# Economics of vaccinating immunocompromised 19–49-years-old adults against herpes zoster in the US

***A SUMMARY REPORT OF CDC & GSK MODELS***

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*Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.*

# Conflict of interest

- CDC model: **Andrew Leidner**, Kai Hong, Tara Anderson, Angela Guo, Jamison Pike, Lisa Prosser, Ismael R. Ortega-Sanchez, Kathleen Dooling
  - No conflicts of interest

- GSK model: Elizabeth La, Desmond Curran, Sara Poston et al., [see complete author list and affiliations]
  - GSK manufacturers the RZV vaccine *and* RTI Health Solutions

# Overview

- **Policy question:** Should adults ≥19 years of age who are or will be immunodeficient or immunosuppressed due to disease or therapy be recommended to receive two doses of RZV for the prevention of herpes zoster and its complications?

| Age | 19–49 years | ≥50 years |
|---|---|---|
| **General (immunocompetent) population** | Not currently under consideration | Recommended |
| **Immunocompromised** | Under consideration<br>HSCT \| Other patient groups | Under consideration |

# Economic analysis

**Question**: Is vaccinating immunocompromised* adults against herpes zoster *cost-effective*?

**Comparator**: Unvaccinated immunocompromised 19–49-years-old adults

**Intervention**: Immunization of immunocompromised 19–49-years-old adults

**Base-case scenario:** What is the incremental *cost-effectiveness* of vaccinating HSCT recipients who are 19–49-years-old using RZV relative to No vaccine?

* Immunocompromised = immunodeficient or immunosuppressed due to disease and/or therapy

# IC populations: Base-case and Scenarios

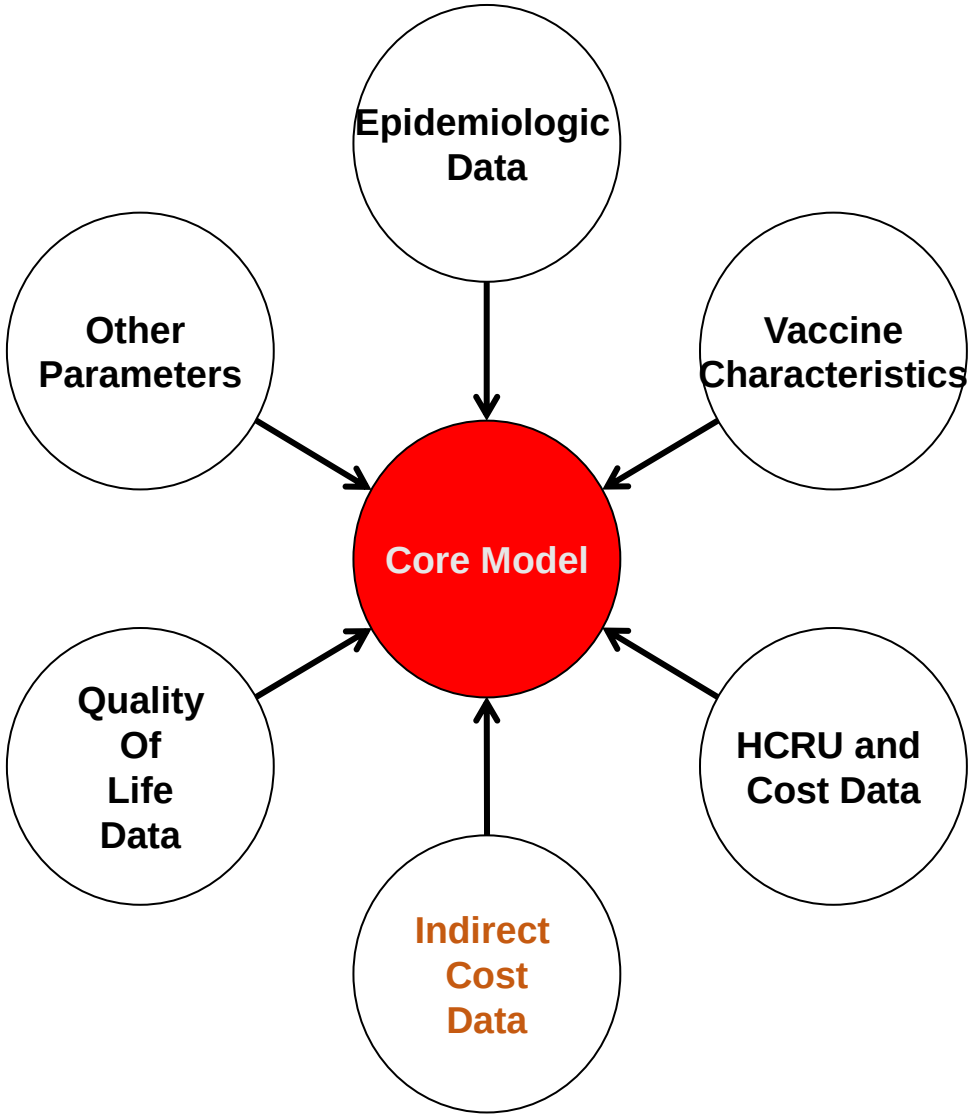
| CDC | GSK |
|---|---|
| **BASE-CASE: Hematopoietic stem cell transplant (HSCT) recipients** | |

