



# **ACIP Recommendations for the use of herpes zoster vaccines**

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# Recommendations of the Advisory Committee on Immunization Practices for Use of Herpes Zoster Vaccines

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**Link live after 1:00pm**

## In October 2017, the ACIP made the following recommendations:

- 1) Recombinant zoster vaccine (RZV) is recommended for the prevention of herpes zoster and related complications for immunocompetent adults aged  $\geq 50$  years.
- 2) RZV is recommended for the prevention of herpes zoster and related complications for immunocompetent adults who previously received zoster vaccine live (ZVL).
- 3) RZV is preferred over ZVL for the prevention of herpes zoster and related complications.

CDC 2018 Herpes Zoster Policy Note recommendations serve as a supplement to the existing recommendations for the use of ZVL in immunocompetent adults aged  $\geq 60$  years.

# Outline

- ACIP Recommendations & CDC Policy Note for Herpes Zoster Vaccines
- Herpes Zoster Disease and Epidemiology
- Rationale for ACIP recommendations
- Clinical guidance for Shingrix

# Background

# Herpes Zoster (HZ): Clinical Manifestations



Courtesy of NIAID



Courtesy of CDC



Courtesy of CDC/Robert Sumpter

# Herpes Zoster & PHN: Clinical Manifestations

## Herpes Zoster

- About 90% of HZ episodes associated with pain
- Treatment: antivirals reduce duration of rash and pain<sup>1</sup>

## PHN

- Pain at least 90 days following resolution of rash
- Treatment: minimal or no efficacy. Side effects, especially in elderly<sup>2</sup>



Courtesy Courtesy of M. Oxman, MDC.

**“My PHN is worse than my cancer and chemotherapy... [it] has made me depressed and suicidal in the past”**

1. Cohen et al, NEJM 2013, 2. Johnson et al, NEJM 2014

# Herpes Zoster (HZ) and Postherpetic Neuralgia (PHN) epidemiology, United States

- ~1 million cases annually<sup>1,2</sup>
- Incidence increases with age, ranging from <1 case/1000 children to >15 cases/1000 population 80 years and older<sup>2,3,4</sup>
- For adults 50 years and older with HZ, 10-18% will go on to develop PHN. Similar to HZ, the incidence increases with age<sup>3</sup>
- Zoster Vaccine Live (ZVL, ZOSTAVAX™) has been licensed in the U.S. since 2006-- 33% of individuals 60 years and older report receipt.<sup>5</sup>

