Overview of two economic models that assess the cost-effectiveness of herpes zoster vaccinations

Advisory Committee on Immunization Practices

June 21, 2017

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Federal contractor for CDC/NCIRD/ISD

Acknowledgements

- This is a presentation of work that was conducted outside of CDC, by two modeling teams from GSK and Merck
  - GlaxoSmithKline (GSK) model team
    - Desmond Curran, Desirée Van Oorschot, Philip O. Buck, Brandon J. Patterson, Bruce Y Lee, Barbara P. Yawn, Katherine A. Hicks and Justin Carrico
  - Merck model team
    - Kelly D. Johnson, Thomas Weiss, Jonathan Graham, Zinan Yi
- CDC and ACIP contributors and reviewers
  - Kathleen Dooling and Rafael Harpaz of CDC/NCIRD/DVD
  - Herpes zoster ACIP workgroup
  - Economists at CDC and colleagues NCIRD/ISD

Views and opinions expressed in this presentation are the authors and do not necessarily represent the views and opinions of the Centers for Disease Control and Prevention.

Conflicts of Interest Statements

- Andrew Leidner: None.
- GSK team
  - Desmond Curran, Desirée Van Oorschot, Philip O. Buck, and Brandon J. Patterson are employees of the GSK group of companies. Desmond Curran, Philip O. Buck, and Brandon J. Patterson hold shares in the GSK group of companies as part of their employee remuneration.
  - Bruce Y. Lee is an employee of John Hopkins University and received fees from the GSK group of companies for this study.
  - Barbara P. Yawn is an employee of the University of Minnesota and received fees from Merck for advisory boards and presentations and from the GSK group of companies for advisory boards and health outcomes studies.
  - Katherine A. Hicks and Justin Carrico are employees of RTI Health Solutions and received research funding for this study from the GSK group of companies.
- Merck team
  - Kelly D. Johnson and Thomas Weiss are employees of Merck & Co., Inc.
  - Merck & Co., Inc. developed and markets the zoster live attenuated vaccine.
  - Jonathan Graham and Zinan Yi (and/or their institutions) received research funding from Merck & Co., Inc., to develop the cost-effectiveness model and for other research studies.

Outline

- Introduction
  - What is a cost-effectiveness ratio (CER)?
  - What are model assumptions and parameters?
- Cost-effectiveness model background and base case results
- Understanding differences in base case results
  - Model assumptions
    - Initial vaccine efficacy*, waning of immunity*, vaccine price
  - Sensitivity analyses comparing the GSK and Merck models
- Overall cost-effectiveness results
- Summary
  - Limitations

* Highly influential parameters regarding differences across models

Introduction

- My objective in this presentation is to describe two cost-effectiveness models, which were developed by two different teams, Merck and GSK
  - Each of these models was described in a report submitted to the ACIP HZ work group as well as in a presentation given to the ACIP HZ work group
  - Both reports went through the CDC economic review following the ACIP Guidance for Health Economics Studies
  - Earlier draft of these slides circulated to Merck and GSK for review

- Cost-effectiveness analysis by CDC team is forthcoming in October

Cost-effectiveness

What is a cost-effectiveness ratio (CER)?

- Cost-effectiveness ratio (CER)
  - An estimated cost per health outcome gained
  - Can be considered a price paid per unit of health gained
    - Outcomes considered in this presentation are quality-adjusted life-years (QALYs)
      - E.g., CER = $/QALY

$$\frac{\text{Costs}_{\text{Vaccination}} - \text{Costs}_{\text{NoVaccination}}}{\text{Outcomes}_{\text{Vaccination}} - \text{Outcomes}_{\text{NoVaccination}}} = \frac{\text{Change in costs}}{\text{Change in outcomes}} = \$/\text{Outcome}$$

- CERs always compare 2 potential strategies
  - E.g., vaccination vs. no vaccination

Cost-effectiveness

What are model assumptions and parameters?

- The CER is the result of calculations based on several assumptions, or parameters, or inputs
  - Parameters can include: intervention (i.e., vaccine) effectiveness, costs of intervention, costs of disease outcomes, and many others
  - Availability of relevant data varies by parameter

- If $CER_A > CER_B$ then intervention A is *less* cost-effective than B

$$\frac{Costs_{Vaccination} - Costs_{NoVaccination}}{Outcomes_{Vaccination} - Outcomes_{NoVaccination}} = \$/Outcome$$

