

Adult Vaccines in 2018: Where do we start?

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Objectives

- Discuss recent outbreaks of vaccine preventable disease, how resistance and vaccines have impacted one another, and implications for vaccine advocacy
- Review both the advantages and potential safety concerns with new vaccine adjuvants
- Describe recent updates to ACIP adult immunization recommendations



“You have to admire its simplicity. It's one billionth our size and it's beating us.”

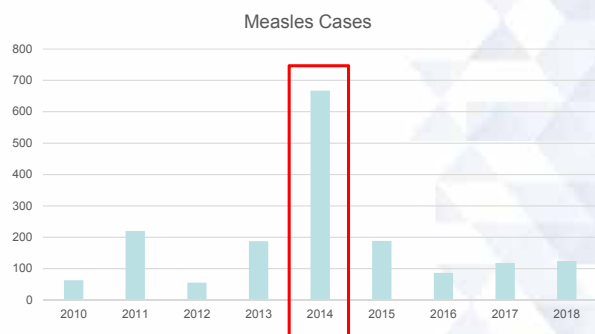
- Dustin Hoffman

“The average person touches their face three to five times every minute. In between that we're touching door knobs, water fountains, and each other.”

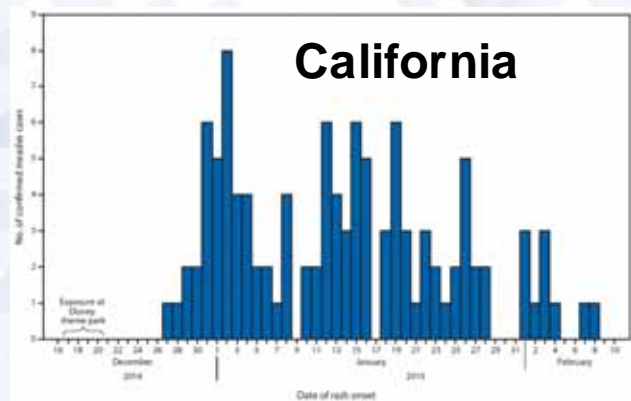
- Kate Winslet



Measles Outbreaks



NCIRD data

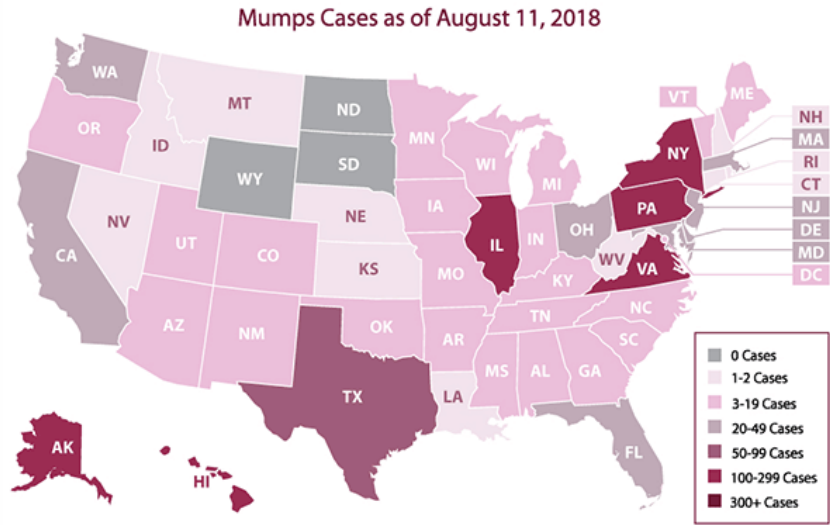


MMWR. February 20, 2015 / 64(06);153-154



<https://www.cdc.gov/measles/cases-outbreaks.html>

From January 1 to August 11, 2018, 47 states and the District of Columbia in the U.S. reported mumps infections in 1,665 people to CDC.



<https://www.cdc.gov/mumps/outbreaks.html>



MMR Vaccine

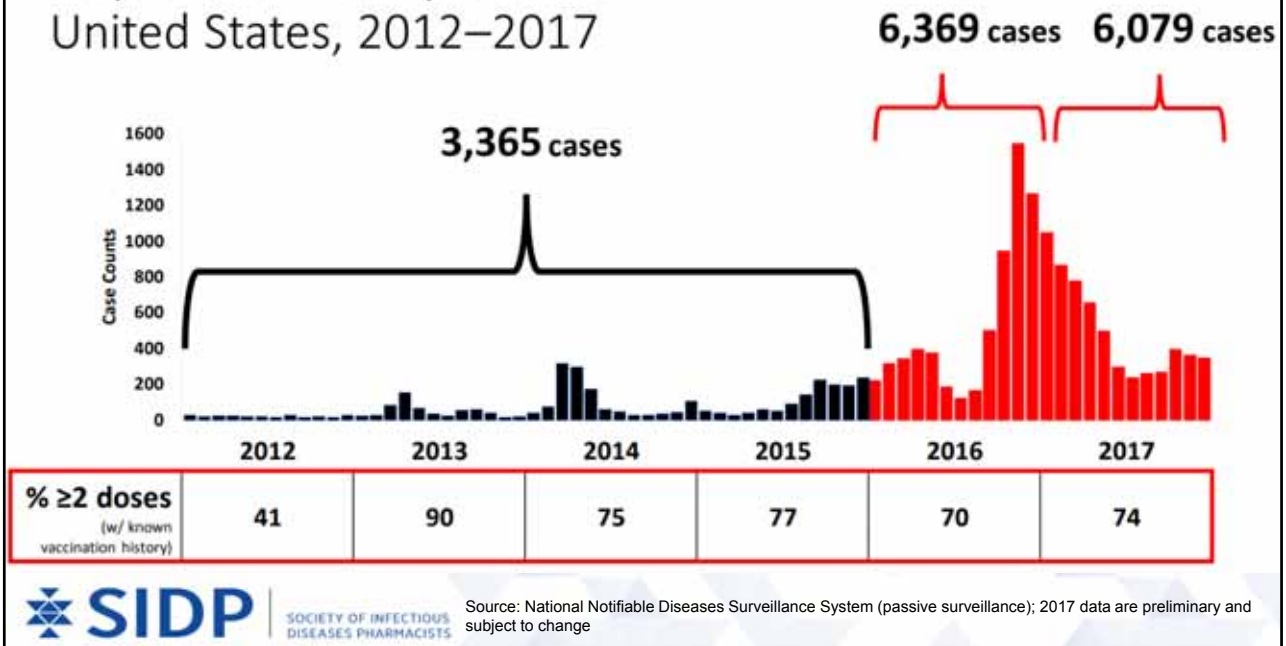
- MMR - Mumps
 - 88% effective 2 doses
 - 78% effective 1 dose

