Adult Immunization Update: A Focus on Zoster and Pneumococcal Vaccines

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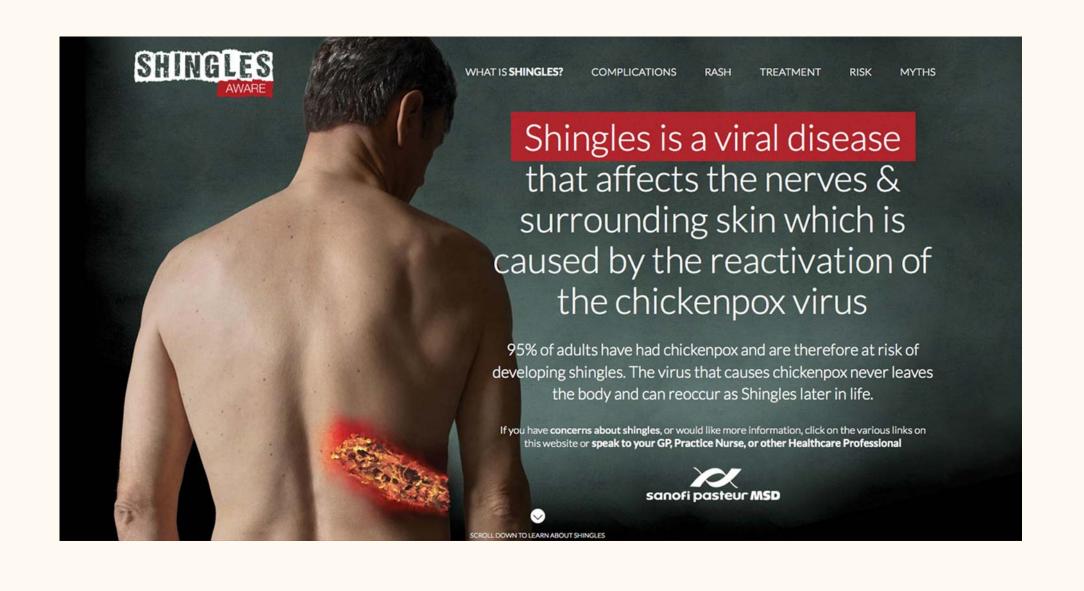
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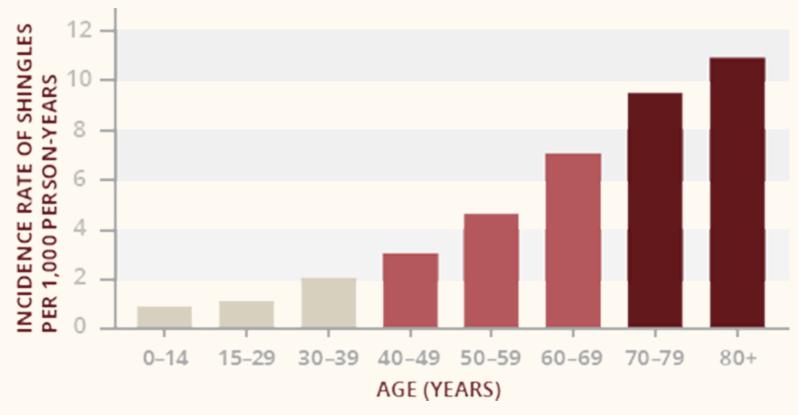
Learning Objectives

By the end of the session, participants may:

- review the pathophysiology related to shingles and pneumonia
- describe the immunization current guidelines to protect against shingles and pneumonia
- evaluate the clinical efficacy of available vaccines



