



ACIP Recommendations for the use of herpes zoster vaccines

Dr. Kathleen Dooling, MD, MPH
Medical Officer, Division of Viral Diseases

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

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https://www.cdc.gov/mmwr/volumes/67/wr/mm6703a5.htm?s_cid=mm6703a5_w

In October 2017, the ACIP made the following recommendations:

- 1) Recombinant zoster vaccine (RZV, [Shingrix]) is recommended for the prevention of herpes zoster and related complications for immunocompetent adults aged ≥ 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 [Zostavax]).
- 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 ≥ 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

Herpes Zoster Epidemiology

Herpes Zoster (HZ): Clinical Manifestations



Courtesy of NIAID



Courtesy of CDC



Courtesy of CDC/Robert Sumpter

Herpes Zoster & Postherpetic Neuralgia (PHN): Clinical Manifestations

Herpes Zoster

- About 90% of HZ episodes associated with pain
- Treatment: antivirals reduce duration of rash and pain¹

PHN

- Pain at least 90 days following resolution of rash
- Treatment: minimal or no efficacy. Side effects, especially in elderly²



Courtesy of M. Oxman, M.D.

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

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

- ~1 million cases annually^{1,2}
- Incidence increases with age, ranging from <1 case/1000 children to >15 cases/1000 population 80 years and older^{2,3,4}
- For adults 50 years and older with HZ, 10-18% will go on to develop PHN. Similar to HZ, the incidence increases with age³
- Zoster Vaccine Live (ZVL) has been licensed in the U.S. since 2006-- 33% of individuals 60 years and older report receipt.⁵

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

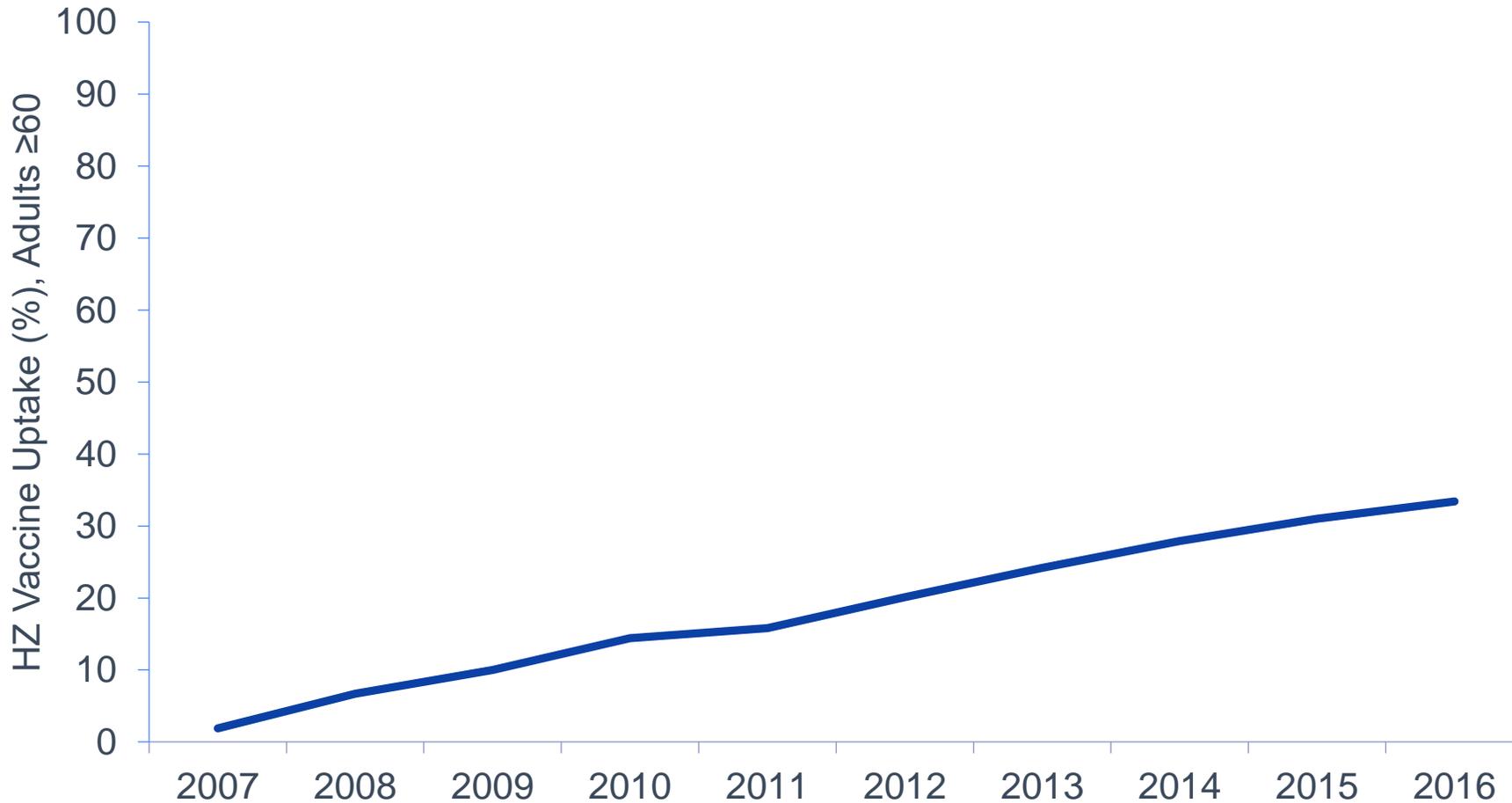
2. Yawn, et al., Mayo Clin Proc. 2007; 82:1341-9