- MMR - Measles
 - 97% effective 2 doses
 - 93% effective 1 dose
- MMR - Rubella
 - 97% effective 1 dose

| Vaccine | Birth | 1 mo | 2 mos | 4 mos | 6 mos | 9 mos | 12 mos | 15 mos | 18 mos | 19-23 mos | 2-3 yrs | 4-6 yrs | 7-10 yrs | 11-12 yrs | 13-15 yrs | 16 yrs | 17-18 yrs |
|--|---|------|-------------|-------|----------------|--------------------------|-------------|--------|-----------|-----------|---------|----------------------|----------|-----------|-----------|--------|-----------|
| Measles, mumps, rubella ^a (MMR) | | | | | See footnote 8 | ← 1 st dose → | | | | | | 2 nd dose | | | | | |
| Vaccine | 19-21 years | | 22-26 years | | 27-49 years | | 50-64 years | | ≥65 years | | | | | | | | |
| MMR ^b | 1 or 2 doses depending on indication (if born in 1957 or later) | | | | | | | | | | | | | | | | |



Reported Mumps Cases: United States, 2012–2017



Third Dose of MMR Vaccine?

- 61-88% 3 MMRs vaccine effectiveness^{1,2,3}
 - Studies had high percentage of patients with 2 doses MMR
 - Three studies ages 9 years through college age
- No serious adverse effects reported after 3 MMR^{2,3,4}
- 3 MMRs appears to provide short-term boost in antibodies and seroconverts most seronegative persons

ACIP Mumps Recommendation

Persons **previously vaccinated with 2 doses** of a mumps virus-containing vaccine who are identified by public health authorities as being part of a group or population at increased risk for acquiring mumps because of an outbreak should receive a **third dose** of a mumps virus-containing vaccine to improve protection against mumps disease and related complications.



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DISEASES PHARMACISTS

Marin M. MMWR Morb Mortal Wkly Rep 2018;67:33–38

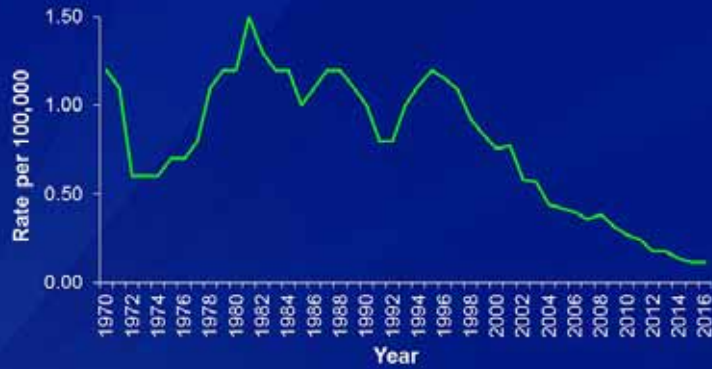
Men B 2013-2014 Outbreak

- Meningococcus serogroup B
- Princeton (9 cases) and UCSB (4)
- 30,000 students vaccinated with Bexsero under IND
- Bexsero (4CMenB)
 - 2 dose (0, 1-6 months)
 - 4 component (non PPS, non conjugate, non adjuvanted)



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Meningococcal Disease Incidence, United States, 1970-2016

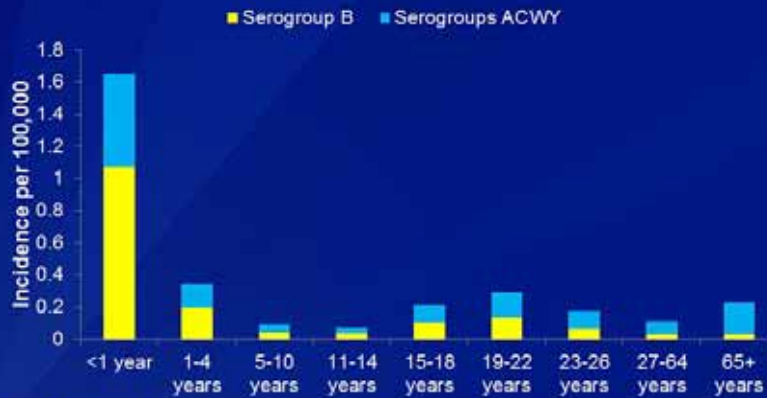


SOURCE: CDC, National Notifiable Diseases Surveillance System



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Meningococcal Incidence by Serogroup* and Age-Group, 2007-2016



SOURCE: CDC, National Notifiable Diseases Surveillance System with additional serogroup data from Active Bacterial Core surveillance and state health departments. Unknown serogroup (19%) and other serogroups (5%) excluded



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Meningococcal B Vaccines

- Trumenba
 - 3-dose series (0, 1-2, 6 months)
 - 2-dose series (0, 6 months)
 - Choice depends upon risk of exposure and patient's susceptibility to Men B disease
- Bexsero
 - 2-dose series (0, 1-6 months)



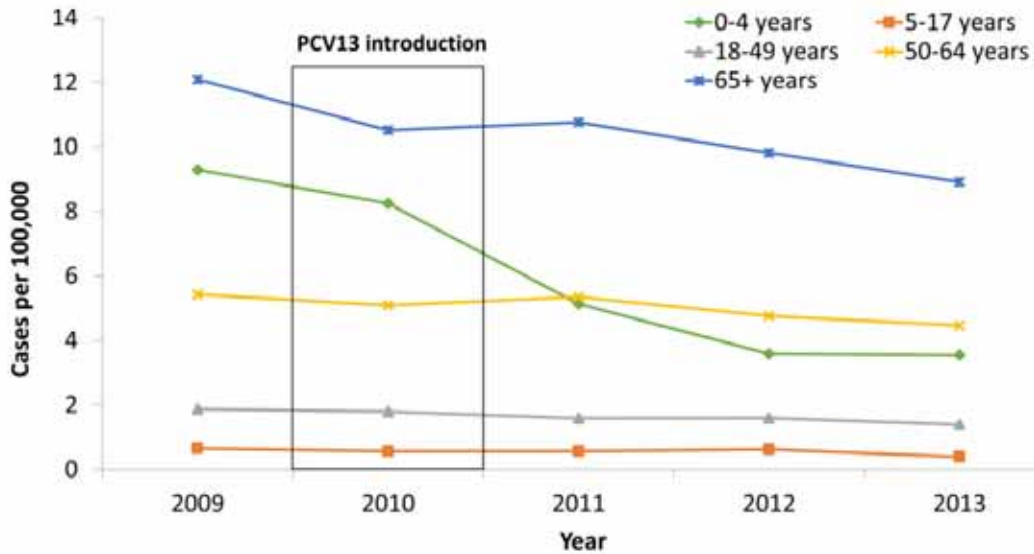
ACIP Recommendations

- Routine use of MenB vaccines in persons at increased risk for serogroup B meningococcal disease, including:
 - During outbreaks of serogroup B meningococcal disease.
 - College campuses that have recently experienced an outbreak of serogroup B meningococcal

"A serogroup B meningococcal (MenB) vaccine series may be administered to adolescents and young adults **16 through 23 years** of age to provide short-term protection against most strains of serogroup B meningococcal disease. The preferred age for MenB vaccination is 16 through 18 years of age **(Category B)**"



Incidences of antimicrobial nonsusceptible IPD



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CDC Active Bacterial Core surveillance, 2009 to 2013

Pneumococcal Vaccine Timing

Age 19-64 Years With Underlying Condition(s)

- Prior doses count towards doses recommended below and do not need to be repeated.
- If PPSV23 given previously – wait one year before giving PCV13
– for group B, wait at least five years before giving a second dose of PPSV23.
- No more than two doses of PPSV23 recommended before 65th birthday and one dose thereafter.

