2018 Adult Immunization Schedule
What’s New?
Disclosures

• I have no financial interests in immunizations discussed here

• I may discuss off-label use of licensed vaccines
Herpes Zoster (HZ) and Postherpetic Neuralgia (PHN) epidemiology, United States

- ~1 million cases annually\(^1,2\)
- Incidence of HZ and PHN increase with age, \(^2,3,4\)
- HZ (cases per 1,000 population)
  - Children: <1
  - 80 years and older >15
- PHN
  - 50 years and older: 10-18% of HZ cases develop PHN
- Zoster Vaccine Live (ZVL, zostavax) licensed in U.S. since 2006
  - 33% of individuals 60 years and older report receipt.\(^5\)

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 CDC, provisional unpublished data from NHIS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**

Recombinant Zoster Vaccine - Shingrix

- **2 components**
  - Glycoprotein E – recombinant protein
  - Adjuvant ASO$_1^B$

- **Efficacy & safety evaluated in 2-part, phase III RCT**
  - >30,000 subjects

- **FDA licensure on Oct 20, 2017**
  - https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm581491.htm
# Zoster vaccines – Important Differences!

<table>
<thead>
<tr>
<th>Zoster vaccine</th>
<th>Storage</th>
<th>Route of injection</th>
<th>Doses in Series</th>
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<tbody>
<tr>
<td>RZV (shingrix)</td>
<td>Refrigerator</td>
<td>IM</td>
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<td>ZVL (zostavax)</td>
<td>Freezer</td>
<td>SQ</td>
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Improperly stored vaccine is useless!
ACIP Recommendations
Zoster vaccines – General Use

• RZV (shingrix) may be used in adults aged ≥50 years, irrespective of prior receipt of varicella vaccine or ZVL (zostavax), and does not require screening for a history of chickenpox (varicella).
• ZVL remains a recommended vaccine for prevention of herpes zoster in immunocompetent adults aged ≥60 years.
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)
  - Efficacy ≥ 85% for 4 years following vaccination in ≥ 70 year olds

- **Harms:**
  - Serious adverse events - No differences detected between vaccinated and comparison populations
  - Grade 3 reactions more commonly reported in vaccinated groups (17%) compared to placebo (3%)
RZV is preferred over ZVL (but no head-to-head trial)

Efficacy
- Estimates of efficacy against HZ higher across all age groups:
  - 60-69 years: 97% vs. 64%
  - 70-79 years: 91% vs. 41%
  - >80 years: 91% vs. 18%
- Waning apparently slower than ZVL over the first 4 years
- Expected to prevent many more cases of HZ and PHN compared to ZVL

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

Economics
- Model - RZV prevents more disease, decreases overall costs (vaccine + expected disease)
HZ - Vaccine efficacy and effectiveness for RZV and ZVL, by age group, during the first 4\(\ddagger\) years following vaccination

\(\ddagger\) Median follow up may be less than 3 yrs: Schmader 2012= 1.3 yrs

\(^\wedge\) 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,
PHN - Vaccine efficacy and effectiveness 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,
Note: The Shingles Prevention Study, Short-term Persistence Study, and Long-term Persistence Study followed the same study population over time.
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\(^1\)
- 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
ACIP Recommendations
Zoster vaccines – Dosing Schedule

- Following dose #1 of RZV, dose #2 should be given 2–6 months later.
  - If dose #2 of RZV is given <4 weeks after #1, repeat dose #2.
  - 2 doses of RZV are necessary regardless of prior history of herpes zoster or prior receipt of ZVL.
  - Based on expert opinion, RZV should not be given <2 months after prior receipt of ZVL.
ACIP Recommendations
Zoster vaccines – History of Zoster

- Persons with a history of zoster should receive shingles vaccine.

- If a patient is experiencing an episode of herpes zoster, vaccination should be delayed until the acute stage of the illness is over and symptoms abate.
ACIP Recommendations
Zoster vaccines – Co-morbidity

• Persons with **chronic medical conditions** (e.g., chronic renal failure, diabetes mellitus, rheumatoid arthritis, and chronic pulmonary disease) should receive RZV.

• **Immunocompromised persons.** No recommendations yet
  ▪ To be discussed as additional data become available.
ACIP Recommendations
Zoster vaccines – Recap

Age 50 years and older
• Administer 2 doses of RZV 2–6 months apart regardless of
  ▪ past episode of herpes zoster, or
  ▪ receipt of past doses of ZVL
    o wait at least 2 months after ZVL before dose of RZV.