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, among adults ≥ 60 yrs, United States, 2007-2016



* 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_B
- ❑ **Efficacy & safety evaluated in a 2-part, phase III RCT, >30,000 subjects**
- ❑ **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 ≥ 50 years.

□ Benefits:

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

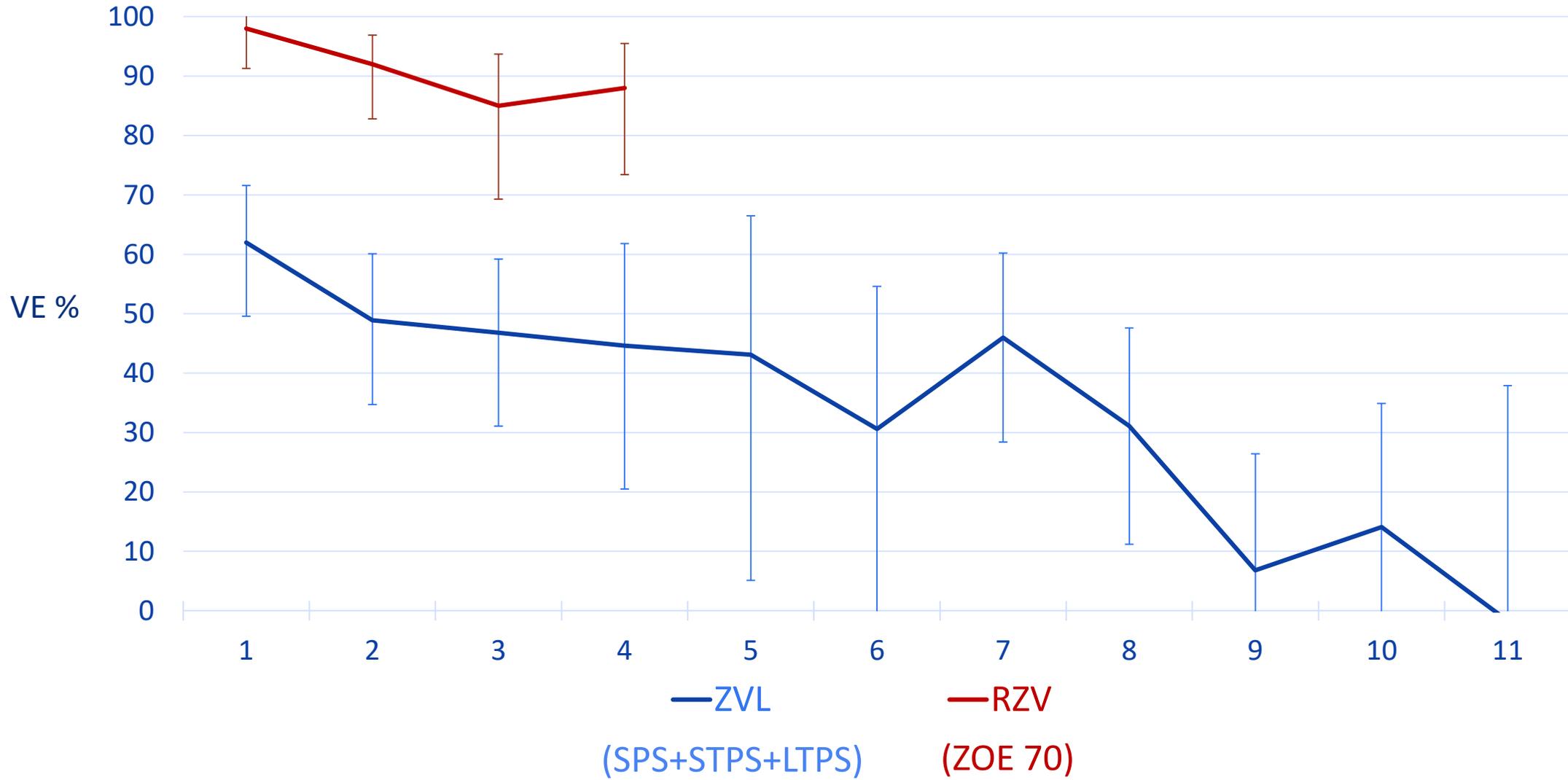
2) RZV is recommended for immunocompetent adults who previously received zoster vaccine live (ZVL)

