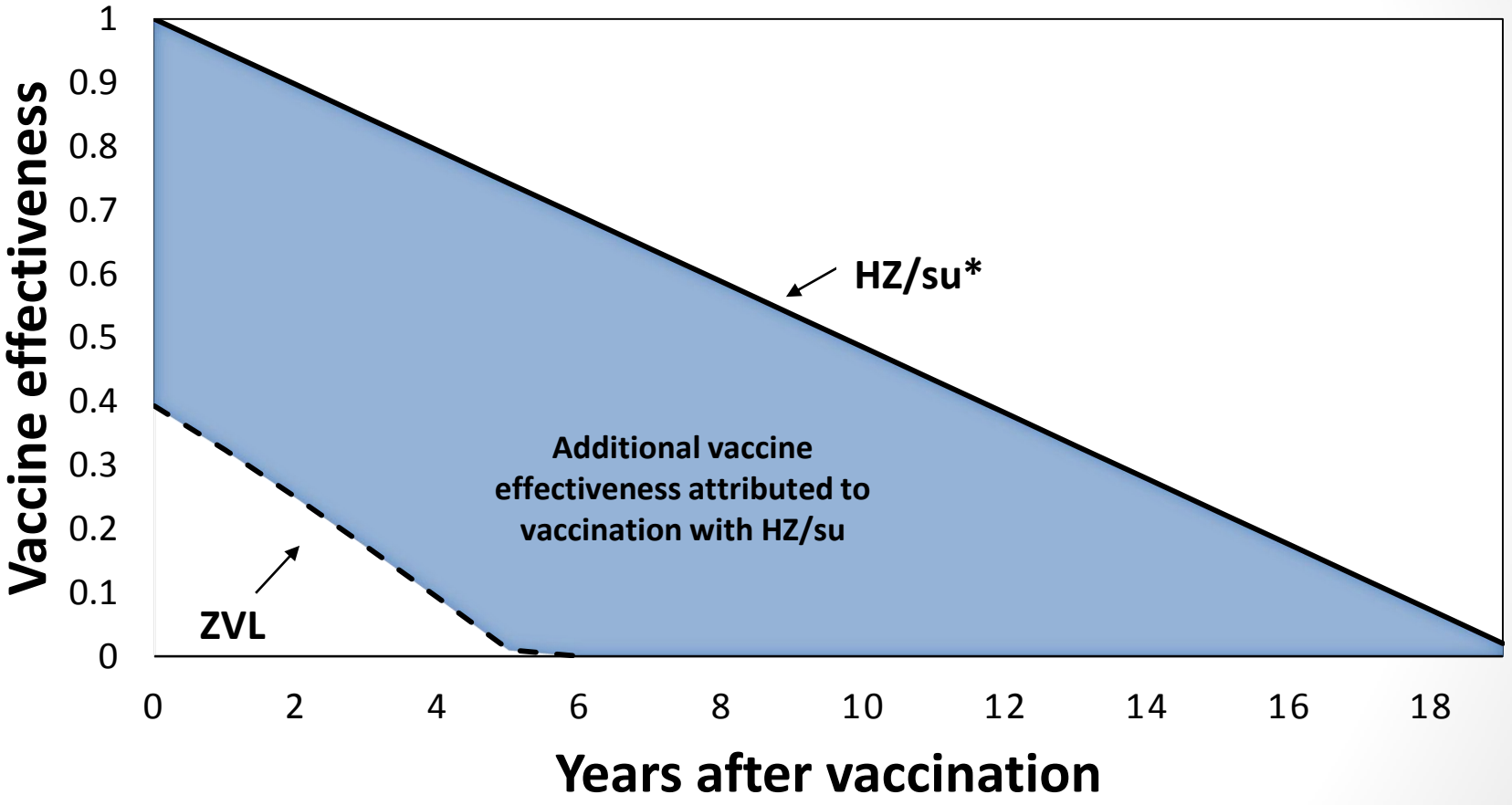


Revaccination - 1 year
VE Assumptions (60-69y)



*2-dose efficacy

Revaccination - 5 years
VE Assumptions (60-69y)



*2-dose efficacy

Scenario Analysis: HZ/su and ZVL Compared to No Vaccination

Terminology: Dominance

Cost and health outcomes, per 1000

Age	Strategy	Costs	QALYs	Incr. Costs	Incr. QALYs	$/QALY
60-69 years	Not vaccinated	$473,485	12138.8			
	Vaccinated- HZ/su	$593,527	12143.5	$120,042	4.67	$25,683
	Vaccinated- ZVL	$614,476	12141.4	$20,949	-2.11	Dominated

Comparing Results Across Models
Base Case Estimates, 60-69 yrs ($/QALY)

	CDC model Societal Perspective
HZ/su*	$26,000
ZVL*	$55,000

*Compared to no vaccination

Comparing Results Across Models
Base Case Estimates, 60-69 yrs ($/QALY)

	Le et al. model Societal Perspective	CDC model Societal Perspective
HZ/su*	$30,000	$26,000
ZVL*	$67,000	$55,000