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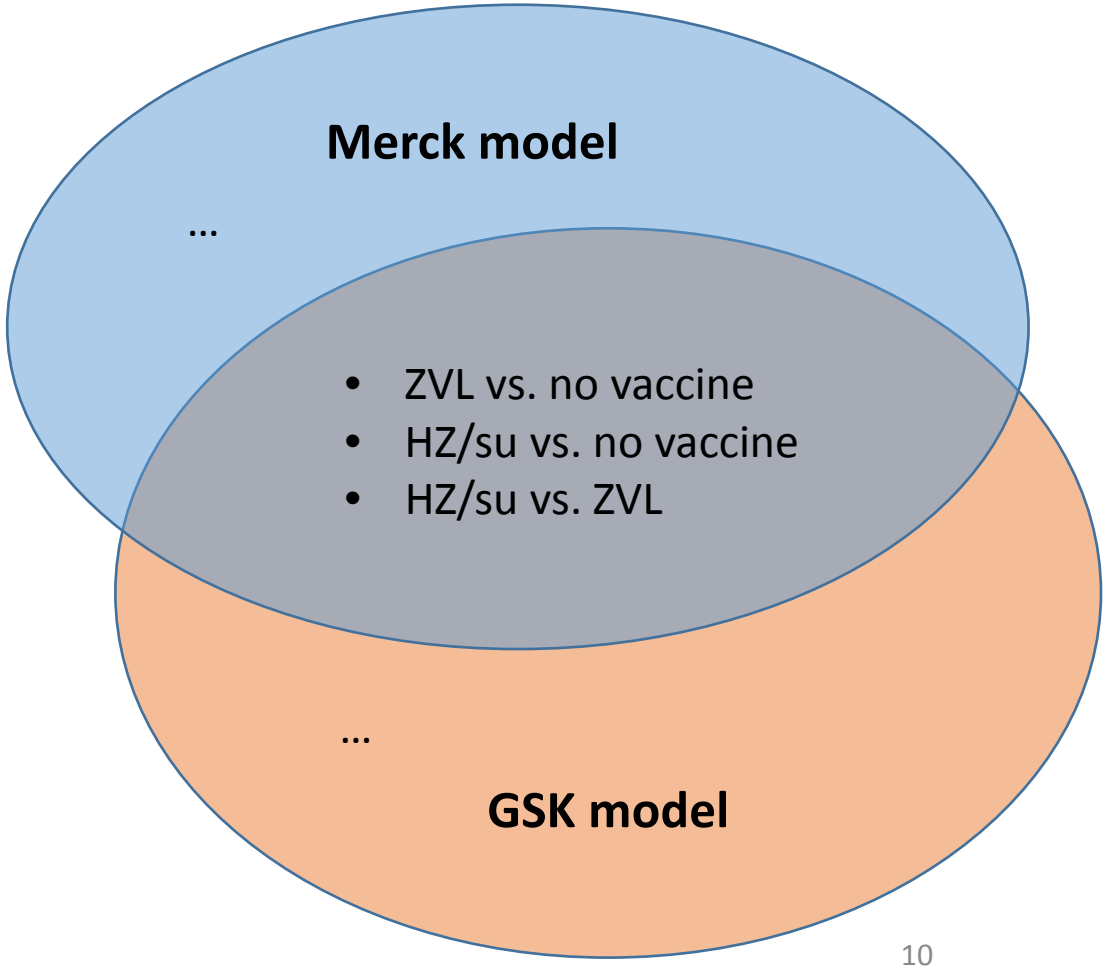
Cost-effectiveness Models
Background

- Current vaccine licensed and recommended
  - Zoster live attenuated vaccine (ZVL or Zostavax) by Merck
  - 1 dose
  - Vaccine received by 20-25 million persons
- Candidate vaccine
  - Herpes zoster subunit vaccine (HZ/su or Shingrix) by GSK
  - 2 doses
- Cost-effectiveness models
  - GSK model and Merck model
  - CDC model (forthcoming)

Cost-effectiveness Models

Research statements

- GSK model and Merck model, cost-effectiveness research objectives
  - Adults 60+ years who have never received a vaccine for HZ
    - ZVL vs. no vaccine
    - HZ/su vs. no vaccine
    - HZ/su vs. ZVL



- Both models contain several additional sub-analyses

Base Case Cost-effectiveness
GSK model & Merck model

- All scenarios among 60+ year olds

	$/QALY	
Model	ZVL vs. no vaccine	HZ/su vs. no vaccine
GSK	$120,000	$12,000
Merck	$125,000	$74,000