Herpes Zoster Virus Epidemiology

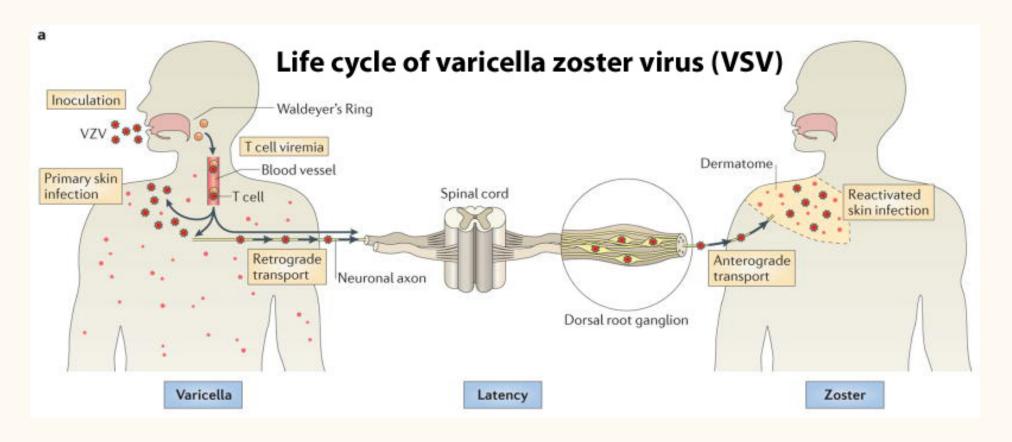


- 1.2 million cases annually in the US
- 1 in 3 people in the US will develop shingles in their lifetime

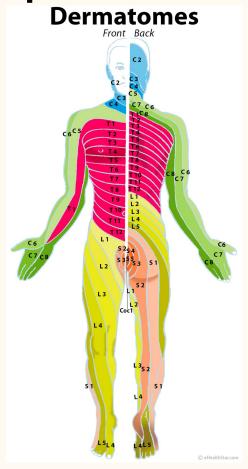
Herpes Zoster Virus Risk Factors

Hx: wild-type VZV Varicella Vaccine Increasing Age Immunocompromising Condition Potential: Gender and Ethnicity

Varicella + Herpes Zoster Virus Pathophysiology



Herpes Zoster Virus Details



- Unilateral vesicular dermatomal eruption
- Impacts T3 to L3 dermatomes
 - <u>+</u> trigeminal nerve
- Localized vs Disseminated
- Initial presentation within 48-72 hours of reactivation
- Vesicular lesions continue to develop for 3-5 days
- Total duration: 7-10 days
- Recovery: 2-4 weeks

Herpes Zoster Virus Complications

NFUROLOGIC

- PHN
- Motor Neuropathy
- Cranial Neuritis
- Meningoencephalitis
- Transverse Myelitis

OPHTHALMIC

- Keratitis
- Iritis
- Retinitis
- Visual Impairment

CUTANEOUS

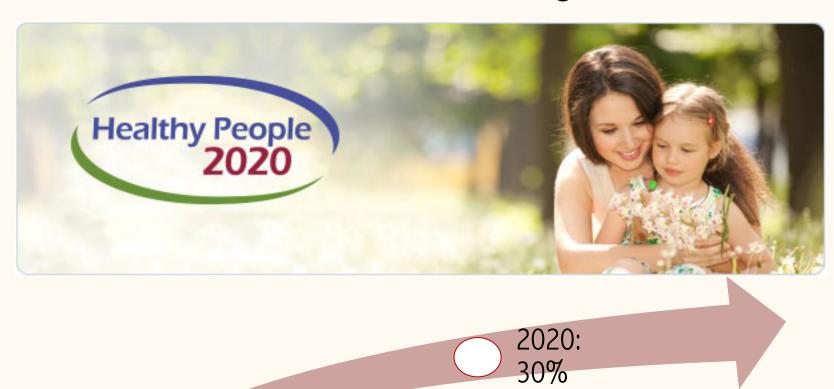
- Bacterial Superinfection
- Scarring
- Disfigurement

VISCERAL

- Pneumonitis
- Hepatitis

Shingles costs approximately \$566 million in healthcare costs Shingles results in the average loss of more than 129 hours per episode.

Herpes Zoster Virus Vaccine Coverage



2008: 6.7%

Herpes Zoster Virus CDC Guidelines



Herpes Zoster Virus Vaccination

ZOSTAVAX SCHEDULE

CDC RECOMMENDATION

≥ 60 Years Old

MERCK RECOMMENDATION

≥ 50 Years of Age

...Why the Difference?..