1. Jumaan et al., JID, 2005, 191:2002-7

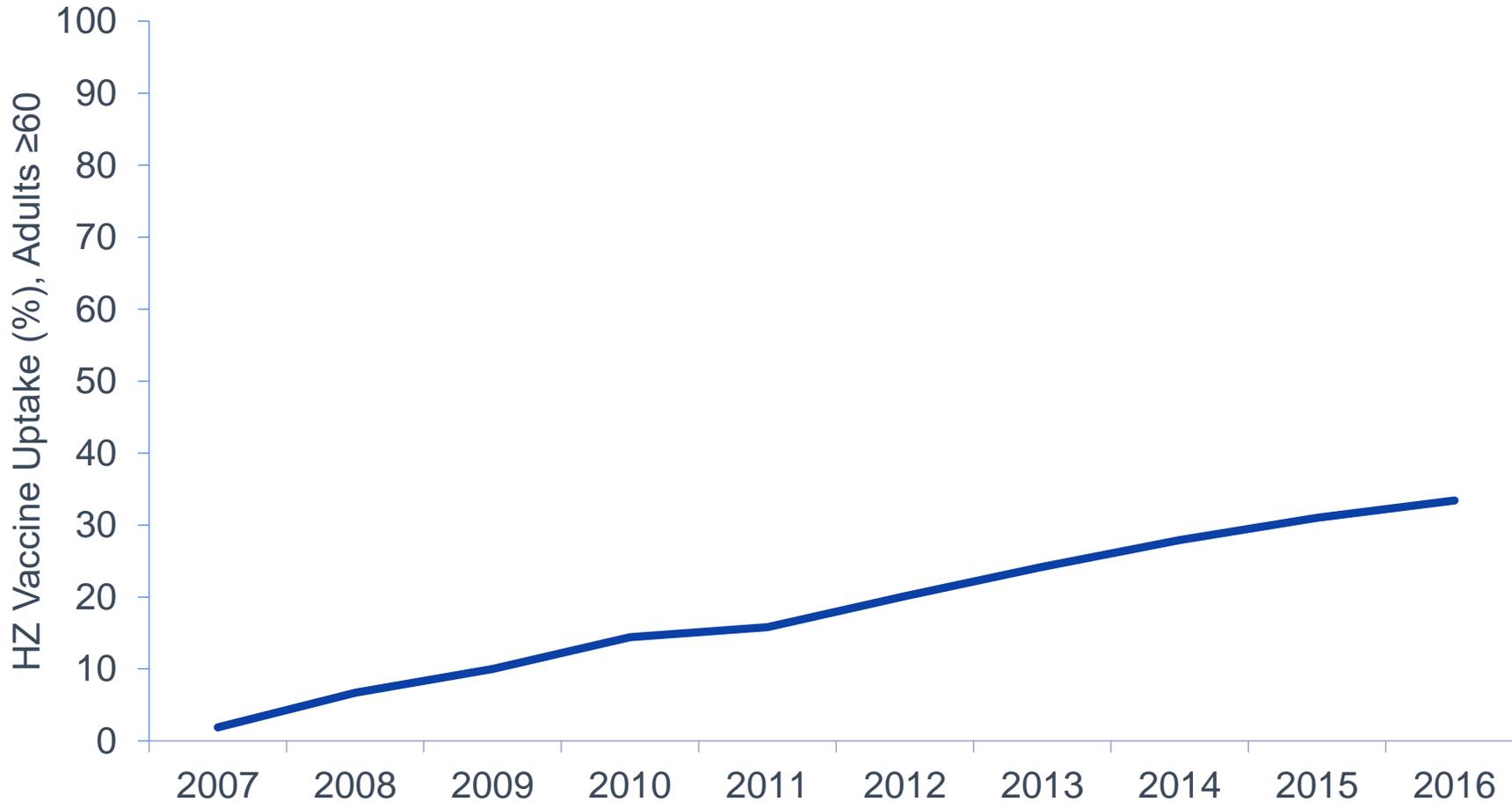
2. Yawn, et al., Mayo Clin Proc. 2007; 82:1341-9

3. Insinga et al., J Gen Intern Med. 2005, 20:748-53

4. Harpaz et al, IDWeek 2015

5. CDC, provisional unpublished data from NHIS

## Vaccination Coverage of Zoster Vaccine Live (ZVL), among adults $\geq 60$ yrs, United States, 2007-2015



\* 2007: National immunization Survey (Lu et al, Vaccine 27:882-7); 2008-13: NHIS (Am J Prev Med 40:e1-6 & MMWR February 5, 2016 / 65(1);1-36), 2016 CDC, unpublished

# Shingrix- Recombinant Zoster Vaccine (RZV)

- ❑ An adjuvanted recombinant protein subunit vaccine (previously referred to as HZ/su)
- ❑ **2 components**
  - Glycoprotein E
  - Adjuvant ASO1<sub>B</sub>
- ❑ **Efficacy & safety evaluated in a 2-part, phase III RCT, >30,000 subjects**
  - ZOE 50 (50+ yrs)
  - ZOE 70 (70+ yrs)
- ❑ **Licensed by the FDA on Oct 20, 2017**
  - <https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm581491.htm>

# 1) RZV is recommended for immunocompetent adults aged $\geq 50$ years.

## □ Benefits:

- High vaccine efficacy against HZ
  - **97%** (50-69 yrs)
  - **91%** ( $\geq 70$  yrs)
- High vaccine efficacy against PHN (**91%** for  $\geq 50$  year olds)
- Maintained efficacy  $\geq$  **85%** for 4 years following vaccination in  $\geq 70$  year olds

## □ Harms:

- No differences detected between vaccinated and comparison populations for serious adverse events
- Grade 3 reactions more commonly reported in vaccinated groups (17%) compared to placebo (3%)