Base Case Cost-effectiveness

GSK model & Merck model

- All scenarios among 60+ year olds

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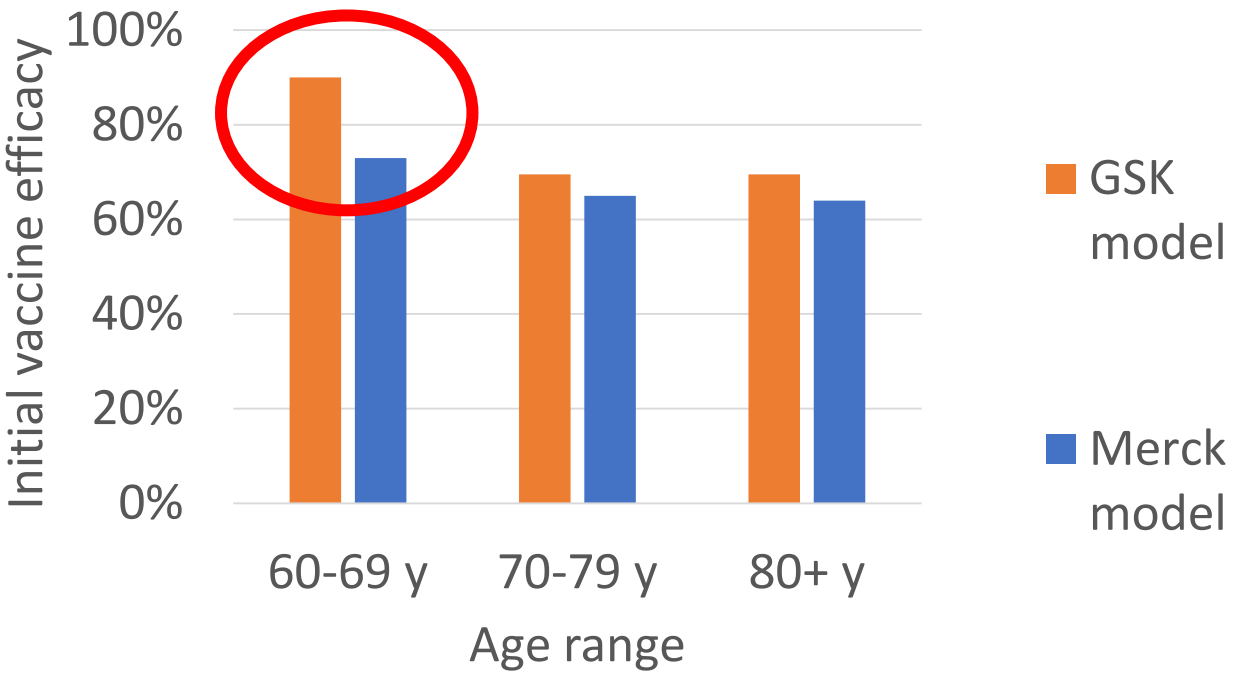
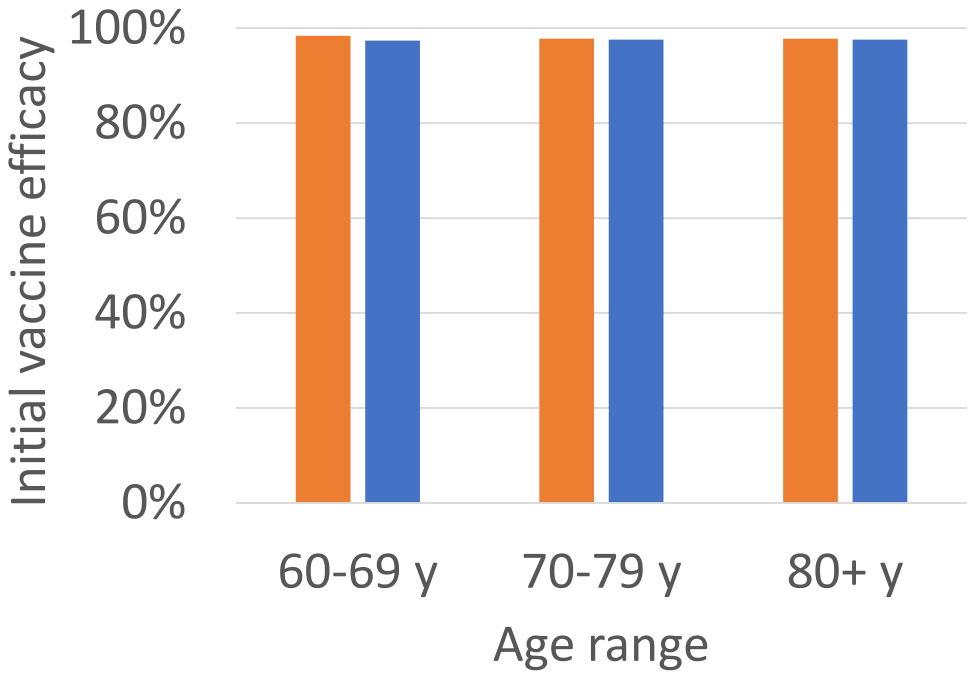
Model Assumptions, Base Case