| People living with Human immunodeficiency virus (HIV) infection | |
|---|---|
| **Multiple Myeloma** | **Renal or other solid organ transplant** |
| **Non-Hodgkin Lymphoma** | **Hodgkin Lymphoma** |
| **Hematologic malignancies** | **Breast cancer** |
| **Autoimmune and other inflammatory** | |

# Design

- Static analytical decision-making models
- Probabilistic simulation and sensitivity analyses
- Hypothetical population
  - Base-case: cohort of 19-49 yo HSCT recipients
- Time Frame: time of vaccination with 1$^{st}$ and 2$^{nd}$ dose of RZV
- Analytic Horizon: Age-specific Life Expectancy or 30 years
- Discount rate: 3% (0%-6%)
- Healthcare & Societal perspectives

# Inputs and main outcomes




Prevention of:

- Uncomplicated HZ cases
- HZ with PHN
- Inpatient care of HZ
- HZ-associated deaths

QALYs saved
$/Case saved
**$/QALY saved**

NNV avert a:

- HZ Case, PHN case
- Hospitalization
- Death

# Cost-saving vs Cost-Effective

**Cost of intervention**: Cost of vaccination program

**Savings from intervention** = Changes in cost of illness (*without* vaccination program costs)

$$\textit{Net cost}_{vacc} = \text{Cost of intervention} - \text{Savings from intervention}$$

**Cost-saving**: Cost of intervention **<** Savings from intervention

*All cost-saving interventions are also cost-effective, but not all cost-effective interventions are cost-savings, not necessarily.*

# Economic evaluation:

Incremental cost-effectiveness ratio (*ICER*) **:**

$$ICER = \frac{C_{vacc} - TC_{saved}}{\sum_{t=0}^{T} \frac{(HO_{unvacc} - HO_{vacc})}{(1+r)^t}}$$

*ICE* < 0 Cost-savings (cost-effective)