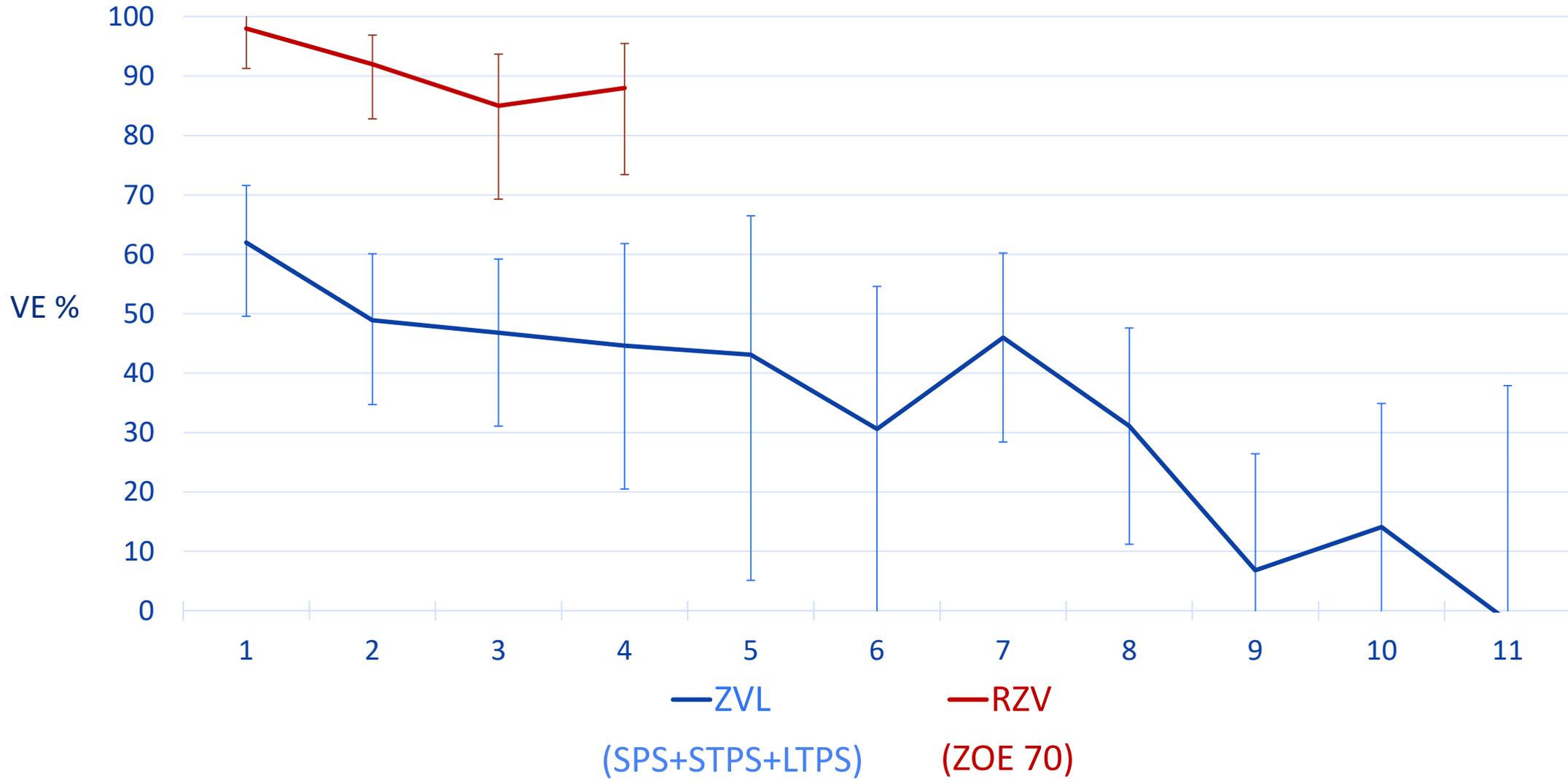
# 1) RZV is recommended for immunocompetent adults aged $\geq 50$ years.

