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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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.

Dooling et al. MMWR Jan 25, 2018

Herpes Zoster Epidemiology

Herpes Zoster & Postherpetic Neuralgia (PHN):

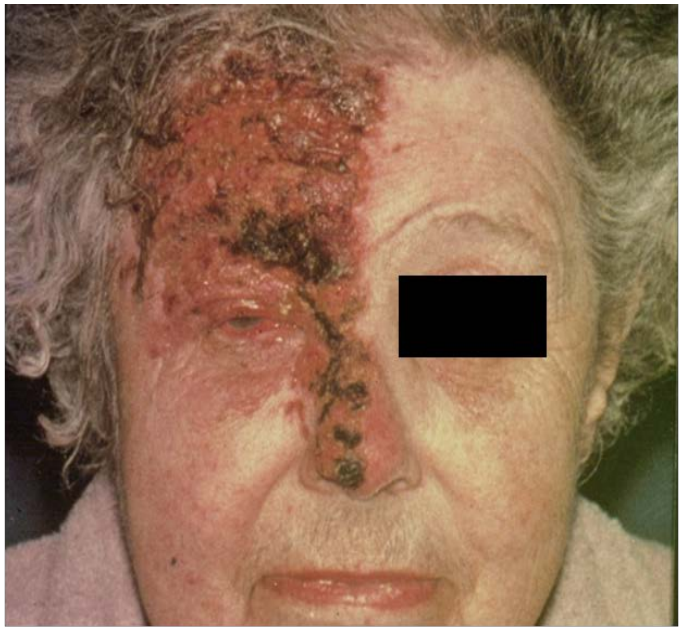
Herpes Zoster

- About 90% of HZ episodes associated with pain
- Treatment: antivirals reduce duration of rash and pain[1]

PHN

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

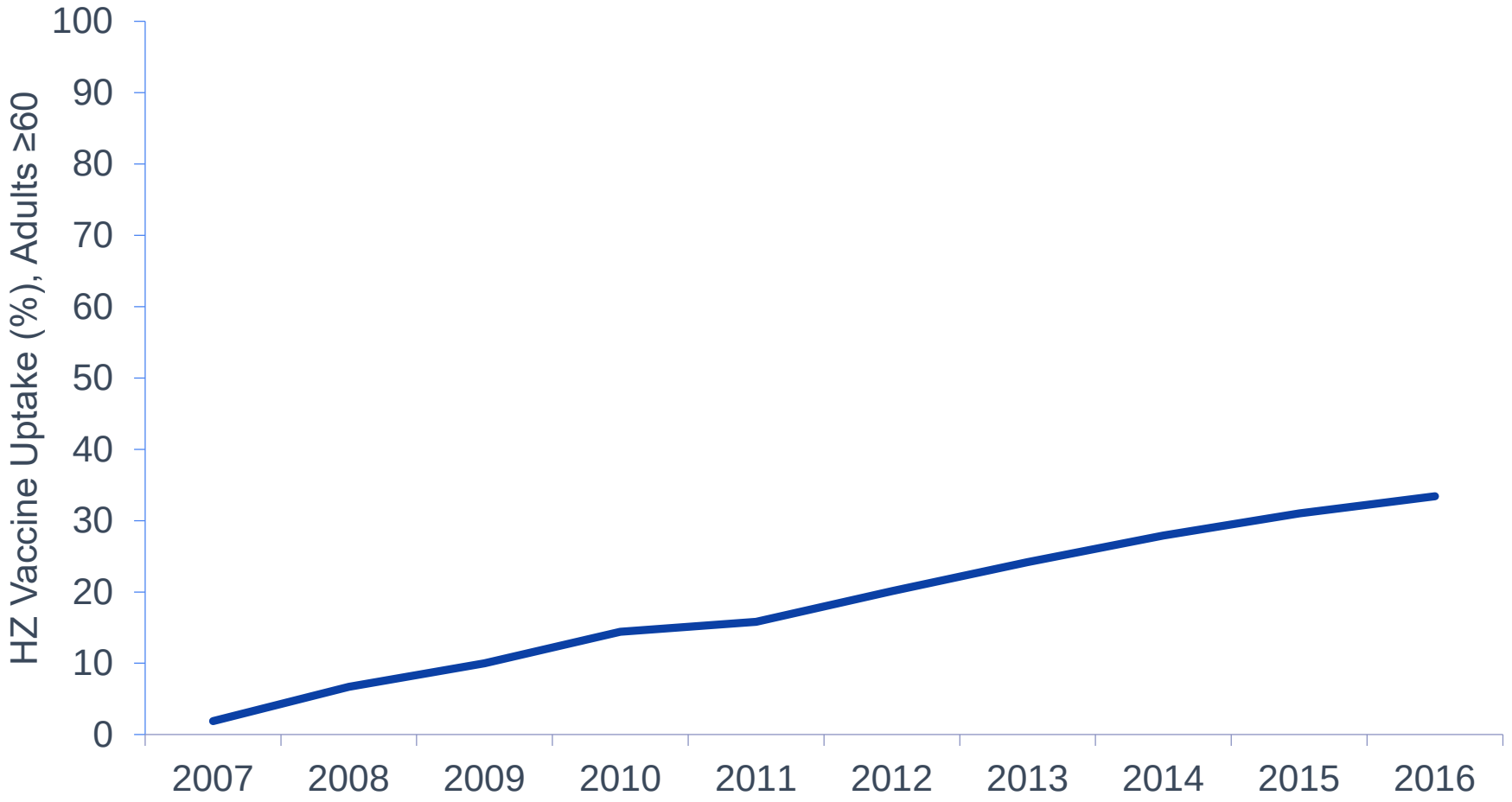
“My PHN is worse than my cancer and chemotherapy… [it] has made me depressed and suicidal in the past”