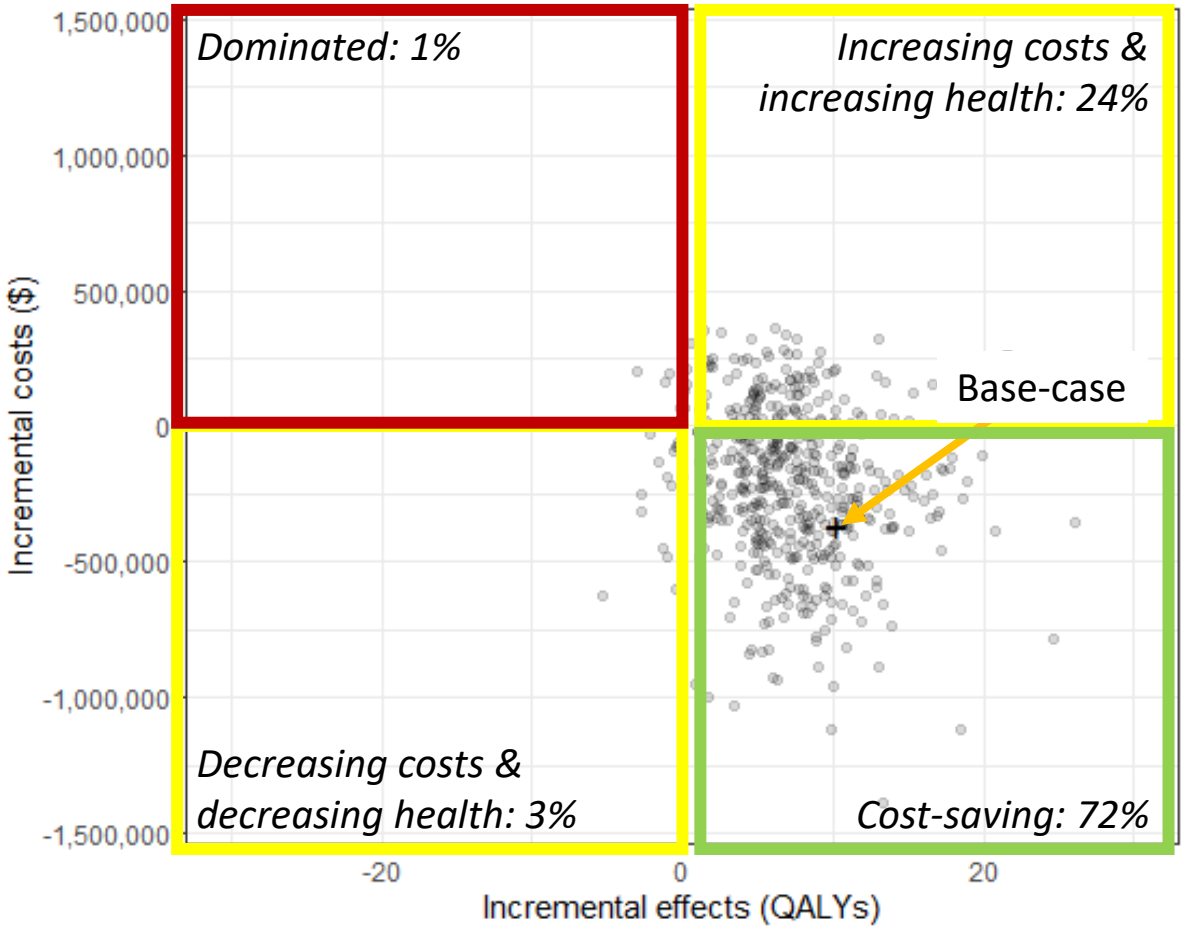
*ICE* > 0 Costly Cost-effective**?**

**Where:**

- ***Cvacc*** **=** Cost of intervention (vaccination program costs)
- ***TCsaved*** **=** Total savings (difference in disease costs under No vaccination vs. RZV vaccination)
- ***HOvacc*** **=** Health outcome of vaccination (ex., HZ cases, QALYs)
- ***HOunvacc*** **=** Health outcome of No vaccination (ex., HZ cases, QALYs)
- ***t*** **=** time in years after immunization *(t=0, 1, 2,…, T)*
- ***r*** **=** discount rate (3%)
- ***T*** **=** Analytical horizon (age-specific, in years)

# CDC: HSCT, base case estimates & PSA

| Summary outcomes | Base-case |
|---|---|
| $ / QALY gained | Cost-saving |
| $ / HZ case averted | Cost-saving |
| $ / hospitalization averted | Cost-saving |
| $ / death averted | Cost-saving |
| NNV avert case | 10 |
| NNV avert hospitalization | 95 |
| NNV avert death | 10,608 |