Initial vaccine efficacy for HZ/su

Single dose of HZ/su



Two doses of HZ/su



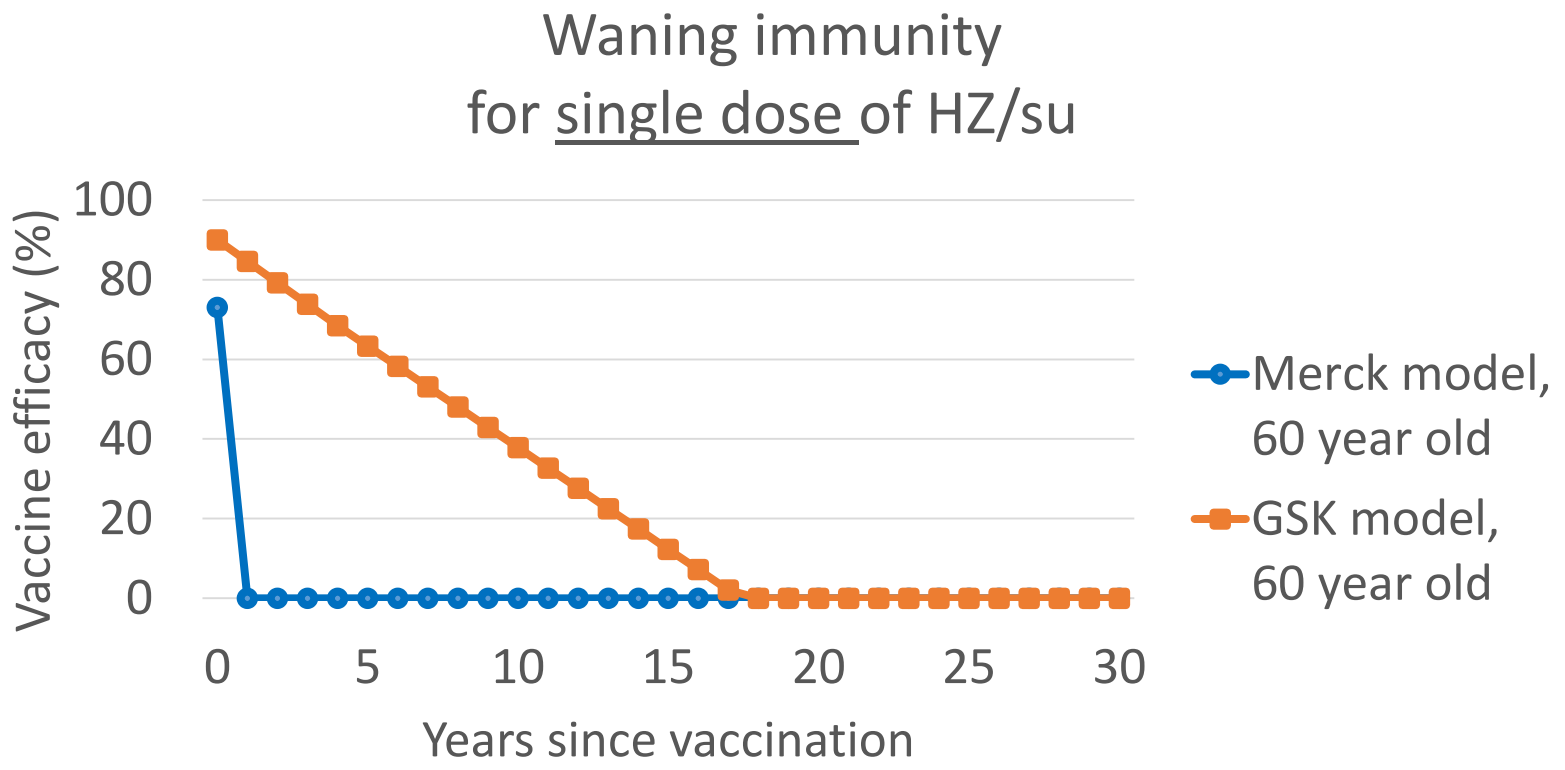
No published data for single dose efficacy or waning immunity

GSK: Single dose initial efficacy based on limited, unpublished data from ZOE-50 and ZOE-70 trials. Initial vaccine efficacy for 60-69 age group with 1 dose is 90%.

Merck: Single dose initial efficacy based on one dose of ZVL. Initial vaccine efficacy for 60-69 age group with 1 dose is 73%.

Model Assumptions, Base Case

Waning immunity from HZ/su vaccine (single dose)



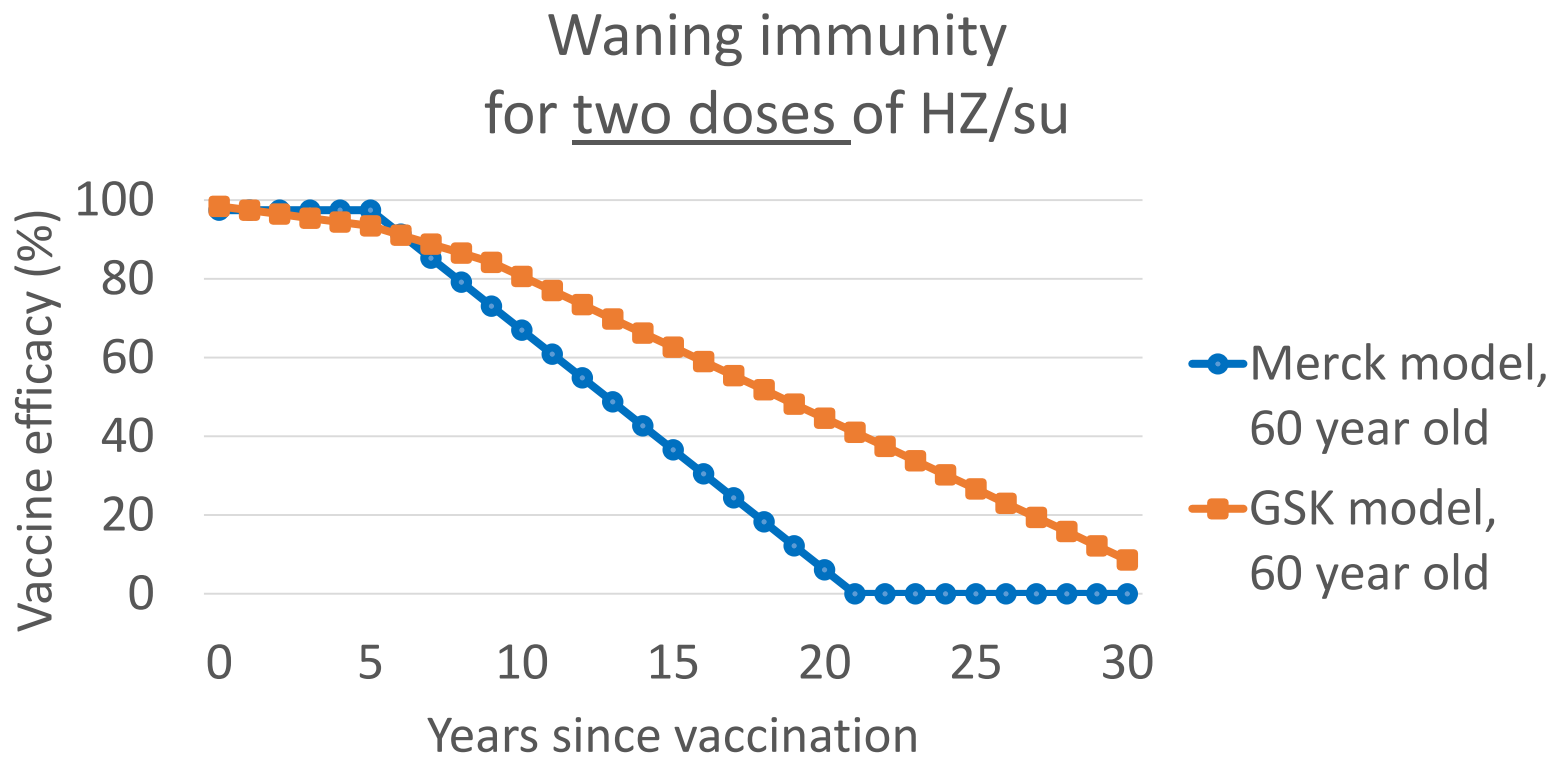
No published data for single dose efficacy or waning immunity