Herpes Zoster Virus Vaccination

ZOSTAVAX SCHEDULE

...Why the Difference?..

CDC RECOMMENDATION

> 60 Years Old

- Zostavax efficacy wanes within 5 years
- Protection beyond 5 years is uncertain
- Lack of long-term data on < 60 years old

A Comparison: Rates of Zostavax Coverage

UNITED STATES (n=208,505)

2015 COVERAGE:

- 35.4%
 - 35.2% Non-Hispanic White
 - 30.2% Asian
 - 16.7% Hispanic
 - 16.0% Black

CALIFORNIA (n=2,406)

2015 COVERAGE:

- 35.5%
 - 42% Non-Hispanic White
 - 25.4% Other Racial/Ethnic Group

Zostavax Awareness and Coverage

UNITED STATES (n=208,505)

AWARENESS:

• 2007: 27%

• 2014: 73.4%

2015: 86.6%

COVERAGE:

• 2007: 1.9%

• 2014: 31.8%

• 2015: 35.4%

2014 Behavioral Risk Factor Surveillance System

• Age: \geq 60 Years

• Gender: Female

• Employment: Not in Workforce

• Household Income: >\$20,000

Region: Midwest, South

• Perceived Health: Fair — Excellent

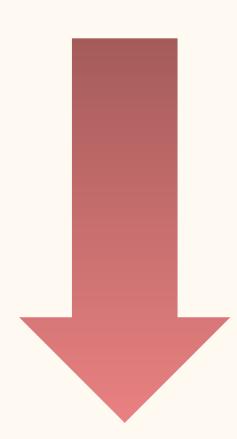
Insurance: Endorses Having

Provider: Endorses Having

• Routine Checkup: Within Previous Year

Barrier to Seeing MD: Endorses No Barrier

Clinical Impact of Zostavax



- 51% decreased shingles incidence
- 61% decreased burden of illness
- 66% decreased PHN incidence

Zostavax Administration Barriers

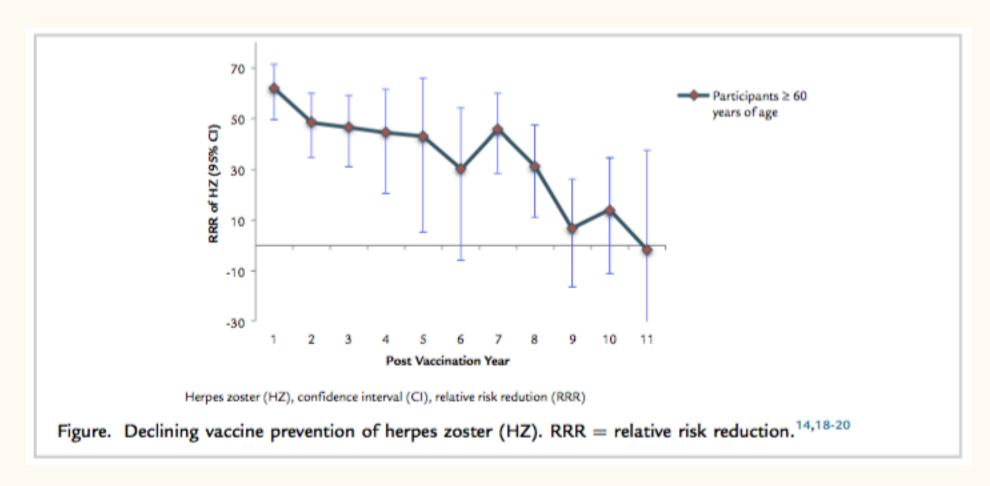
ZOSTAVAX BARRIERS

- High cost
- Freezer storage
- Medicare Part D coverage
- Lack of urgency to vaccinate
- Lack of urgency to be vaccinated

STRATEGIES TO OVERCOME

- Pharmacist involvement
- Reminder/recall systems
- Educational campaigns
- Standing orders
- Linking immunization
- Routine vaccine status assessment