A. Smoker, or

Chronic conditions:

- heart disease (excluding hypertension)
- lung disease (including asthma)
- liver disease (including cirrhosis)
- diabetes
- alcoholism

PPSV
23

B. Immunocompromised (including HIV infection),

- ##### Chronic renal failure, Nephrotic syndrome, or Asplenia (including sickle cell)

PCV
13

8 weeks

PPSV
23

5 years

PPSV
23

C. CSF leaks or Cochlear implants

PCV
13

8 weeks

PPSV
23



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<http://eziz.org/assets/docs/IMM-1152.pdf>

Pneumococcal Vaccine Timing - Adults

Age 65 Years or Older

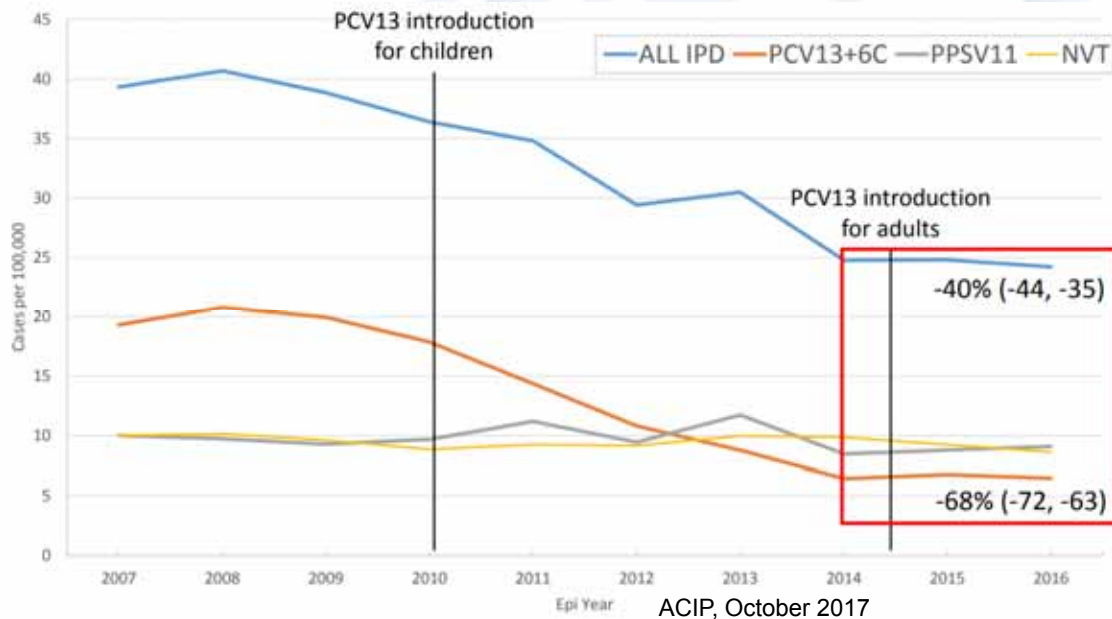
• If PCV13 was given before age 65 years, no additional PCV13 is needed.



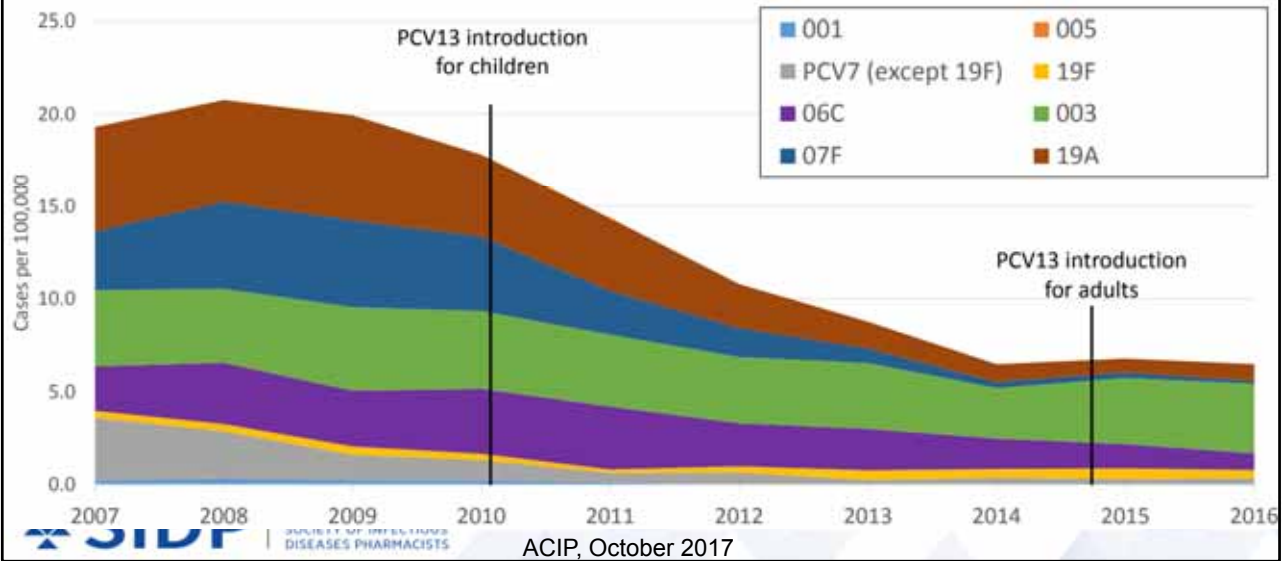
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<http://eziz.org/assets/docs/IMM-1152.pdf>