GSK: Single dose efficacy wanes at rate of ZVL

Merck: Single dose efficacy wanes to 0% after 1 year

Model Assumptions, Base Case

Waning immunity from HZ/su vaccine (two doses)



No published data for long term, two dose waning immunity

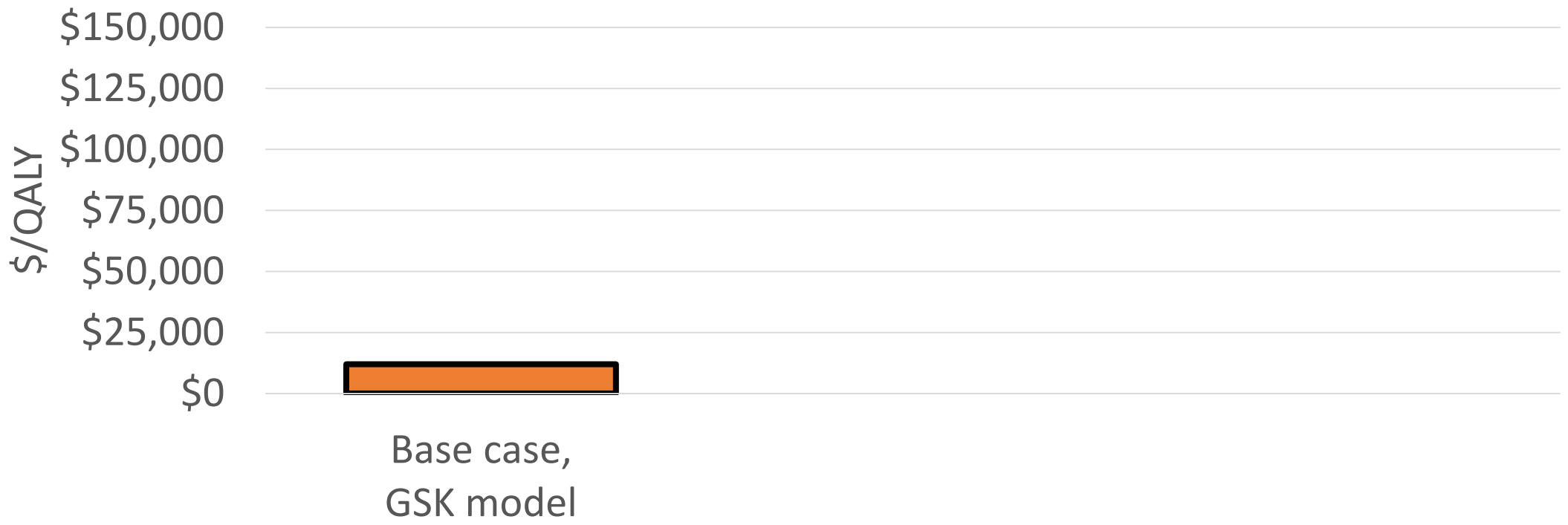
GSK: Two dose waning rate based on extrapolation from trial data