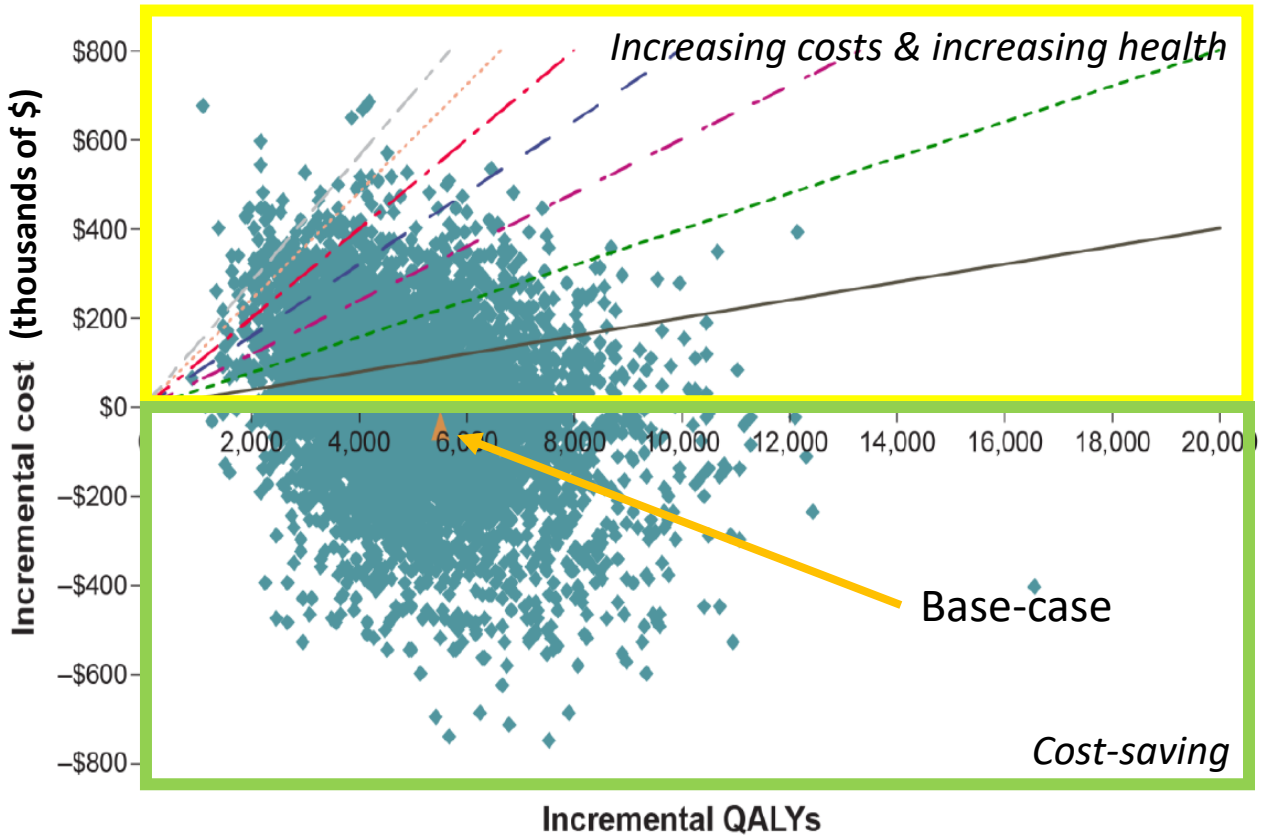

**Probabilistic sensitivity analysis (PSA)**

# GSK: HSCT, base case estimates & PSA

| Summary outcomes | Base-Case |
|---|---|
| $ / QALY gained | Cost-saving |
| $ / HZ case averted | Cost-saving |
| $ / hospitalization averted | n/r |
| $ / death averted* | n/r |
| NNV avert case | 8.6 |
| NNV avert PHN | 46.6 |
| NNV avert death* | n/r |

n/r = not reported

* Difference in number of HZ deaths between "No Vaccination" and "RZV vaccination" was reported to be zero by GSK model