Age 60 years or older
• Administer either RZV (preferred) or ZVL
  ▪ wait at least 2 months after ZVL before dose of RZV
Shingrix- Recombinant Zoster Vaccine (RZV)
Clinical Guidance

CONTRAINDICATION
- History of severe allergic reaction, such as anaphylaxis, to any component of RZV

PRECAUTIONS
- Current herpes zoster infection
- Pregnancy and breastfeeding
Shingrix- Recombinant Zoster Vaccine (RZV) Reactogenicity

- Before vaccination, counsel about expected reactogenicity
  - pain (78%)
  - myalgia (45%)
  - fatigue (45%)

- Reactions to 1st dose didn’t predict reactions to 2nd dose

- Vaccine recipients should be encouraged to complete the series even if they experienced a grade 1–3 reaction to the first dose.
RZV may be co-administered with other vaccines

- RZV+ QIV (Fluarix) -- no interference or safety problems
- RZV+ PPSV23 (Pneumovax23) or Tdap (Boostrix) – studies ongoing
- RZV+ Fluarix – have not been studied

https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm581491.htm
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Mumps

- Outbreaks in 2016 and 2017
  - Mostly in young adults in college settings.
  - Also, >3,000 cases in Arkansas outbreak
  - Intensity of exposure to the virus in close-contact settings (such as a college campus)

https://www.cdc.gov/mumps/outbreaks.html
Other Changes to Schedule - Mumps

- Persons ≥12 months who previously received ≤2 doses of mumps-containing vaccine and are identified by public health authorities to be at increased risk during a mumps outbreak should receive a dose of mumps-virus containing vaccine.
Reminder to vaccinate persons with chronic liver disease

- Hepatitis C virus [HCV] infection
- Cirrhosis
- Fatty liver disease
- Alcoholic liver disease
- Autoimmune hepatitis
- ALT or AST level greater than twice the upper limit of normal
Low coverage rates, HAV + HBV vaccines

2014 and 2015 National Health Interview Surveys
Adults aged ≥ 18 years self-reporting receipt of vaccines

HAV
- 19% ≥1 dose  12% ≥2 doses  Chronic Liver Disease (CLD)
- 15% ≥1 dose  9% ≥2 doses  No CLD

HBV
- 36% ≥1 dose  29% ≥3 doses  CLD
- 30% ≥1 dose  25% ≥3 doses  No CLD

Yue X et al., Vaccine 2018;36:1183  https://doi.org/10.1016/j.vaccine.2018.01.033
## Hepatitis A Outbreak Cases as of 11/10/17
### Hospitalization or Death for Persons with CLD

<table>
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<th>San Diego</th>
<th>Santa Cruz</th>
<th>Los Angeles</th>
</tr>
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<tr>
<td><strong>Start of outbreak</strong></td>
<td>11/2016</td>
<td>4/2017</td>
<td>9/2017</td>
</tr>
<tr>
<td><strong>Cases</strong></td>
<td>546</td>
<td>76</td>
<td>11</td>
</tr>
<tr>
<td><strong>Deaths</strong></td>
<td>20</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Homeless or illicit drug use (%)</strong></td>
<td>69%</td>
<td>81%</td>
<td>55%</td>
</tr>
<tr>
<td><strong>Hospitalized (%)</strong></td>
<td>68%</td>
<td>43%</td>
<td>73%</td>
</tr>
<tr>
<td><strong>HCV or HBV coinfection (%)</strong></td>
<td>19%</td>
<td>39%</td>
<td>-</td>
</tr>
<tr>
<td><strong>Male (%)</strong></td>
<td>68%</td>
<td>63%</td>
<td>91%</td>
</tr>
<tr>
<td><strong>Median age (years)</strong></td>
<td>43</td>
<td>37</td>
<td>40</td>
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New Hepatitis B Vaccine for Adults

- Single-antigen HepB (HEPLISAV-B, Dynavax Technologies Corp.)
- 11/2017: Licensed by FDA for persons ≥ 18y years of age
- 2/2018: ACIP voted to recommend – published recommendations to follow
- Joins other inactivated HBV vaccines in U.S
  - Engerix-B, Recombivax HB, Pediarix, Twinrix