IPD rates among adults ≥ 65 years, 2007–2016

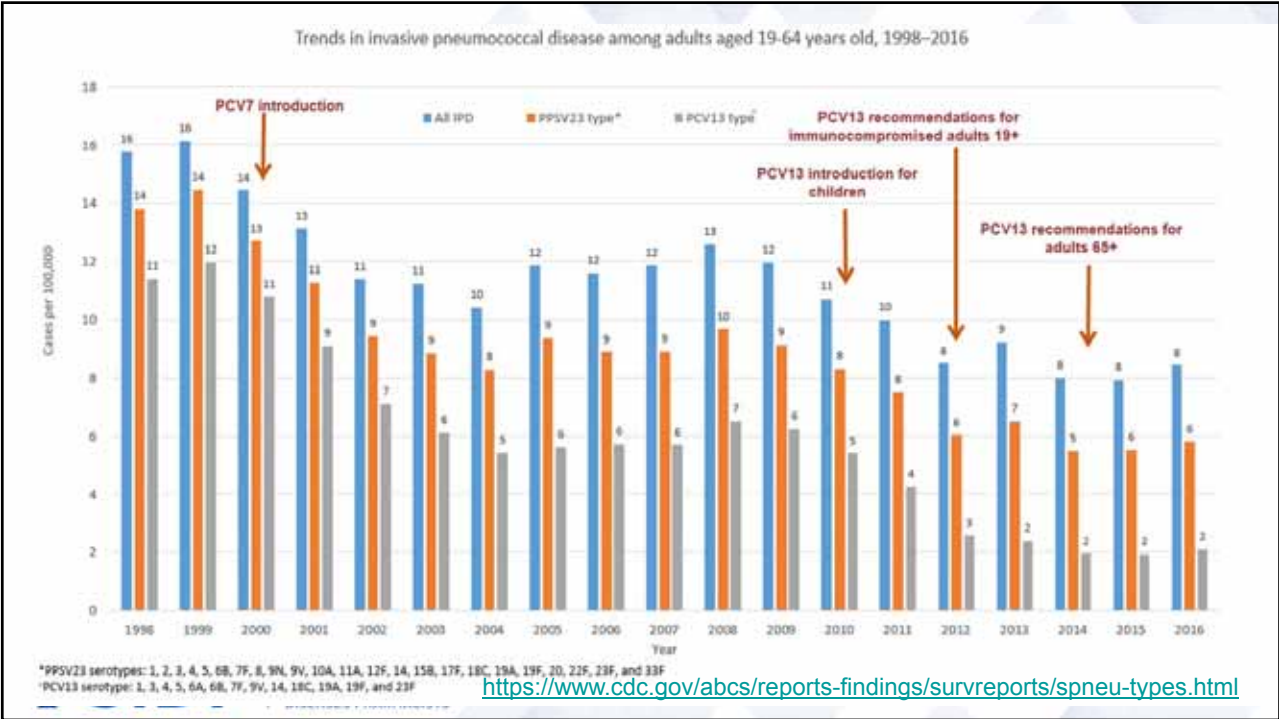
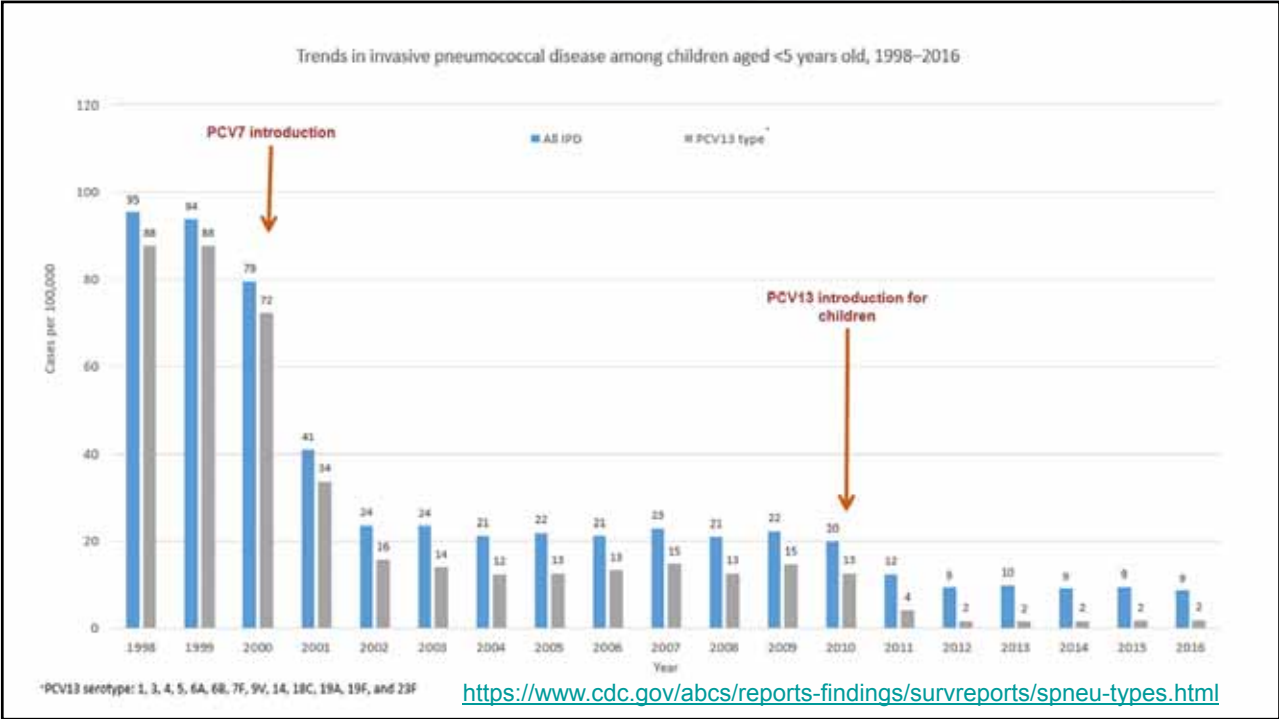