- Long-term immunogenicity:
  - CD4+ T cell response maintained from 4 years through 9 years at  $>3$  times baseline
  - Immune response maintained in the oldest age group ( $>70$  yrs)
  - However, there is no established correlate of protection
  
- Number needed to vaccinate to prevent 1 case:
  - HZ: 11 – 17
  - PHN: 70 – 187
  
- Cost-effectiveness:
  - \$31,000/QALY (average 50 yrs+)
    - \$9,700/QALY (80-89 yo)- \$47,000/QALY (50-59 yo)

## 2) RZV is recommended for immunocompetent adults who previously received zoster vaccine live (ZVL)

- ❑ RZV is more efficacious than ZVL in all age categories; differences are larger at older ages
- ❑ Experimental and observational studies indicate significant waning of protection from ZVL:
  - VE drops the first year after receipt (15-25%)
  - By 6 yrs post vaccination, VE <35%
  - Negligible protection by 10 years
- ❑ RZV is significantly more efficacious over 4 years, with VE > 97% in the first year which is maintained ≥85% during the first 4 years for all ages
- ❑ In a small study, vaccination with RZV 5 yrs following ZVL did not alter the safety or immunogenicity of RZV.

# Vaccine efficacy against HZ for ZVL and RZV, by year following vaccination



Note: The Shingles Prevention Study, Short-term Persistence Study, and Long-term Persistence Study followed the same study population over time.

## 2) RZV is recommended for immunocompetent adults who previously received zoster vaccine live (ZVL)

- ~20 million people have been vaccinated with ZVL and potentially eligible for RZV<sup>1</sup>
- Cost-effectiveness ratio of revaccination at a minimal interval (~8 weeks\* post ZVL) is similar to or lower than other adult vaccines:
  - \$15,000 /QALY (80-89 yrs) to \$117,000 /QALY (50-59 yrs)

1. Source: IMS

\* Revaccination at 8 weeks was approximated in the CEA model by revaccination immediately following ZVL

### 3) RZV is preferred over ZVL

These vaccines have not been studied in a head to head efficacy trial

#### **Efficacy**

- ❑ RZV estimates of efficacy are significantly higher than ZVL estimates across all age groups:
  - 60-69 years: 97% vs 64%
  - 70-79 years: 91% vs 41%
  - >80 years 91% vs 18%
- ❑ HZ/su appears to wane at a slower rate than ZVL over the first 4 yrs
- ❑ The expected cases of HZ and PHN averted are far greater with HZ/su compared to ZVL