- ❑ 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 more efficacious than ZVL in all age categories; differences are larger at older ages

- ❑ RZV is significantly more efficacious than ZVL over the first 4 years
 - RZV VE > 97% in the first year
 - RZV VE maintained ≥85% during the first 4 years for all ages

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 RZV¹
- In a small study, vaccination with RZV 5 yrs following ZVL did not alter the safety or immunogenicity of RZV.
- 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%
- ❑ RZV 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 RZV compared to ZVL

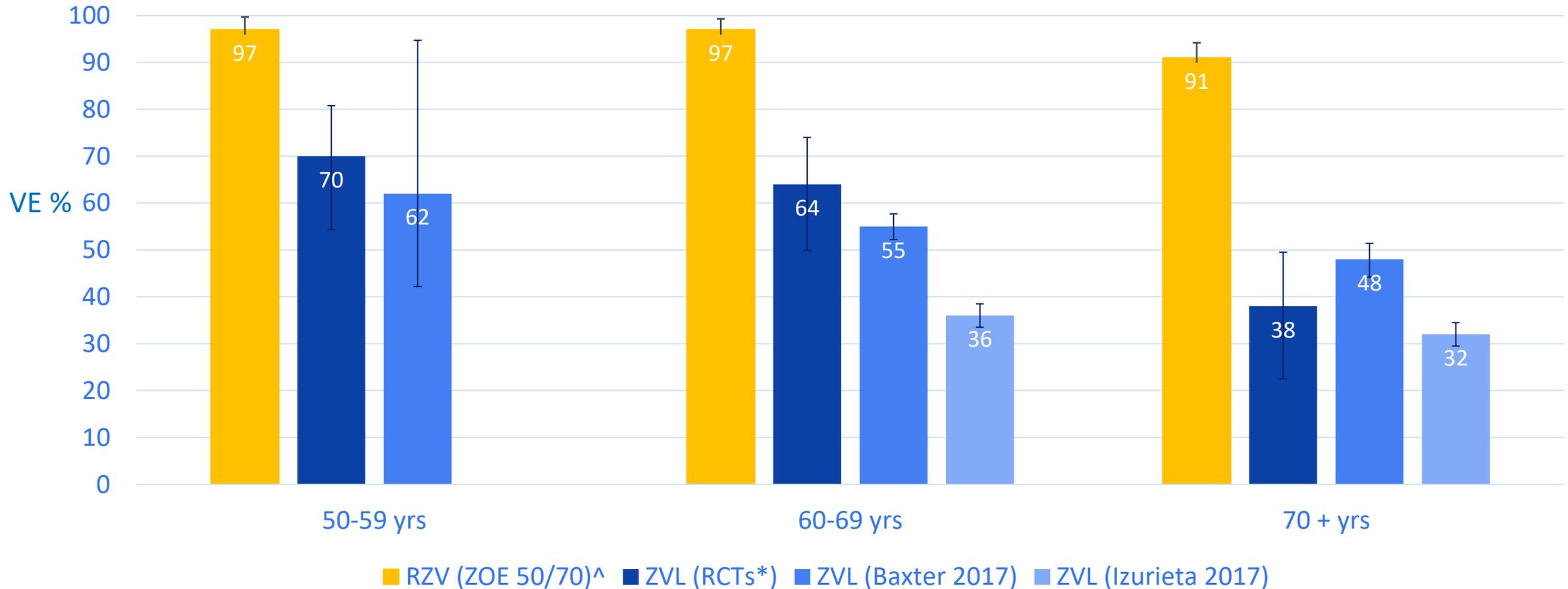
Adverse Effects

- ❑ 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[‡] years following vaccination