**Probabilistic sensitivity analysis (PSA)**

# GSK and CDC models comparison (I): analytical approach and inputs

- Age groups considered
  - CDC: Three groups: 19-29yos, 30-39yos and at 40-49yos
  - GSK: 19-49yos (0ne group only) starting of age 35yrs
- Annual HZ incidence in HSCT
  - CDC: 40.2 (range 35.6 to 45.12) per 1000 PY
  - GSK: 60 (range 40 to 80) per 1000 PY
- Probability of PHN
  - CDC: Base case 9.1% (range 6% to 41%)
  - GSK: Base case 12.9% (range 8.5% to 17.3%)
- Antiviral prophylaxis following HSCT
  - CDC: Prophylaxis period 6mos, SA 1mo to 2yrs
  - GSK: No specific/not explicit
- Vaccination coverage
  - CDC: Dose-specific 1st dose <93% & 2nd dose <86%
  - GSK: 1st dose & 2nd dose 100% (Base-case), SA 76%-100%
- Utilities-Background
  - CDC: age specific and reduction for IC to 86%
  - GSK: adjusted for baseline quality of life among IC
- Duration/transition to IC status
  - CDC: 2yrs for HSCT
  - GSK: 5yrs for HSCT (range 2 to 30yrs scenario-specific)
- Initial VE & waning of VE in time
  - CDC Initial VE per dose: 1$^{st}$ 39%, 2$^{nd}$ 68% in 21months follow-up
    Years until no VE 1$^{st}$ dose 11yrs, 2$^{nd}$ 20yrs.
  - GSK Initial VE per dose: 1$^{st}$ 58%, 2$^{nd}$ 72.5%,
    Annual VE waning per dose 1$^{st}$ 18.2%, 2$^{nd}$ 9.1% during IC status
- Unitary cost of HZ outcomes
  - CDC: **Direct cost**: non PHN, non inpatient HZ episode ($1,549), with PHN ($4,906), as inpatient non PHN ($37,852)
  - GSK: **Direct cost**: non PHN HZ episode ($3,578), with PHN ($8,513). **Indirect**: HZ case ($199)

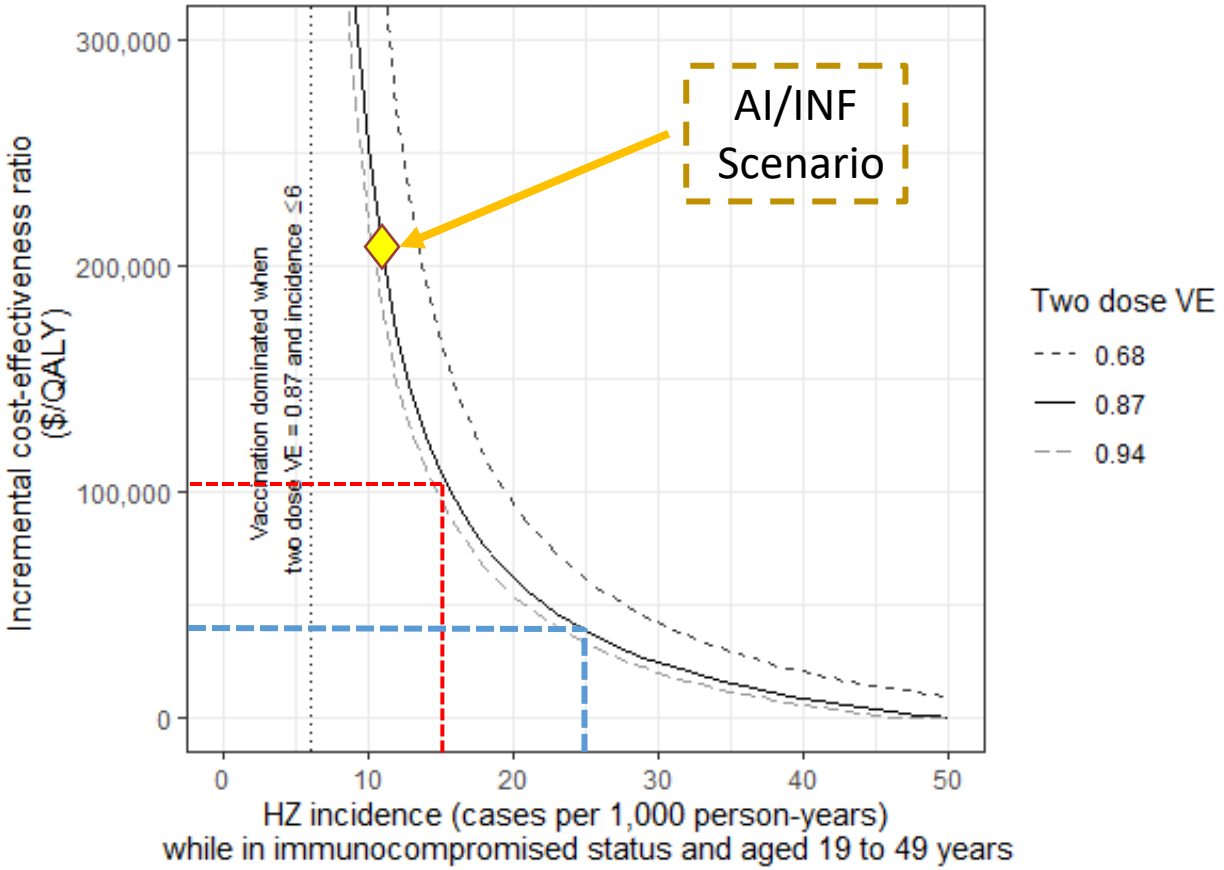
# GSK and CDC models comparison (II): base case & scenario results