Immunosenesence Related to Zostavax



Determining the Optimal Zostavax Schedule: a CE Analysis

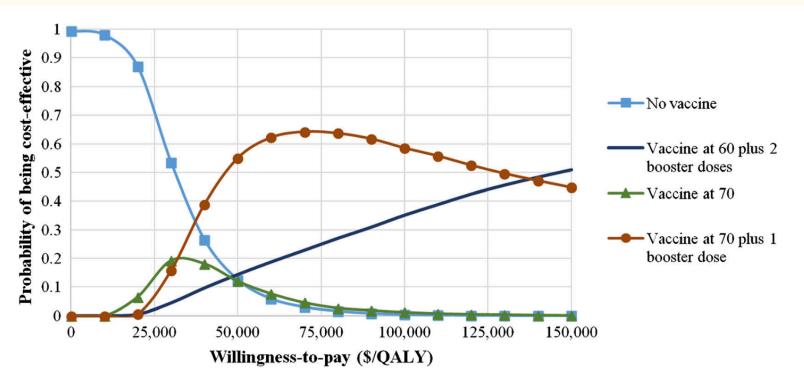


Figure 4. Cost-effectiveness acceptability curve of different vaccination strategies. Only strategies with > 5 % the probability of being cost-effective at different willingness-to-pay values were included. QALY, quality-adjusted life year.

In the Pipeline: Shingrix

Licensed by GlaxoSmithKline

HZ/su contains:

- 50 μg lyophilized recombinant gE antigen
- 0.5 ml liposome-based ASO1_B adjuvant system
- 50 μg 3-*O*-desacyl-4'-monophosphoryl lipid A (MPL)
- 50 μg Quilaja saponaria Molina, fraction 21

Pending Indication: Prevention of herpes zoster in adults \geq 50 years

- Non-live recombinant vaccine
- 0.5 ml IM immunization administered at 0 and 2-6 months

Shingrix: ZOE-50 Trial Efficacy

Randomized | Observer-blind | Placebo-controlled | Multi-Center | Multinational | Phase III

Table 1. Vaccine Efficacy against the First or Only Episode of Herpes Zoster using Poisson Method (Modified Total Vaccinated Cohort)(1)

Age Strata	Group	N	Confirmed HZ Cases*	Incidence Rate of HZ Cases	Vaccine Efficacy† % (95% CI)
			(n)	(per 1000	
				person-years)	
50–59 Years	HZ/su	3492	3	0.3	96.6 (89.6-99.3)
	Placebo	3525	87	7.8	-
60–69 Years	HZ/su	2141	2	0.3	97.4 (90.1-99.7)
	Placebo	2166	75	10.8	-
≥70 Years‡	HZ/su	1711	1	0.2	97.9 (87.9-100.0)
	Placebo	1724	48	9.4	-
Overall§	HZ/su	7344	6	0.3	97.2 (93.7-99.0)
	Placebo	7415	210	9.1	-

CI = Confidence Interval; HZ/su = Herpes zoster subunit vaccine; Modified total vaccinated cohort = Excluded subjects who did not receive the second dose or who developed a confirmed case of herpes zoster within 1 month after the second dose

§Vaccine efficacy adjusted by age strata and region

^{*193} case confirmed by polymerase-chain reaction and 23 case confirmed by herpes zoster ascertainment committee \dagger For all efficacy comparisons, P < 0.0001; analyzed using the Poisson method

[‡]Vaccine efficacy adjusted by region

Shingrix: ZOE-50 Trial Safety

Randomized | Observer-blind | Placebo-controlled | Multi-Center | Multinational | Phase III

Table 2. Solicited Injection Site and Systemic Adverse Reactions Reported Within 7 Days After Vaccination (Total Vaccinated Cohort)⁽¹⁾