Courtesy of M.Oxman

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

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(Lu et al, Vaccine 27:882-7); 2008-13: NHIS (Am J Prev Med 40:e1-6 & MMWR February 5, 2016 / 65(1);1–36), 2016 CDC, unpublished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

ACIP Recommendations

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 ≥ **85%** for 4 years following vaccination in ≥ 70 year olds

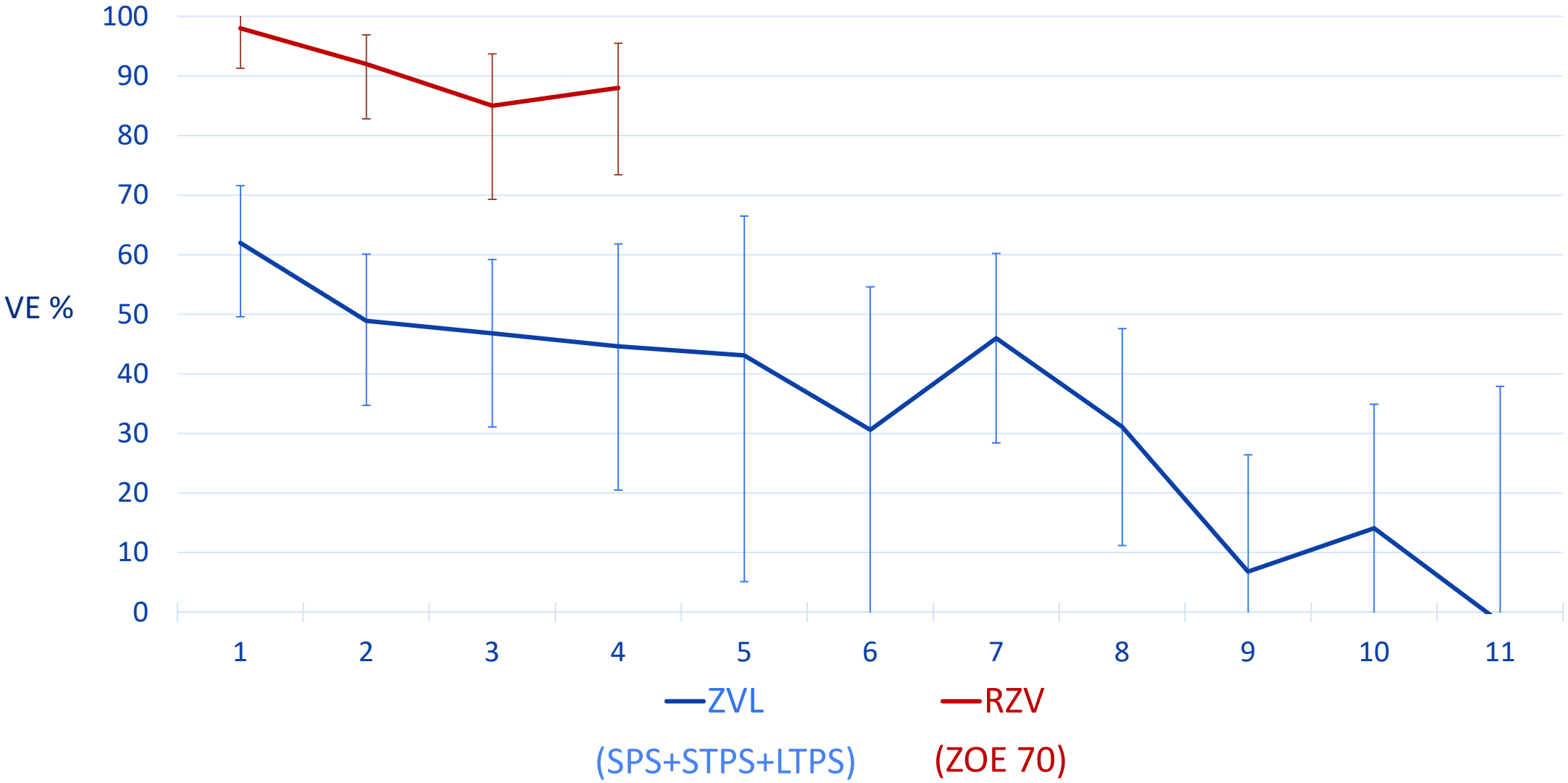
- **Harms:**
  - No differences detected between vaccinated and comparison populations for serious adverse events
  - Grade 3 reactions more commonly reported in vaccinated groups (17%) compared to placebo (3%)

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

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.

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%

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)

Shingrix- Clinical Guidance

Shingrix- Recombinant Zoster Vaccine (RZV) Clinical Guidance

- **Refrigerator stable, requires reconstitution prior to administration**
  - adjuvant suspension (diluent) + lyophilized gE protein
  - After reconstitution, administer RZV immediately or store between 2-8^{o}C (max=6hrs)
- **2 doses at 0 & 2-6 months**
- **Administer IM**

- **RZV may be co-administered with other vaccines**
  - RZV+ QIV (Fluarix)
  - RZV+ PPSV23 (Pneumovax23) or Tdap (Boostrix)
  - RZV+ Fluad

  - 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 >70yrs-- protection from ZVL is 38% over ~3yrs
- Minimal interval between ZVL and RZV= 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%)
- **1 in 6 patients may experience reactogenicity that prevents regular activities.**
- **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?