- Yeast-derived recombinant HBsAg
- 1018 adjuvant
  - 22-mer oligonucleotide sequence containing CpG that binds Toll-like receptor 9 to stimulate directed immune response
- 2 doses given at least 1 month apart
Heplisav-B – Seroprotection and Safety

- **Immunogenicity**
  - Healthy: 90%–100% vs. 71%–90% (3 doses Engerix-B)
  - Diabetes Type II: 90% vs. 65% (3 doses Engerix-B)
  - Chronic kidney disease: 90% (3 doses) vs. 81% (4 double doses Engerix-B)

- **Safety and reactogenicity**
  - Mild adverse events 46% vs. 46% (Engerix-B)
  - Serious adverse events 5% vs. 6% (Engerix-B)
  - Cardiovascular events 0.27% vs. 0.14% (Engerix-B)
  - Potentially immune-mediated events (e.g., granulomatosis + polyangiitis, Grave’s disease) 0.1%–0.2% vs. 0%–0.7% (Engerix-B)


Influenza – 2/18 ACIP Meeting

- Live attenuated influenza vaccine returns as one of many vaccine options for 2018-2019 influenza season
- 2017-18 (A/Slovenia) vs. 2015-16 (A/Bolivia) H1N1 strains
  - Increased reproduction in human cells, more immunogenic
  - No effectiveness data yet
- License indication unchanged: healthy, 2-49 years of age
WHO recommends that vaccines for use in the 2018-2019 northern hemisphere influenza season contain:

**Trivalent**
- A/Michigan/45/2015 (**H1N1**)pdm09-like virus;
- A/Singapore/INFIMH-16-0019/2016 (**H3N2**) - **CHANGE**
- B/Colorado/06/2017-like virus (**B/Victoria/2/87** lineage) – **CHANGE**

**Quadrivalent** – above +
- B/Phuket/3073/2013-like virus (**B/Yamagata/16/88** lineage)

Hepatitis A Post-exposure Prophylaxis

ACIP vote February 22, 2018 – not final until published

- Ages 12 months and older - Hep A vaccine
- Ages 40 years and older
  - Hep A vaccine
  - +/- Immune globulin, “depending on the provider's risk assessment.”
- Age 6-12 months travelling internationally
  - Early Hep A vaccine dose
  - + regular 2-dose series on or after 1st birthday
Thank you - Questions?

Many thanks to following CDC staff for sharing their slides:

• Kathleen Dooling, MD MPH  –  Zoster
• David Kim, MD  –  Hepatitis B
Shingrix Rollout for VFA Providers

• Availability of vaccine
  • Timeline uncertain at this time but vaccine should be available in Q2 or Q3 ordering period
  • Reminder it is a 2 dose series licensed down to 50 yrs of age

• Letter describing vaccine recommendations and availability will be released in upcoming weeks

• VFA providers should continue to offer Zostervax until Shingrix is available—do not miss opportunities to vaccinate VFA-eligible patients
## Key Differences Between Zoster IZs

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<th>Zostavax (ZVL)</th>
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<tr>
<td><strong>Storage</strong></td>
<td><strong>Refrigerator</strong> (between 36°F and 46°F) - Store both vials together in refrigerator before reconstitution. <strong>DO NOT FREEZE.</strong></td>
<td><strong>Freezer</strong> (between -58°F and +5°F) for powder containing vial. Diluent should be stored at room temperature or refrigerator.</td>
</tr>
<tr>
<td><strong>Vaccine Type</strong></td>
<td>Recombinant, adjuvanted (non-live)</td>
<td>Live</td>
</tr>
<tr>
<td><strong>Route of Administration</strong></td>
<td>Intramuscular (IM) – 0.5ml / dose</td>
<td>Subcutaneous (SQ) – 0.65ml / dose</td>
</tr>
<tr>
<td><strong>Dose Interval</strong></td>
<td>2 dose series, spaced 2 to 6 months apart*</td>
<td>Single dose</td>
</tr>
<tr>
<td><strong>Recommended Age</strong></td>
<td>≥ 50 years**</td>
<td>≥ 60 years (FDA licensure is ≥ 50 years)</td>
</tr>
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*Minimum interval for Shingrix immunization after Zostavax is 8 weeks.

**Even people who have had shingles or previously got Zostavax can be vaccinated with Shingrix.
Thank you - Questions?

- my317vaccines@cdph.ca.gov