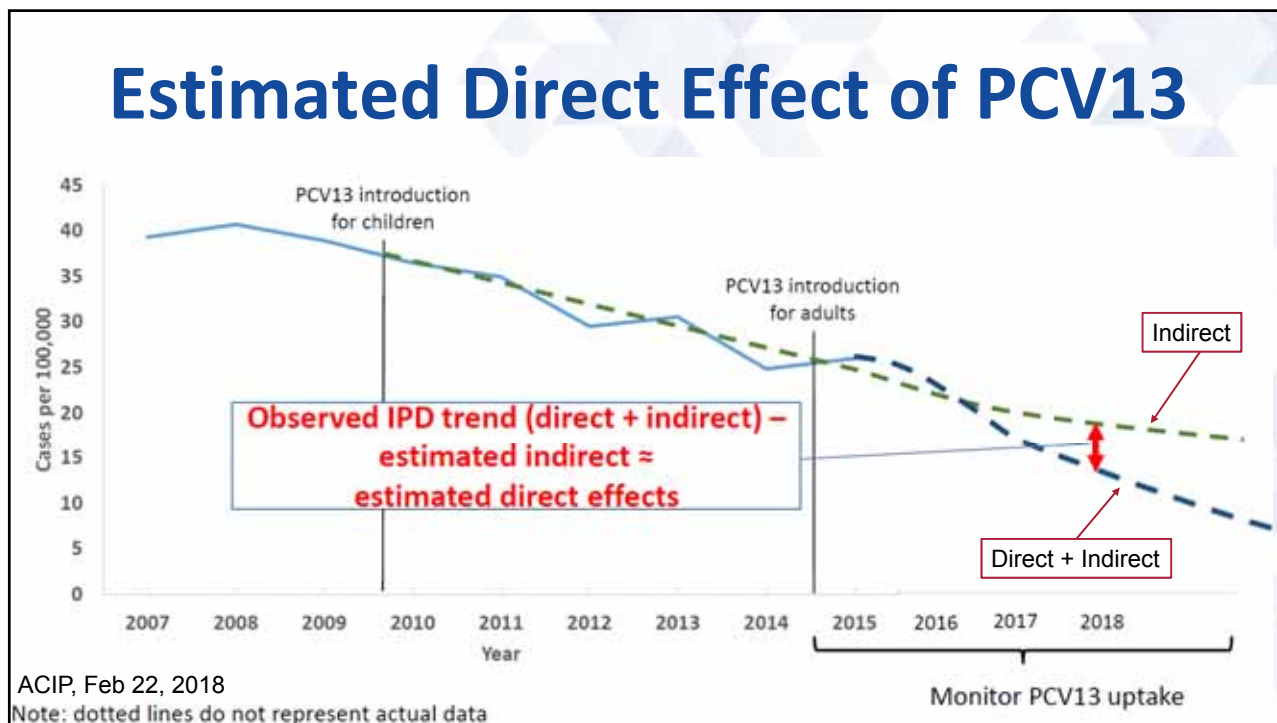
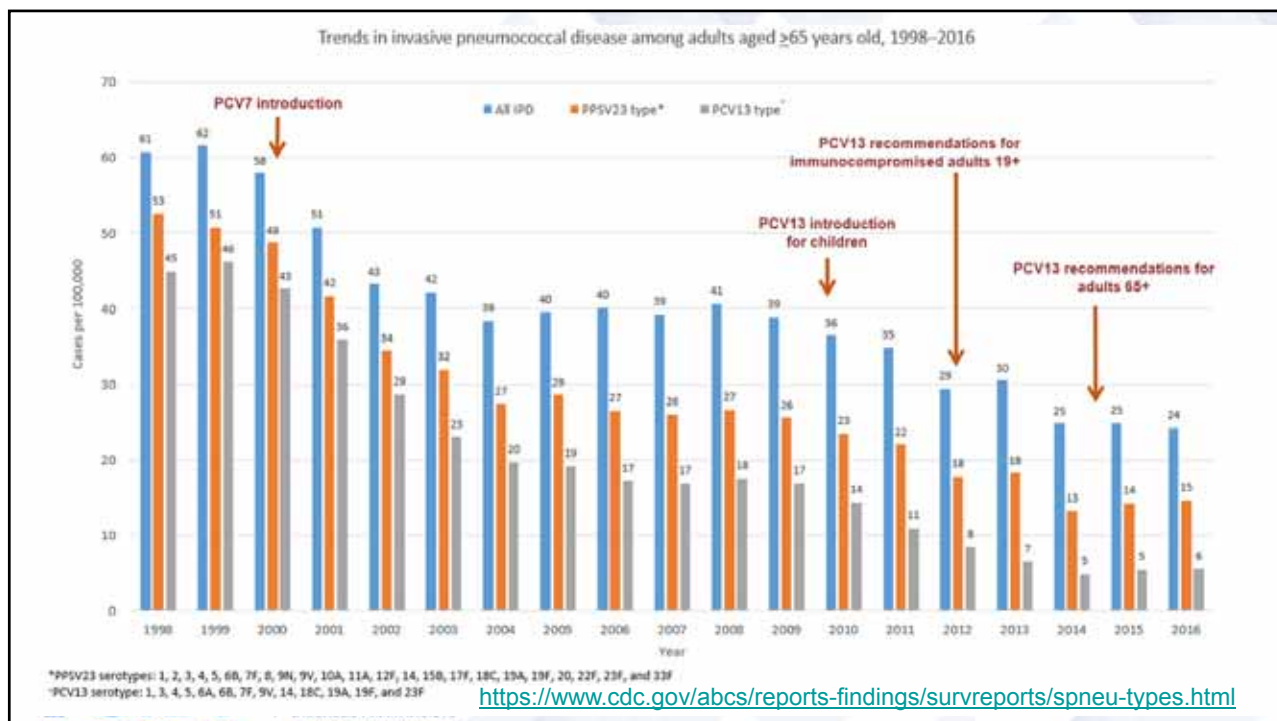
IPD rates among adults ≥ 65 years by PCV13 plus 6C serotypes, 2007–2016



PCV13 Impact on IPD

- Pneumococcal carriage among adults ≥ 65 years old very low (1.8%)
 - PCV13-type carriage 0.2% in 2015-2016
- PCV13 coverage ≥ 65 years old $\sim 40\%$
- Invasive pneumococcal disease (IPD)
 - PCV13-type IPD declined among all age groups
 - IPD incidence in adults ≥ 65 years old plateaued in 2014-2016
 - Modeled direct and indirect effects project relatively few cases prevented
 - Serotype 3 IPD does not follow the same pattern as other PCV13-types





Influenza Vaccine Excipients

Residuals

- Inactivating: formaldehyde
- Antibiotics: Neomycin, Polymyxin B
- Egg protein

Additives

- stabilizers: albumin, gelatin
- buffers: phosphate

Preservatives

(thimerosal, EDTA, phenol)



Adjuvants

(Aluminum, MF59, ASO, CpG)