| Scenario | GSK | CDC |
|---|---|---|
| **HSCT (Base case)** | Cost-saving, $140* | Cost-saving |
| Multiple Myeloma | n/r | Cost-saving |
| Renal transplant | Cost-saving | n/r |
| Hematologic malignancy | n/r | $10,000 |
| HIV | $33,000 | $79,000 |
| Breast cancer | $68,000 | n/r |
| Hodgkin lymphoma | $96,000 | n/r |
| Non-Hodgkin lymphoma | n/r | $99,000 |
| Autoimmune & inflammatory | 150,000 ** | $208,000 |

* Cost-savings **from societal perspective**, $140 from healthcare perspective. n/r = not reported.

** Implicit AI/INF scenario: Assuming starting age 25 years, HZ incidence 10/1000PY *and* duration of IC status 5 years

# CDC model: Autoimmune/inflammatory conditions




**Scenario inputs**

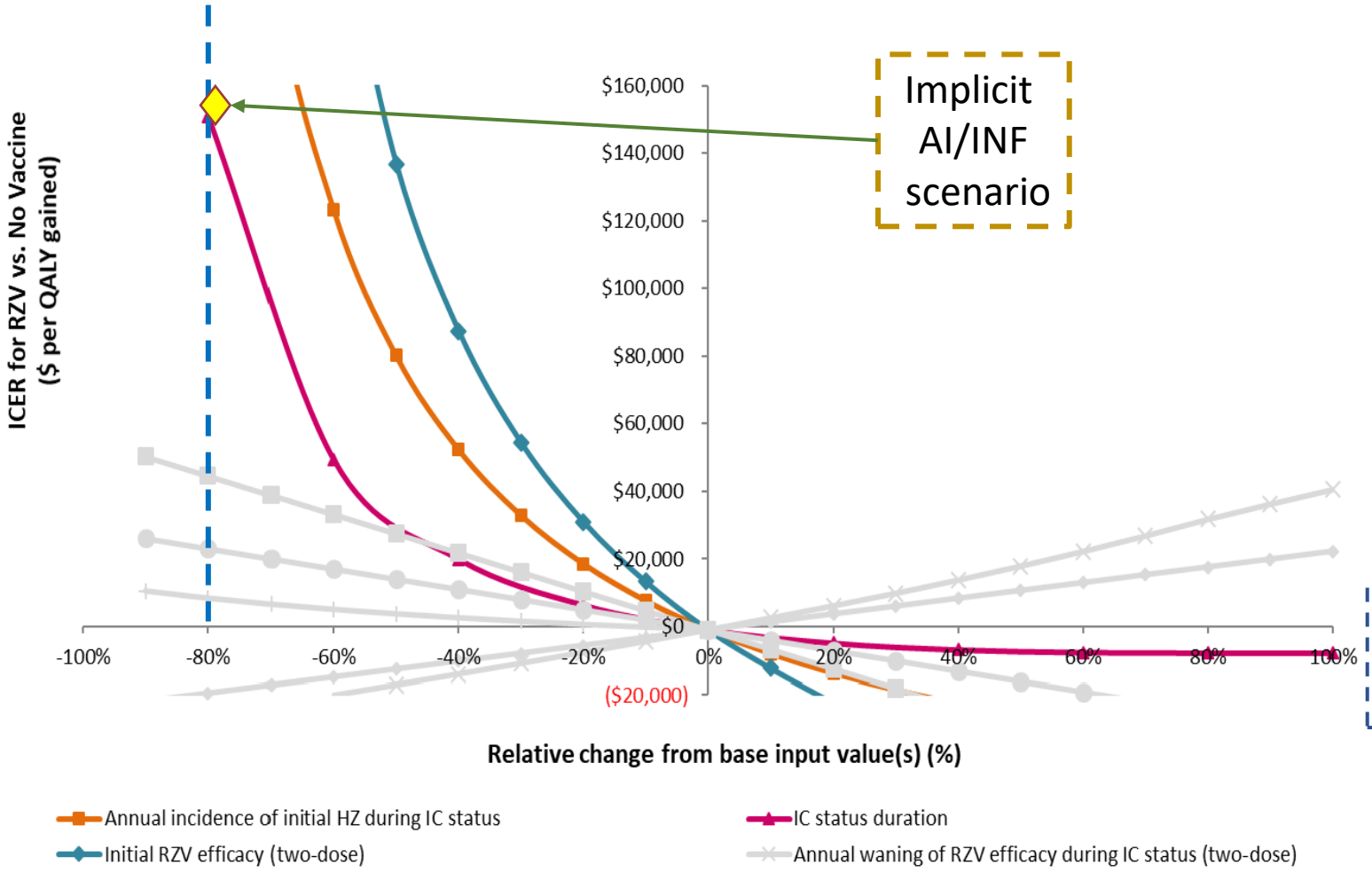
- Lower health care costs
- Higher VE
- Lower incidence
- Lower risks of death

**Incidence (cases/1,000 person-years) among 21–50-year-olds with select AI/INF conditions[1]:**

- Systemic lupus erythematosus: 15.2—24.6
- Rheumatoid arthritis: 6.6—10.0
- Psoriasis: 3.7—6.4

[1] Yun et al. 2016. "Risk of Herpes Zoster in Autoimmune and Inflammatory Diseases", *Arthritis and Rheumatology* 68(9): 2328-2337.