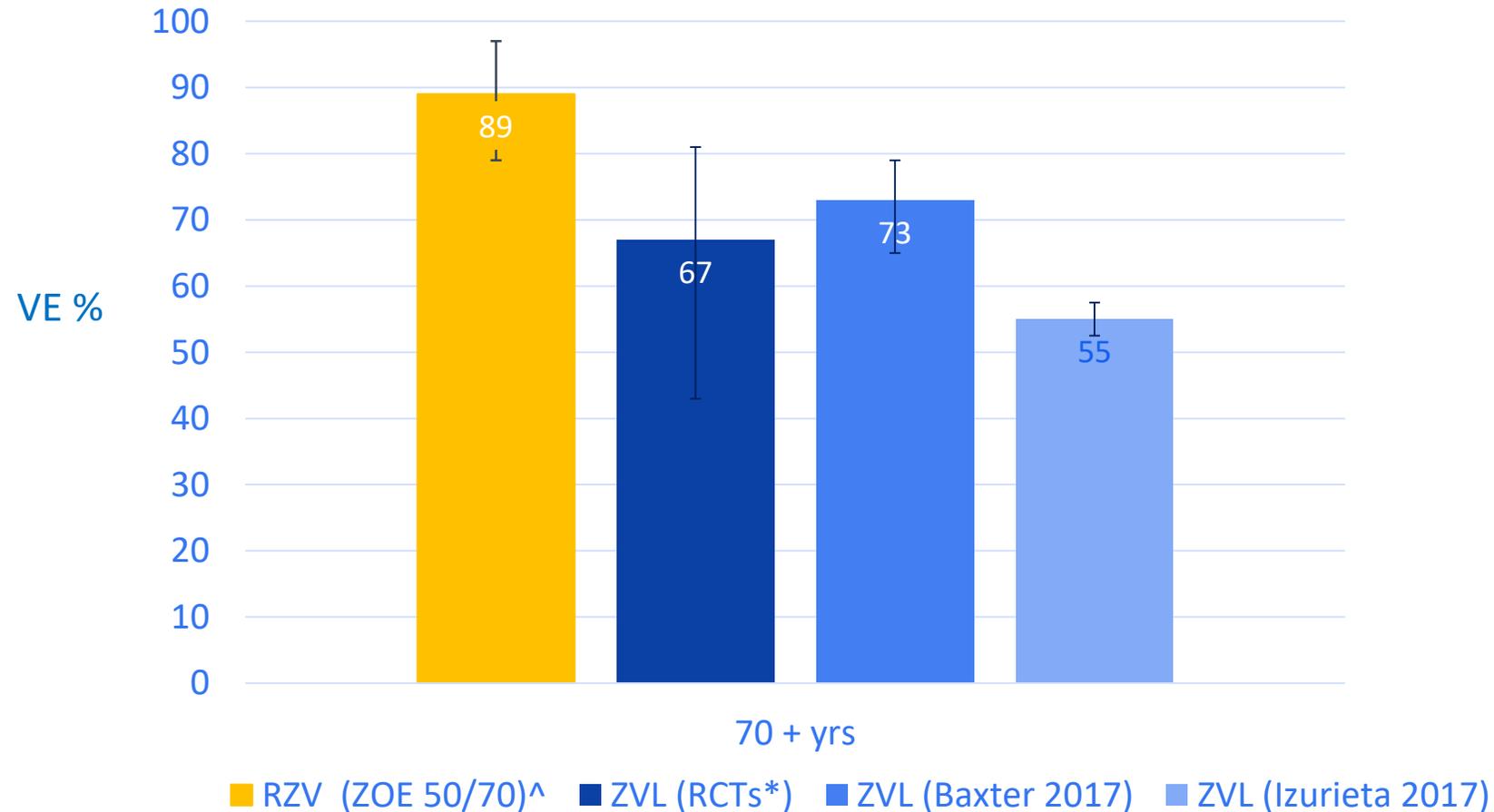


[‡] Median follow up may be less than 3 yrs: Schmader 2012= 1.3 yrs

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

^{*} RCTs= 50-59 yrs: Schmader 2012, 60-69 and 70+ yrs: Oxman 2005,

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



^ Pooled ZOE 50/70: Cunningham 2016

* 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**

- ❑ **RZV may be co-administred 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 ≥ 5 years after ZVL
- ❑ Consider a shorter interval if individual is >70 yrs-- protection from ZVL is 38% over ~ 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?