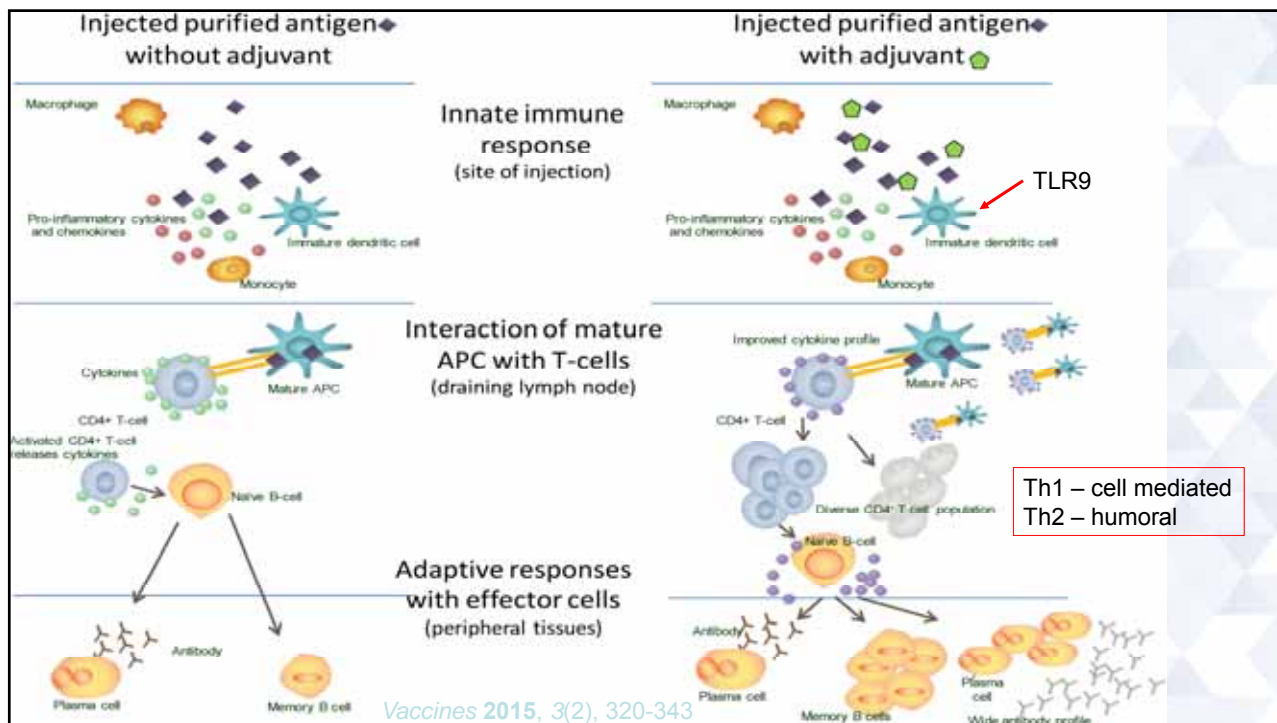
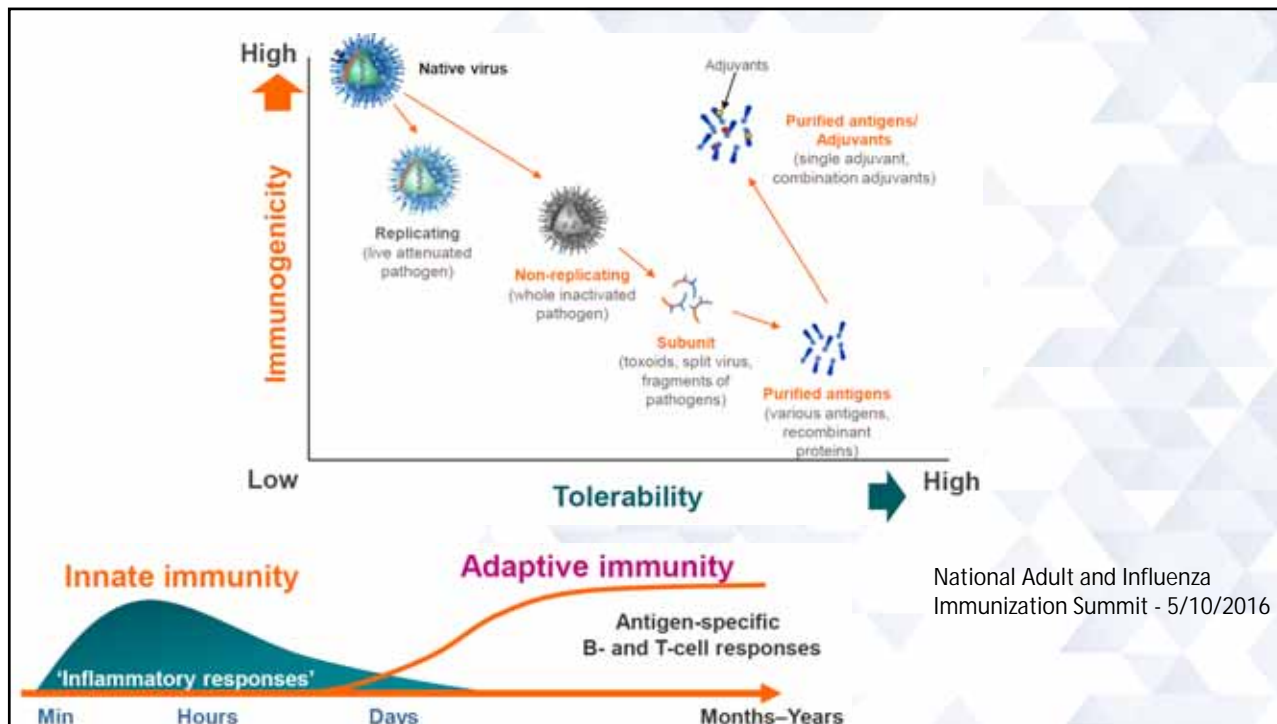
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Adjuvants

- Benefits
 - Improve immunogenicity
 - Reduce dose of the vaccine antigen
 - Reduce the number of doses needed for immunity
 - Improve efficacy in special populations
 - ◆ Newborns, elderly, immunocompromised, renal, etc
- Challenges
 - Increased reactogenicity
 - Potential for pre-existing immunity to carrier protein
 - Need to be approved by the FDA in addition to the vaccine