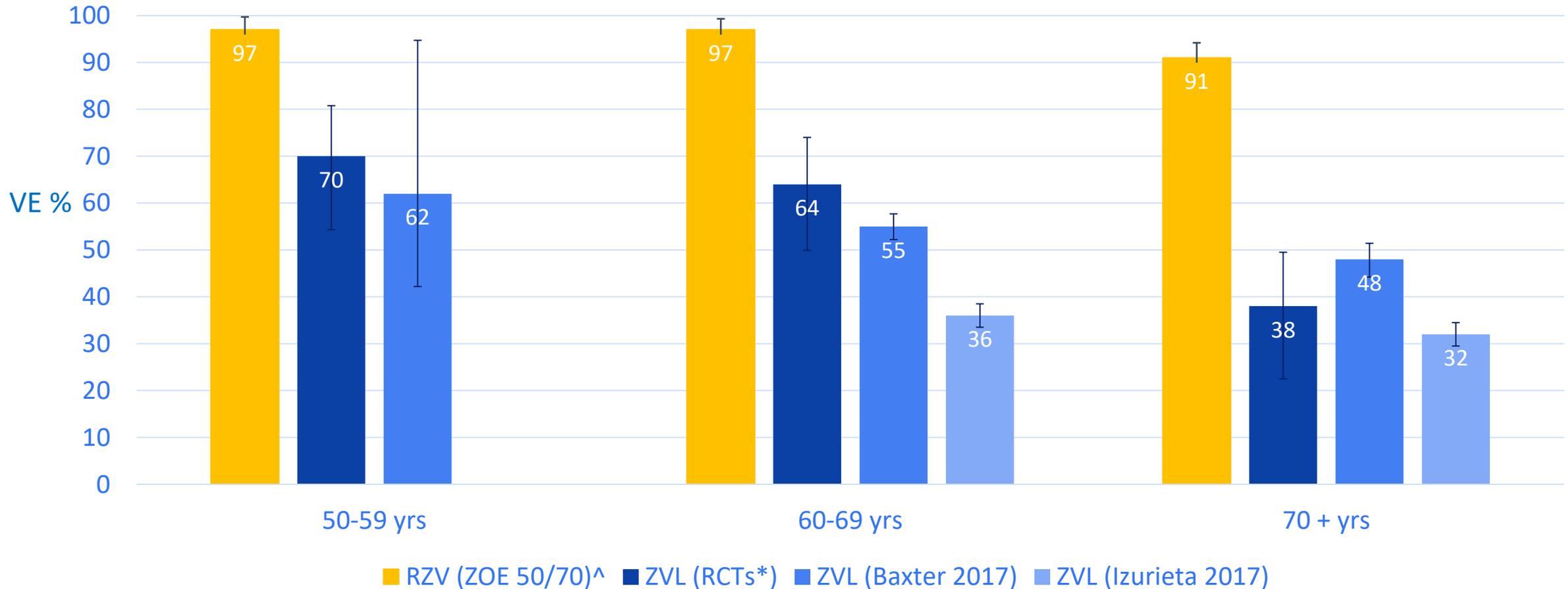
#### **Adverse Effects**

- ❑ Neither vaccine is associated with serious adverse events in immunocompetent persons
- ❑ RZV is more reactogenic than ZVL

#### **Economics**

- ❑ RZV leads to more disease prevention and decreased overall costs (vaccine + expected disease costs)

# Vaccine efficacy and effectiveness against HZ for RZV and ZVL, by age group, during the first 4<sup>‡</sup> years following vaccination