		HZ/su	Placebo N = 4466		
	N	V = 4460			
	n	% (95% CI)	n	% (95% CI)	
Injection Site	3571	81.5 (80.3-82.6)	522	11.9 (11.0-12.9)	
Reaction					
Pain	3464	79.1 (77.8-80.2)	499	11.2 (10.3-122)	
Redness	1664	38.0 (36.5-39.4)	59	1.3 (1.0-1.7)	
Swelling	1153	26.3 (25.0-27.6)	46	1.1 (0.8-1.4)	
Grade 3	417	9.5 (8.7-10.4)	16	0.4 (0.2-0.6)	
Systemic					
Fatigue	2008	45.9 (44.4-47.4)	728	16.6 (15.2-17.8)	
Fever	939	21.5 (20.3-22.7)	132	3.0 (2.5-3.6)	
Gastrointestinal	788	18.0 (16.9-19.2)	387	8.8 (8.0-9.7)	
Symptoms					
Headache	1716	39.2 (37.8-40.7)	700	16.0 (14.9-17.1)	
Myalgia	2025	46.3 (44.8-47.8)	530	12.1 (11.2-13.1)	
Shivering	1232	28.3 (26.8-29.5)	259	5.9 (5.2-6.7)	
Grade 3	498	11.4 (10.5-12.4)	106	2.4 (2.0-2.9)	

CI = Confidence interval; Grade 3 = Preventing normal everyday activities; HZ/su = Herpes zoster subunit vaccine; Total vaccinated cohort = all subjects who received at least 1 dose of HZ/su or placebo

Shingrix: ZOE-70 Trial Efficacy

Randomized | Observer-blind | Placebo-controlled | Multi-Center | Multinational | Phase III

Table 1. Vaccine Efficacy Against the First or Only Episode of Herpes Zoster (HZ) (Modified Total Vaccinated Cohort)⁽¹⁾

Age Strata	Group	N	Confirmed HZ cases (n)	Incidence Rate of HZ Cases (per 1000 person-years)	Vaccine Efficacy* % (95% CI)
ZOE-70					
Overall	Herpes zoster subunit vaccine	6,541	23	0.9	89.8 (84.2-93.7)
	Placebo	6,622	223	9.2]
70-79	Herpes zoster subunit vaccine	5,114	17	0.9	90.0 (83.5-94.4)
	Placebo	5,189	169	8.8]
≥80	Herpes zoster subunit vaccine	1,427	6	1.2	89.1 (74.6-96.2)
	Placebo	1,433	54	11.0	

Shingrix: ZOE-70 Trial Efficacy

Randomized | Observer-blind | Placebo-controlled | Multi-Center | Multinational | Phase III

Table 1. Vaccine Efficacy Against the First or Only Episode of Herpes Zoster (HZ) (Modified Total Vaccinated Cohort)⁽¹⁾

Age Strata	Group	N	Confirmed HZ	Incidence Rate	Vaccine Efficacy*
			cases (n)	of HZ Cases (per 1000 person-years)	% (95% CI)
Pooled Analy	sis				
Overall	Herpes zoster subunit vaccine	8,250	25	0.8	91.3 (86.8-94.5)
	Placebo	8,346	284	9.3	
70-79	Herpes zoster subunit vaccine	6,468	19	0.8	91.3 (86.1-94.9)
	Placebo	6,554	216	8.9	
≥80	Herpes zoster subunit vaccine	1,782	6	1.0	91.4 (80.2-97.0)
	Placebo	1,792	68	11.1	

Shingrix: ZOE-70 Trial Safety

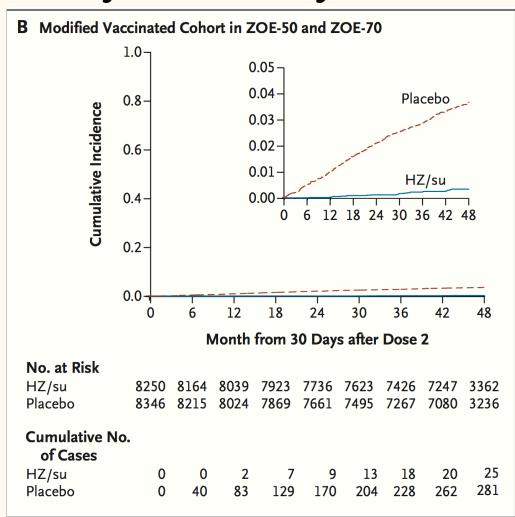
Table 2. Solicited Injection Site and Systemic Adverse Reactions Reported Within 7 Days After Vaccination (Analyses in the Reactogenicity Subgroup)⁽¹⁾