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US Vaccine Adjuvants

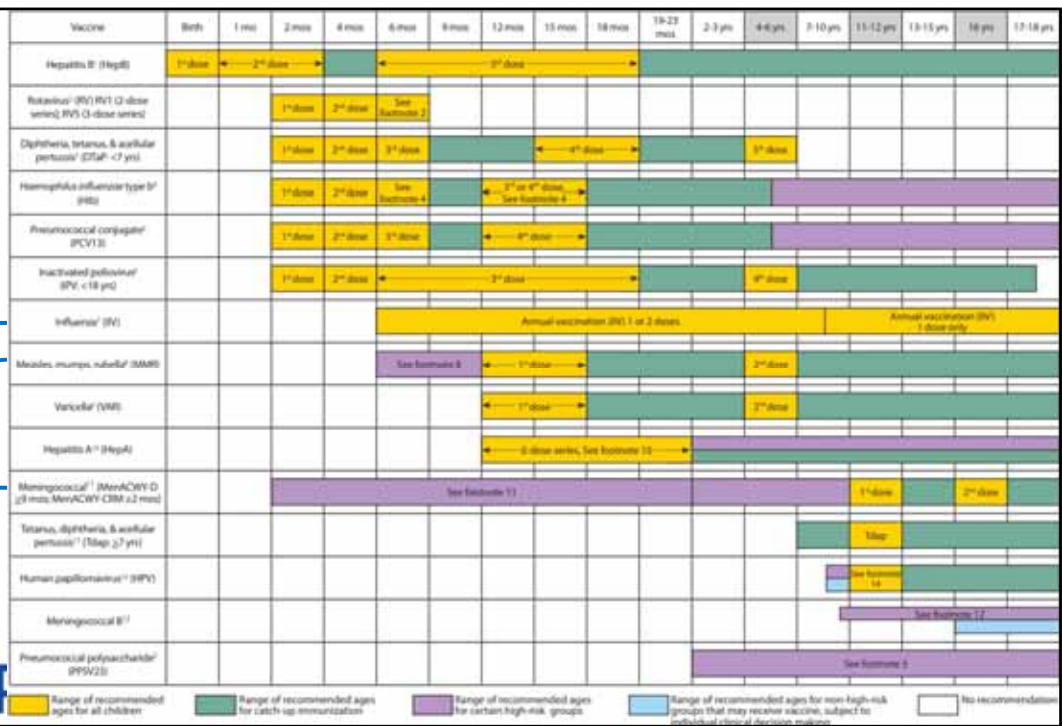
| Adjuvant | Vaccine | Component | Immune Effect |
|---|--|---|---|
| Aluminum (1940s) (hydroxide, phosphate, alum, mixed salts) | D, T, pertussis, IPV, hepatitis A & B, HPV, meningococcal and pneumococcal | Aluminum as salts mixed with antigen (adsorption) | Only increases antibody production; no CMI |
| ASO4 (2009) | Cervarix (not marketed) | Alum + MPL | ↑ Ab and Th1 responses |
| ASO3 (2013) | Pandemic H5N1 vaccine (not commercially available) | VitE + squalene | ↑ Ab and Th1 responses |
| MF59 (2015) | Fluad | Squalene (oil-in-water emulsion) | Increases APC recruitment and activation. Th1/Th2 |
| CpG 1018 (2017) | Hepelisav-B | Synthetic DNA sequences | Enhances B and T cell responses; TLR9 agonist |
| ASO1B (2017) | Shingrix | MPL + QS-21 | |



Vaccine Updates

2018 Pediatric Schedule

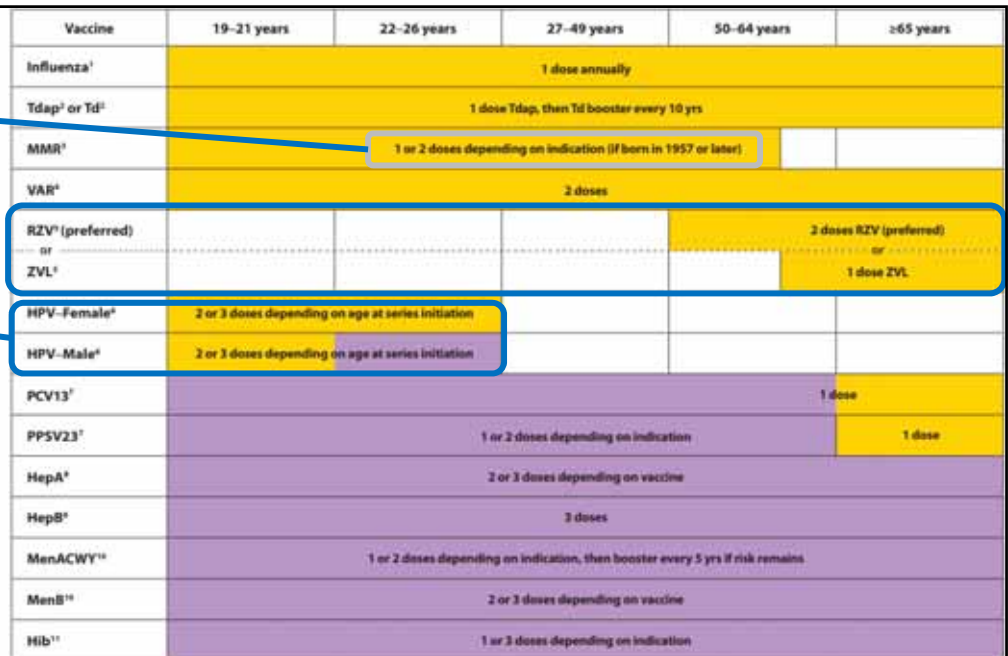
LAIV is back
 3rd dose mumps
 outbreak
 MenHibrix D/C'd



Legend:
 Yellow: Range of recommended ages for all children
 Green: Range of recommended ages for catch-up immunization
 Purple: Range of recommended ages for certain high-risk groups
 Light blue: Range of recommended ages for non-high-risk groups that may receive vaccine, subject to individual clinical decision-making
 White: No recommendation

2018 Adult Schedule

Mumps outbreak
 2 dose: <15 yrs



Legend:
 Yellow: Recommended for adults who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection
 Purple: Recommended for adults with other indications
 White: No recommendation

2018 Adult Schedule

Not Contraindicated

| Vaccine | Pregnancy ^{1,4} | Immu- compromised (excluding HIV infection) ^{5,11,12} | HIV infection CD4+ count (cells/ μ L) ^{13,14} | Asplenia, complement deficiencies ^{15,16,17} | End-stage renal disease, on hemodialysis ¹⁸ | Heart or lung disease, alcoholism ¹⁹ | Chronic liver disease ²⁰ | Diabetes ²¹ | Health care personnel ^{22,23} | Men who have sex with men ^{24,25} |
|--|--|--|---|---|--|---|-------------------------------------|------------------------|--|--|
| Influenza ¹ | 1 dose annually | | | | | | | | | |
| Tdap ² or Td ² | 1 dose Tdap each pregnancy | 1 dose Tdap, then Td booster every 10 yrs | | | | | | | | |
| MMR ³ | contraindicated | | 1 or 2 doses depending on indication | | | | | | | |
| VAR ⁴ | contraindicated | | 2 doses | | | | | | | |
| RZV ⁶ (preferred) or ZVL ⁷ | contraindicated | | 2 doses RZV at age \geq 50 yrs (preferred) or 1 dose ZVL at age \geq 60 yrs | | | | | | | |
| HPV-Female ⁸ | 3 doses through age 26 yrs | | 2 or 3 doses through age 26 yrs | | | | | | | |
| HPV-Male ⁸ | 3 doses through age 26 yrs | | 2 or 3 doses through age 21 yrs | | | | | | 2 or 3 doses through age 26 yrs | |
| PCV13 ⁹ | 1 dose | | | | | | | | | |
| PPSV23 ¹⁰ | 1, 2, or 3 doses depending on indication | | | | | | | | | |
| HepA ¹¹ | 2 or 3 doses depending on vaccine | | | | | | | | | |
| HepB ¹¹ | 3 doses | | | | | | | | | |
| MenACWY ¹² | 1 or 2 doses depending on indication, then booster every 5 yrs if risk remains | | | | | | | | | |
| MenB ¹² | 2 or 3 doses depending on vaccine | | | | | | | | | |
| Hib ¹¹ | 3 doses HibCT recipients only | | 1 dose | | | | | | | |