*Compared to no vaccination

Comparing Results Across Models
Base Case Estimates, 60+ yrs ($/QALY)

	Le et al. model Societal Perspective	CDC model Societal Perspective	CDC model Healthcare Perspective	GSK model Healthcare + Prod. Loss	Merck model Healthcare + Prod. Loss
HZ/su*	$30,000**	$19,000	$29,000	$12,000	$107,000
ZVL*	$67,000**	$80,000	$89,000	$120,000	$83,000

*Compared to no vaccination

**Vaccinated at age 60

Uncertainty Analyses

Uncertainty Analysis: PSA
100% 2-dose completion, $/QALY (95% CI)

Age	HZ/su vs No vaccination	ZVL vs No vaccination
50-59 y	**$46,824** (CS*- 133,244)	**$85,026** (65,441 - 118,116)
60-69 y	**$25,683** (CS - 74,875)	**$54,920** (39,090 - 78,879)
70-79 y	**$11,561** (CS - 39,954)	**$58,703** (44,556 - 81,773)
80-89 y	**$9,739** (CS - 29,570)	**$137,631** (110,262 - 184,955)
90-99 y	**$27,310** (14,718 - 43,534)	**$364,224** (285,501 - 494,097)

*Cost saving

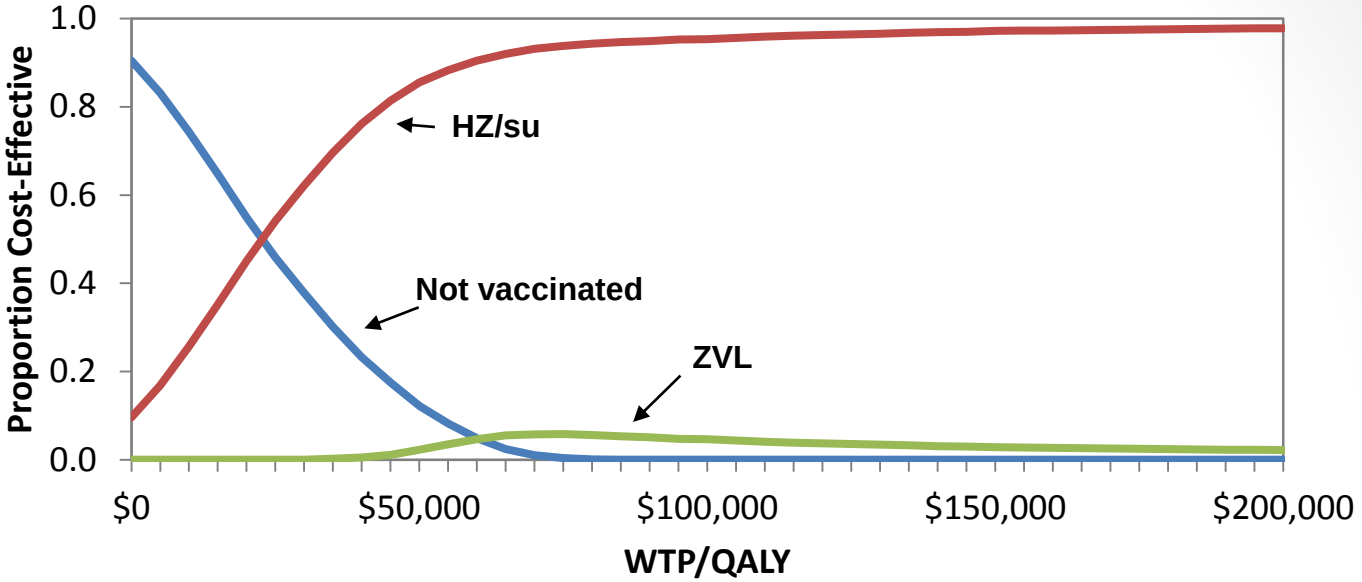
Uncertainty Analysis: PSA
73.5% 2-dose completion, $/QALY (95% CI)

Age	HZ/su* 100% 2-dose completion	HZ/su * 73.5% 2-dose completion	ZVL*
50-59 y	**$46,824** (CS**- 133,244)	**$40,662** (CS* - 90,254)	**$85,026** (65,441 - 118,116)
60-69 y	**$25,683** (CS - 74,875)	**$21,773** (CS – 52,548)	**$54,920** (39,090 - 78,879)
70-79 y	**$11,561** (CS - 39,954)	**$14,208** (CS - 37,978)	**$58,703** (44,556 - 81,773)
80-89 y	**$9,739** (CS - 29,570)	**$12,119** (CS – 30,208)	**$137,631** (110,262 - 184,955)
90-99 y	**$27,310** (14,718 - 43,534)	**$27,669** (9,992 – 44,364)	**$364,224** (285,501 - 494,097)