Merck: Two dose waning rate wanes to 0% in year 20

Sensitivity Analyses

HZ/su vs. no vaccine, comparing the two models

- All scenarios among 60+ year olds



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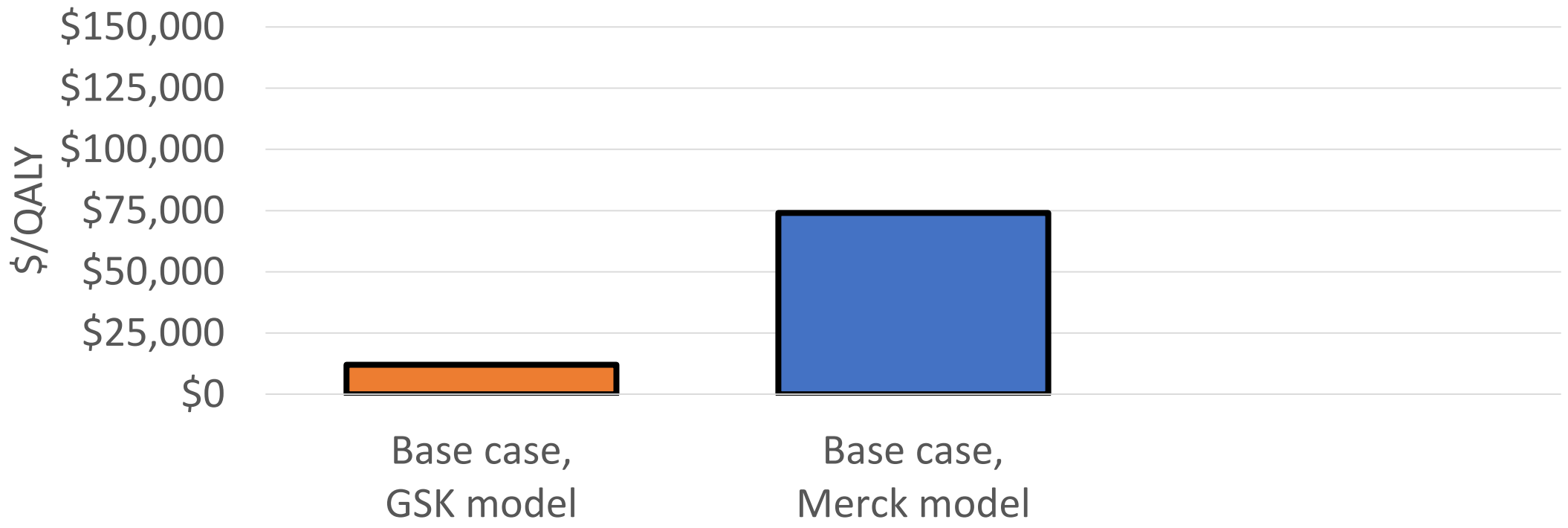

Sensitivity Analyses

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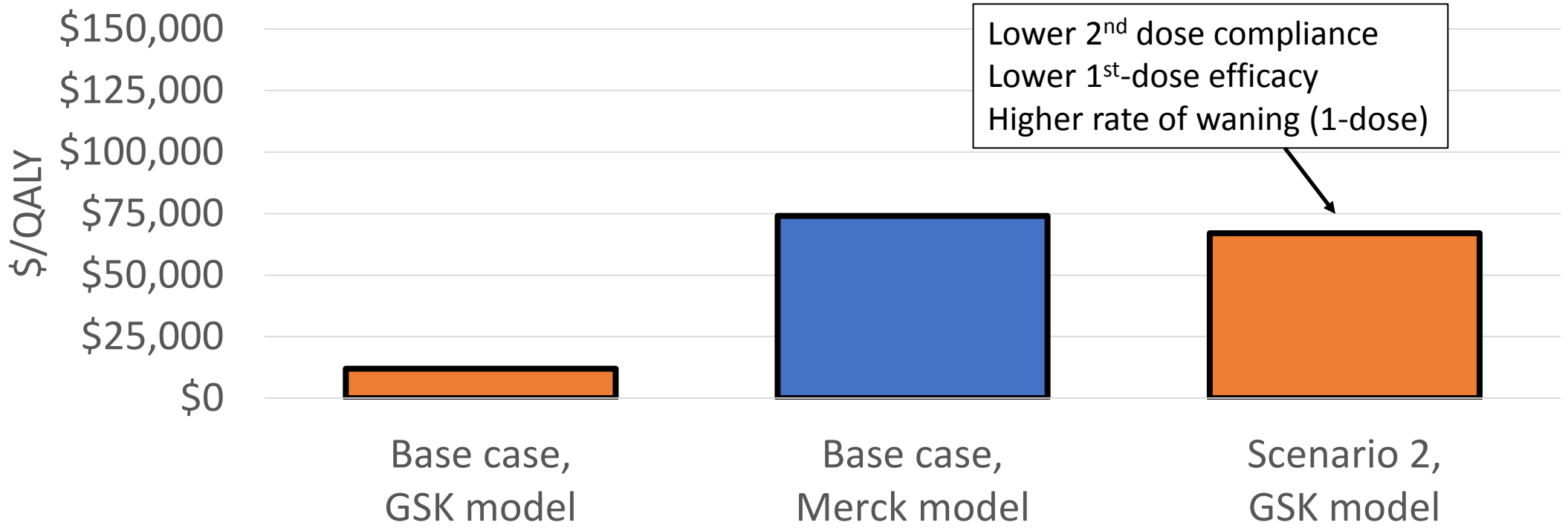

Model Assumptions, Base Case

Vaccination costs

Single dose costs	GSK model	Merck model
ZVL	$197	$213
HZ/su	$140	$106
Total vaccination cost (with administration fees)	**GSK model**	**Merck model**
ZVL (1 dose)	$217	$233
HZ/su (1 dose)	$160	$126
HZ/su (2 doses)	$320	$253