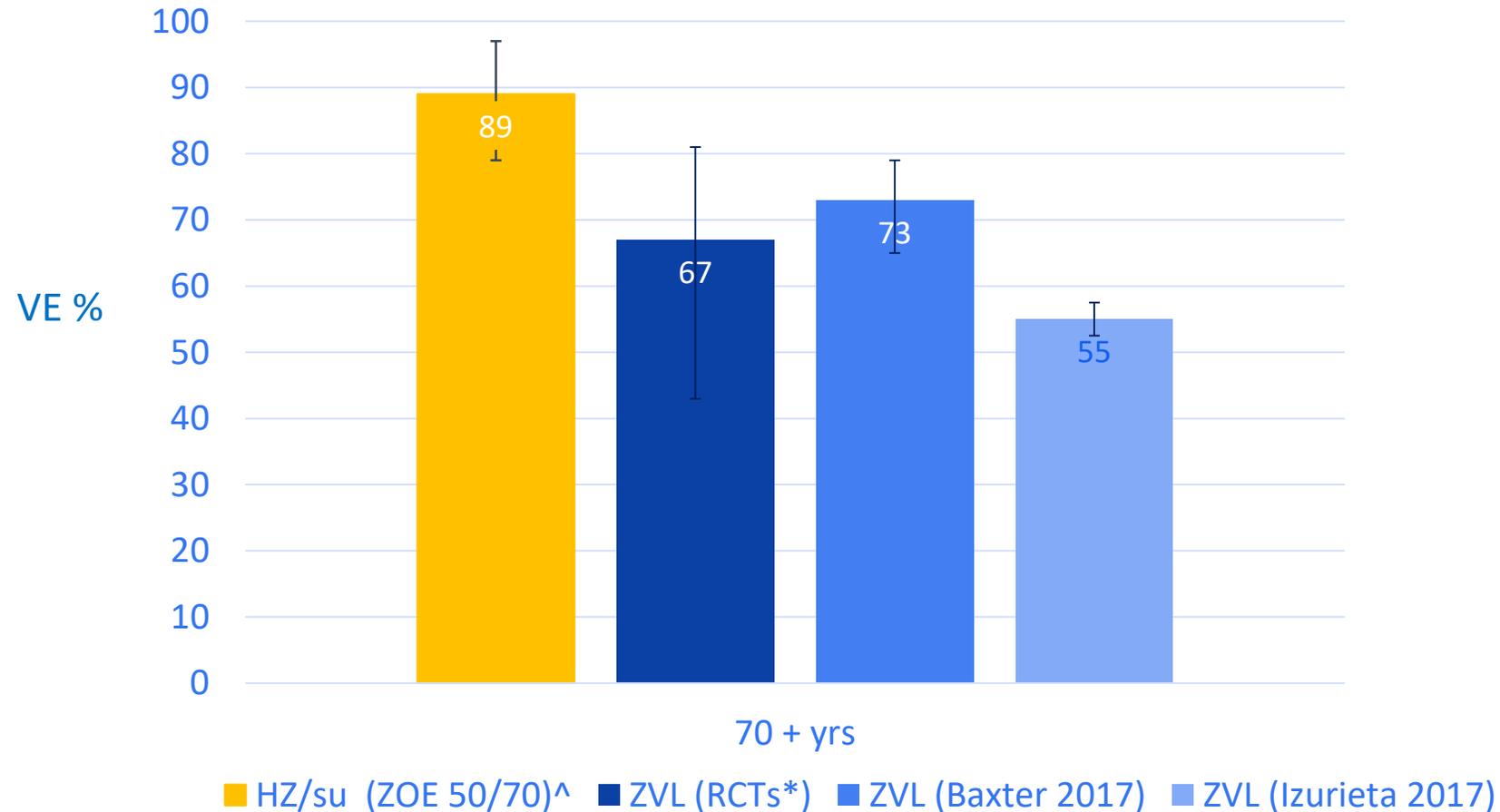


<sup>‡</sup> Median follow up may be less than 3 yrs: Schmader 2012= 1.3 yrs

<sup>^</sup> ZOE 50/70= 50-59 & 60-69yr: Lal 2015, 70+yrs: Cunningham 2016

<sup>\*</sup> RCTs= 50-59 yrs: Schmader 2012, 60-69 and 70+ yrs: Oxman 2005,

# Vaccine efficacy and effectiveness against PHN for HZ/su and ZVL, in adults 70 years and older during the first 4 years following vaccination



<sup>^</sup> Pooled ZOE 50/70: Cunningham 2016

<sup>\*</sup> Shingles Prevention Study: Oxman 2005,

# Shingrix- Recombinant Zoster Vaccine (RZV) Clinical Guidance

- ❑ **Refrigerator stable, requires reconstitution prior to administration**
  - adjuvant suspension + lyophilized gE protein
  - After reconstitution, administer RZV immediately or store between 2-8°C (max=6hrs)
- ❑ **2 doses at 0 & 2-6 months**
- ❑ **Administer IM**
  
- ❑ **Co-Administration with other vaccines**
  - RZV+ QIV (Fluarix) --no interference or safety problems
  - RZV+ PPSV23 (Pneumovax23) or Tdap (Boostrix)– studies ongoing
  - RZV+ Fluad– have not been studied
  
- <https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm581491.htm>

# Shingrix- Recombinant Zoster Vaccine (RZV) Clinical Guidance

## Recommended populations:

- ❑ Adults with chronic medical conditions
- ❑ Adults taking low-dose immunosuppressive therapy, anticipating or have recovered from immunosuppression\*
- ❑ Give irrespective of prior receipt of varicella vaccine, ZVL, or herpes zoster episode
- ❑ HZ vaccines do not require screening for a history of chickenpox (varicella)

*\*Immunocompromised persons were excluded from Phase III efficacy studies, thus, ACIP has not made recommendations regarding the use of RZV in these patients. This topic is will be discussed at ACIP meetings as additional data become available.*

# Shingrix- Recombinant Zoster Vaccine (RZV) Clinical Guidance

For adults who previously received ZVL:

- ❑ No interference or safety problems when RZV vaccination administered  $\geq 5$  years after ZVL
- ❑ Consider a shorter interval if individual is  $>70$  yrs-- protection from ZVL is 38% over  $\sim 3$  yrs
- ❑ Minimal interval of 8 weeks (expert opinion)

# Shingrix- Recombinant Zoster Vaccine (RZV) Clinical Guidance

## CONTRAINDICATION:

- ❑ Allergy: RZV should not be administered to persons with a history of severe allergic reaction, such as anaphylaxis, to any component of this vaccine.

## PRECAUTIONS:

- ❑ Current herpes zoster infection:
- ❑ Pregnancy and breastfeeding:

# Shingrix- Recombinant Zoster Vaccine (RZV) Clinical Guidance

## Counseling for Reactogenicity.

- ❑ **Before vaccination, counsel about expected systemic and local reactogenicity**
  - pain (78%)
  - myalgia (45%)
  - fatigue (45%)
- ❑ **Reactions to the first dose did not strongly predict reactions to the second dose**
- ❑ **vaccine recipients should be encouraged to complete the series even if they experienced a grade 1–3 reaction to the first dose.**

**QUESTIONS?**