	Herpes zoster	r subunit vaccine	Placebo				
	n/N	% (95% CI)	n/N	% (95% CI)			
Any solicited reaction							
All	399/505	79.0 (75.2-82.5)	149/505	29.5 (25.6-33.7)			
Grade*	60/505	11.9 (9.2-15.0)	10/505	2.0 (1.0-3.6)			
Solicited injection s	ite reactions						
All	374/505	74.1 (70.0–77.8)	50/505	9.9 (7.4–12.8)			
Pain	347/505	68.7 (64.5–72.7)	43/505	8.5 (6.2–11.3)			
Redness	198/505	39.2 (34.9–43.6)	5/505	1.0 (0.3–2.3)			
Swelling	114/505	22.6 (19.0–26.5)	2/505	0.4 (0.0–1.4)			
Grade 3*	43/505	8.5 (6.2–11.3)	1/505	0.2 (0.0–1.1)			
Solicited systemic reactions							
All	267/504	53.0 (48.5–57.4)	127/505	25.1 (21.4–29.2)			
Fatigue	166/504	32.9 (28.8–37.2)	77/505	15.2 (12.2–18.7)			
Myalgia	157/504	31.2 (27.1–35.4)	41/505	8.1 (5.9–10.9)			
Headache	124/504	24.6 (20.9–28.6)	55/505	10.9 (8.3–13.9)			
Shivering	75/504	14.9 (11.9–18.3)	22/505	4.4 (2.7–6.5)			
Fever	62/504	12.3 (9.6–15.5)	13/505	2.6 (1.4–4.4)			
Gastrointestinal	55/504	10.9 (8.3–14.0)	40/505	7.9 (5.7–10.6)			
symptoms							
Grade 3*	30/504	6.0 (4.1–8.4)	10/505	2.0 (1.0–3.6)			

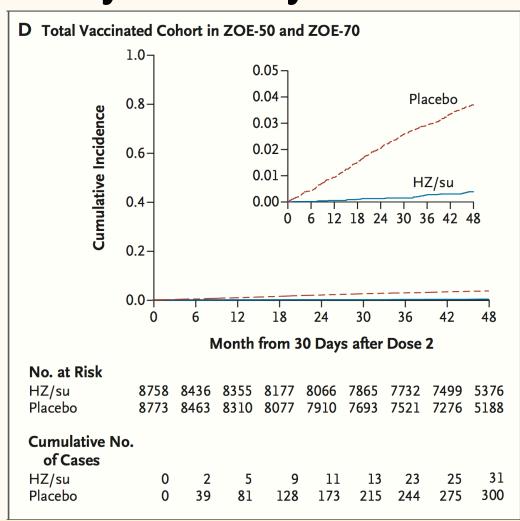
CI = Confidence Interval

^{*}Redness and swelling at the injection site were scored as 0 for <20 mm diameter, 1 for ≥20 to ≤50 mm, 2 for >50 to ≤100 mm, and 3 for >100 mm. Fever was scored as 0 for <37.5°C, 1 for 37.5°C to 38°C, 2 for 38.1°C to 39°C, and 3 for >39°C (the preferred route for recording temperature was oral). All other symptoms were scored as 0 for absent, 1 for easily tolerated, 2 for interferes with normal activity and 3 for prevents normal activity.