- Administration fee (incurred for each dose) was $20 in both models
- HZ/su cost (or price) for one dose
  - GSK model assumptions based on a GSK estimate with a range of $125 to $175
  - Merck model assumptions based on price parity with ZVL vaccine with a range of $85 to $128
- ZVL prices came from the CDC vaccine price list

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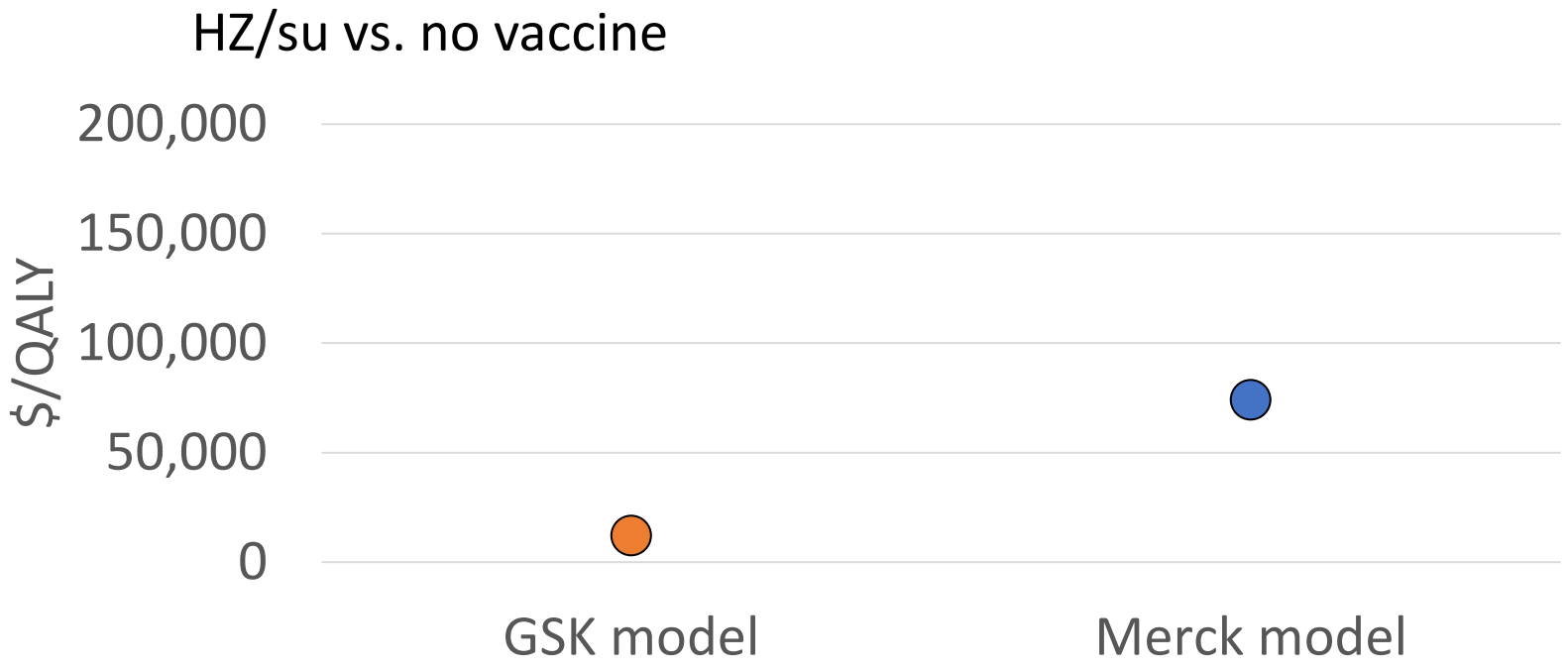
Overall Cost-effectiveness