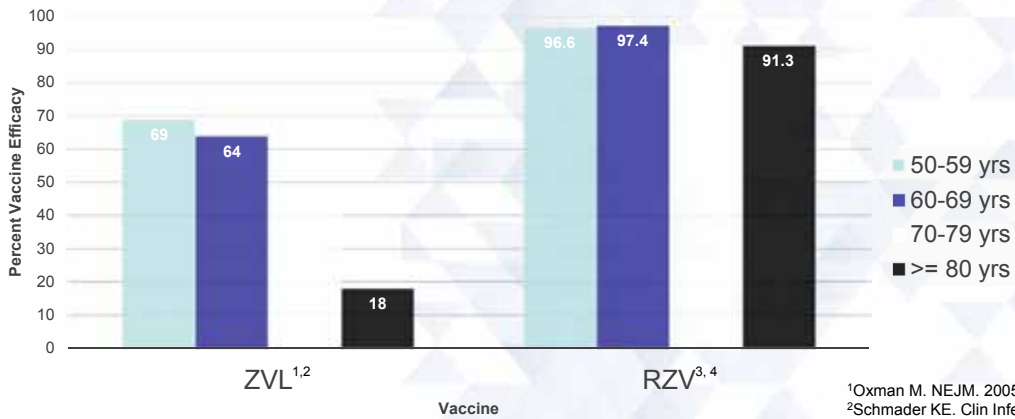
Recommended for adults who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection
 Recommended for adults with other indications
 Contraindicated
 No recommendation

Comparison of Zostavax (ZVL) and Shingrix (RZV)

| | Zostavax (ZVL) | Shingrix (RZV) |
|--------------------------|-----------------------|--|
| Type of vaccine | Live | Inactivated |
| Adjuvant | None | AS01 _B |
| Storage | Frozen | Refrigerate* |
| Regimen | 1 dose | 2 doses (2 months apart) |
| Efficacy against disease | 51.3% (varies by age) | 97.2% \geq 50 years |
| Duration | 7-8 years | 3.2 years (model predicts 19 yrs to zero efficacy) |
| SAE/ADR | 1.9% / 48.3% | 1.1% / 84.4% (17% Grade 3) |

* Discard 6 hours after reconstitution if not administered

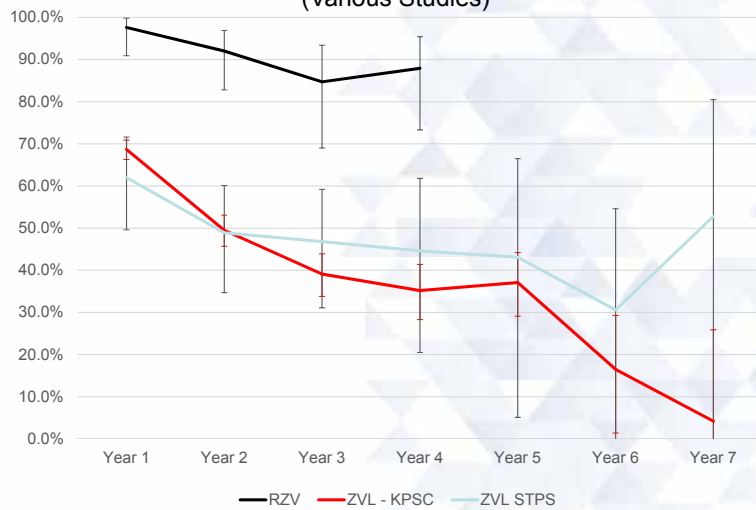
Shingles Vaccines Efficacy Comparison



¹Oxman M. NEJM. 2005;352:2271-84;
²Schmader KE. Clin Infect Dis. 2012;54:922-928;
³Lal et al., NEJM 2015;372(22):2087-96. (ZOE-50);
⁴Cunningham AL. NEJM. 2016;375:1019-32 (ZOE-70)



RZV and ZVL Efficacy Persistence Against HZ (Various Studies)



Cunningham et al., NEJM 2016;375(11):1019-32.
 Oxman et al., NEJM 2005, 352:2271-84.
 Schmader et al., Clin Infect Dis 2012, 55(10):1320-8.
 Tseng et al., J Infect Dis 2016, 123(12):1872-5.



Live Attenuated Influenza Vaccine (LAIV4) Past and Future



Heplisav-B® (Dynavax)

- In the U.S.: 850,000-2.2 million with chronic HBV
 - ↑ since 2014 likely due to heroin and opioid epidemic
 - 5,000 people die from HBV per year from chronic liver disease
- Hepatitis B Vaccine (Recombinant), Adjuvanted – Heplisav-B
 - FDA licensed November 9, 2017 for 18 years and older
 - Series of 2 doses, separated by 1 month
 - Adjuvant stimulates TLR9, combined with HBsAg → elicits anti-HBsAg Ab
 - Seroprotection 90.0%-100.0%
 - ◆ 70.5%-90.2% with existing Hepatitis B vaccines
 - ◆ Better response in diabetes, kidney disease than current HepB vaccines
 - ◆ Better choice for immediate departure travelers
 - Local & systemic AEs similar to other Hep B vaccines
 - ◆ Signal with CV disease – will monitor in post-marketing studies

2018–19 Influenza Vaccines

| Vaccine (manufacturer)* | Approved Age Indications | |
|--|--------------------------|-----------------------|
| Inactivated Influenza Vaccine | | |
| Fluzone (Sanofi Pasteur) IIV4 | 6 months and older | IIV3/4-ID - Withdrawn |
| Fluvirin (Seqirus) IIV3 | 4 years and older | |
| Fluarix (GSK) IIV4 | 6 months and older | |
| FluLaval (GSK) IIV4 | 6 months and older | |
| Afluria (Seqirus) IIV3 | 5 years and older | |
| Afluria (Seqirus) IIV4 | 5 years and older | |
| Fluzone High-Dose (Sanofi Pasteur) IIV3-HD | 65 years and older | |
| Flucelvax (Seqirus)–cell cultured (canine kidney cell) ccIIV4 | 4 years and older | |
| Flublok (Sanofi Pasteur) RIV3/RIV4 | 18 years and older | |
| Fluad (Seqirus) IIV3 | 65 years and older | |
| Live Attenuated Influenza Vaccine | | |
| FluMist (MedImmune) LAIV4 | 2 years to 49 years | |

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