# GSK model: Thresholds in HSCT used to project $/QALY for Autoimmune/inflammatory conditions




**Base-case value of annual HZ incidence for HSCT**

- 60 (40 - 85) per 1000 PY

**HZ incidence in selected AI/INF[1,2] conditions**

- 11.5 (3.7-24.6) per 1000 PY

About 80% relative reduction in HZ incidence from base value


1. Chen, S.-Y., et al., *Incidence of herpes zoster in patients with altered immune function.* Infection, 2014. 42(2): p. 325-334
2. Yun et al. 2016. "Risk of Herpes Zoster in Autoimmune and Inflammatory Diseases", *Arthritis and Rheumatology* 68(9): 2328-2337

# Discussion

- **Neither model assessed $/QALY in patients ≥50-years-old**
- **Base-case: HSCT patients**
  - Economic value of RZV vaccine appears to be *favorable* (i.e., cost-saving)
    - High(er) HZ incidence and HZ-related health care costs combined with reasonable VE
  - Clinical trial data support VE assumptions
  - Smaller patient population
- **Scenarios: Other patient groups (e.g., HIV, AI/INF)**
  - With lower risk of HZ and healthcare costs, the economic value of RZV vaccination is less favorable relative to HSCT patients
  - Some AI/INF conditions may have *the least favorable* estimates of RZV use, depending on the underlying risk of HZ
  - Larger patient population

# End of Summary