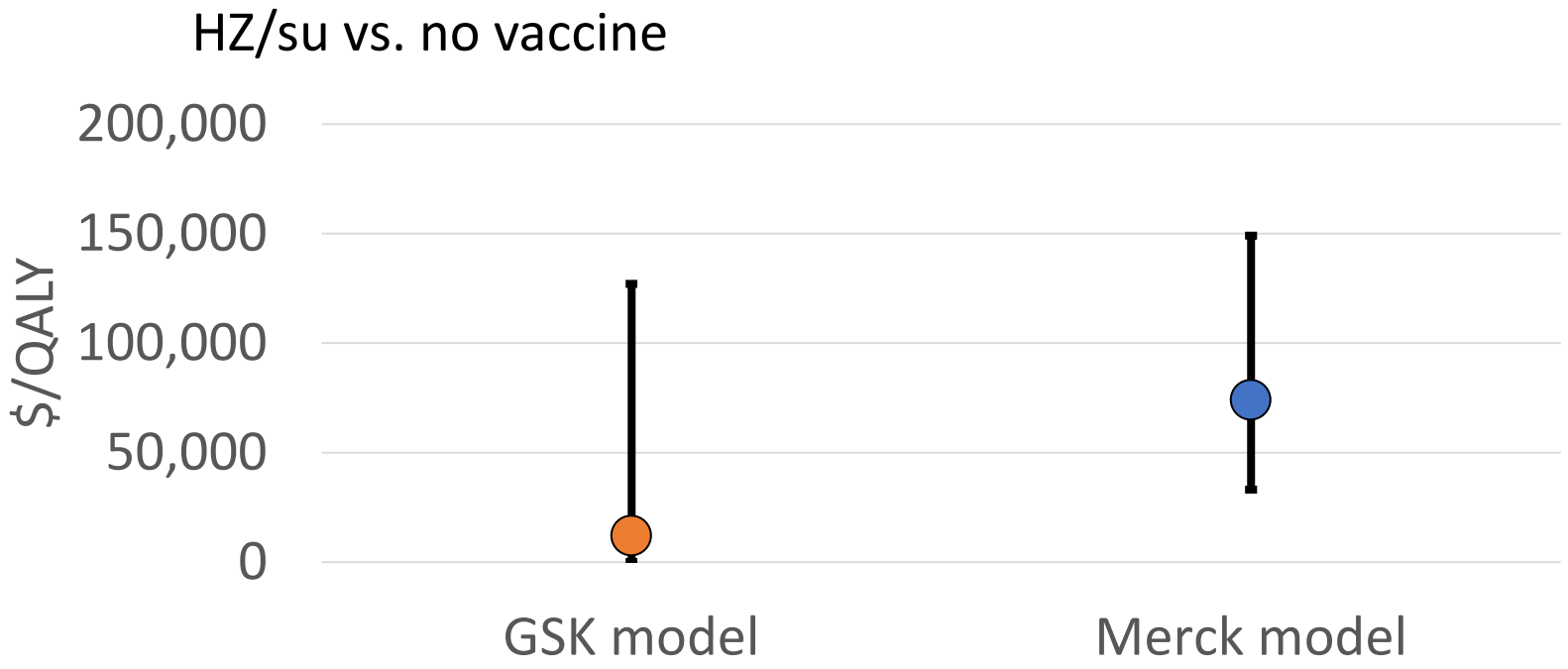
HZ/su vs. no vaccine, base case with sensitivity analyses

- All scenarios among 60+ year olds
- Base case estimates are represented with data points



Overall Cost-effectiveness
HZ/su vs. no vaccine, base case with sensitivity analyses

- All scenarios among 60+ year olds
- Base case estimates are represented with data points
- Ranges based on sensitivity analyses[a] are represented with error bars



[a.] One way and scenario analyses were used to construct ranges. In probabilistic sensitivity analyses, a portion of scenarios may have produced CERs that exceeded these ranges.

Overall Cost-effectiveness

HZ/su vs. ZVL, base case with sensitivity analyses[a]

- All scenarios among 60+ year olds
- HZ/su vs. ZVL

Model	Scenario description	Which vaccine is cost-saving[c]?
GSK[b]	Base case	HZ/su
	Most favors HZ/su	HZ/su
	Most favors ZVL	HZ/su
Merck	Base case	HZ/su
	Most favors HZ/su	HZ/su
	Most favors ZVL	ZVL

[a.] Only one way or scenario analyses was used to develop this table.

[b.] All of the one way sensitivity scenarios in the GSK model indicated cost-savings. A portion of scenarios from the probabilistic sensitivity analyses were not cost-saving.

[c.] Cost-saving is defined as a cost-effectiveness ratio with negative costs (or savings) and positive health outcomes.

Overall Cost-effectiveness

HZ/su vs. ZVL, base case with sensitivity analyses[a]

- All scenarios among 60+ year olds
- HZ/su vs. ZVL

Model	Scenario description	Which vaccine is cost-saving[c]?
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Overall Cost-effectiveness

HZ/su vs. ZVL, base case with sensitivity analyses[a]

- All scenarios among 60+ year olds
- HZ/su vs. ZVL

Model	Scenario description	Which vaccine is cost-saving[c]?
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- Sensitivity analyses exploring cost-effectiveness in general
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Summary

Cost-effectiveness among adults aged 60+ years old

- HZ/su vs. no vaccine
  - Base case (both models): From $12,000 to $74,000 per QALY gained
  - Sensitivity analyses (both models): From cost-saving to $150,000 per QALY gained

- ZVL vs. no vaccine
  - Base case (both models): From $120,000 to $125,000 per QALY gained
  - Sensitivity analyses (Merck model): From $60,000 to $260,000 per QALY gained

- HZ/su vs. ZVL
  - Base case (both models): HZ/su is cost-saving relative to ZVL
  - Sensitivity analyses (both models): From HZ/su being cost-saving relative to ZVL to ZVL being cost-saving relative to HZ/su

Summary

Cost-effectiveness among adults aged 60+ years old

- Important factors influencing observed range in values between the two models
  - Assumptions with relatively greater uncertainty and limited evidence base
    - Efficacy and waning immunity for 1st dose for HZ/su vaccine
    - Long-term waning immunity for 2-doses of HZ/su vaccine

- Important factors influencing observed range in overall cost-effectiveness
    - HZ/su vaccine cost
    - HZ/su regimen completion
    - HZ incidence
    - Cost to treat a case of HZ with and without post-herpetic neuralgia (PHN)
    - Initial efficacy of a single dose of HZ/su
    - Rate of waning immunity from HZ/su

Limitations

- Uncertainty around several key parameters
  - Limited empirical data
    - Efficacy and waning immunity for 1st dose for HZ/su vaccine
    - 2-dose regimen completion of HZ/su outside of clinical trials
    - Long-term waning immunity for 2-doses of HZ/su vaccine
  - A price has not been published for the HZ/su vaccine

Acknowledgements

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