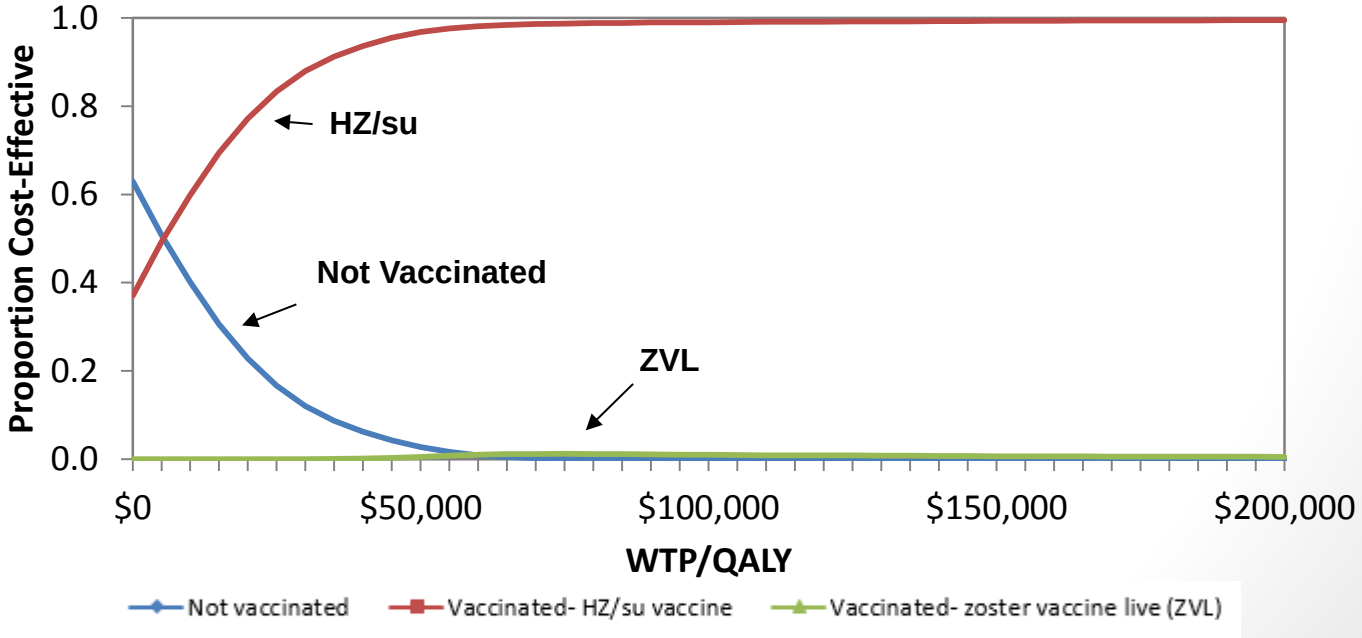
* vs no vaccination; **Cost saving

Results: C/E Acceptability Curves, 60-69 years

100% 2-dose completion



73.5% 2-dose completion



Multi-Way Sensitivity Analysis: HZ/su 2-Dose Completion Rate, 1-dose Vaccine Waning Duration, Initial Efficacy

Age	1-dose lower bound initial VE; Waning duration= 1 yr		
	2-dose completion rate		
	20%	50%	100%
60-69 y	$46,171	$35,450	$25,683
70-79 y	$36,194	$22,681	$11,561
80-89 y	$41,959	$22,872	$9,739
90-99 y	$61,059	$40,938	$27,310

Multi-Way Sensitivity Analysis: HZ/su 2-Dose Completion Rate, Vaccine Waning Duration, Initial Efficacy

Age	1-dose initial VE=0.85; waning 1 y 2-dose initial VE=0.95; waning 10 y			1-dose initial VE=0.95; waning 17.5 y 2-dose initial VE=1.0; waning 30 y		
	2-dose completion rate			2-dose completion rate		
	20%	50%	100%	20%	50%	100%
60-69 y	$64,171	$54,920*	$569,324**	Cost Saving	$403	$7,902
Age	**1-dose initial VE=0.64; waning 1 y 2-dose initial VE=0.92; waning 10 y**			**1-dose initial VE=0.74; waning 13.4 y 2-dose initial VE=1.0; waning 30 y**		
70-79 y	$51,493	$49,865	$48,050***	Cost Saving	Cost Saving	Cost Saving
80-89 y	$57,244	$44,879	$34,505	Cost Saving	Cost Saving	$2,212
90-99 y	$70,968	$54,681	$42,465	$6,902	$13,564	$21,971

* ZVL dominates HZ/su; ** No dominant strategy; *** HZ/su dominates ZVL by extended dominance

Limitations

- Adverse event data
- Healthcare utilization associated with adverse events
- Long-term effectiveness of vaccination
- Proportion of individuals completing 2-dose series
- Healthcare utilization associated with 2nd dose

Summary

- Results vary by age at vaccination
- Most sensitive to changes in:
  - Duration of VE
  - Incidence of HZ, PHN
  - Cost of HZ, PHN episode
- Differences across models
  - Time costs
  - Incidence of PHN by age
  - Vaccine effectiveness
  - 2-dose completion