Shingrix: Pooled Analysis Efficacy



Shingrix: Pooled Analysis Safety



In the Pipeline: Shingrix

Licensed by GlaxoSmithKline

HZ/su contains:

- 50 μg lyophilized recombinant gE antigen
- 0.5 ml liposome-based ASO1_B adjuvant system
- 50 μg 3-*O*-desacyl-4'-monophosphoryl lipid A (MPL)
- 50 μg Quilaja saponaria Molina, fraction 21

Pending Indication: Prevention of herpes zoster in adults \geq 50 years

- Non-live recombinant vaccine
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Epidemiology

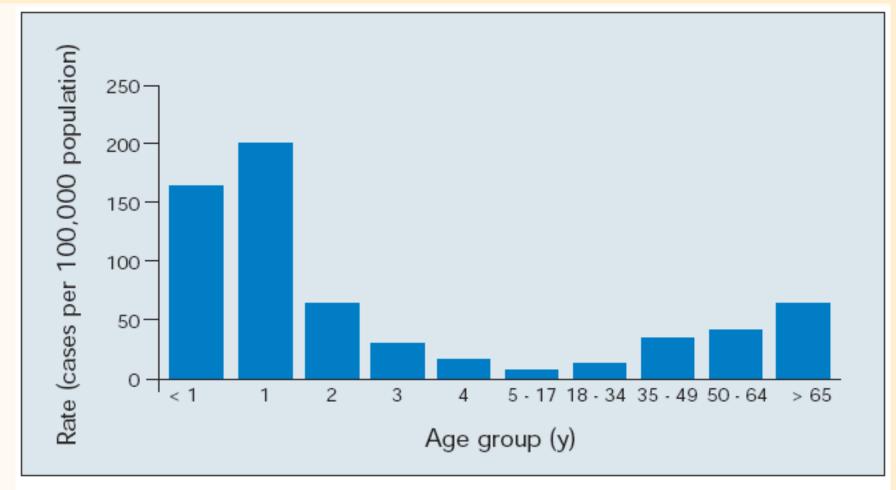


Figure 1 – The incidence of invasive pneumococcal disease varies according to age group. Although the highest rates of disease are seen in young children, the incidence increases with age among adults.

(From Epidemiology and Prevention of Vaccine-Preventable Diseases. 7th ed.⁶)

Pneumococcal Risk Factors

COMMUNITY ACQUIRED PNEUMONIA

- Cigarette Smoking
- Elderly
- Indoor Air Pollution
- Underlying Pulmonary Condition
- Recent URTI
- Alcohol Use
- Immunocompromised Condition
- Immunocompromising Medications

HOSPITAL ACQUIRED PNEUMONIA

- Prolonged Hospitalization
- Use of Gastric Acid Suppressants
- Nasogastric Intubation
- Prolonged Antibiotic Exposure
- Intensive Care Unit Setting
- Contaminated Personnel
- Inadequate Hygienic Procedures

COPD | Asthma | Chronic Liver Disease | Chronic Cardiovascular Disease | Diabetes

Pneumococcal Pathophysiology

PREVENTATIVE MEASURES **BUGS** ROUTES • S. pneumoniae **Inhaled Particles** Hand washing • H. influenza • Extrapulmonary Infection **Immunization** Oropharyngeal Aspiration • M. pneumoniae • Legionella • C. pneumoniae Viral Superinfections

Pneumococcal Complications

COMMUNITY ACQUIRED PNEUMONIA

One of the MOST common causes of severe sepsis and infections cause of death in children and adults in the United States.

Bacteremia

Pleural Effusion

Renal Failure

Septic Shock

Empyema

Respiratory Failure

Lung Abscesses

Pleurisy

Multiple Drug Resistance

Otitis Media

Pneumococcal Meningitis

Death

Pneumococcal Vaccine Coverage





GOALS

- Noninstitutionalized Adults
 - \geq 65 Years Old: 90% by 2020
 - 18 to 64 Years Old: 60% by 2020

- Institutionalized Adults
 - 90% by 2020

CDC Pneumococcal Guideline



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



Age 65 Years or Older

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

No history of pneumococcal vaccine

PCV 13 Prevnar 13°

1 year

(8 weeks for groups B & C as defined below)

PPSV 23 Pneumovax® 23

Received PPSV23 before age 65

1 year

PCV 13

1 year

(8 weeks for groups B & C as defined below) **and 5 years** after prior dose of PPSV23

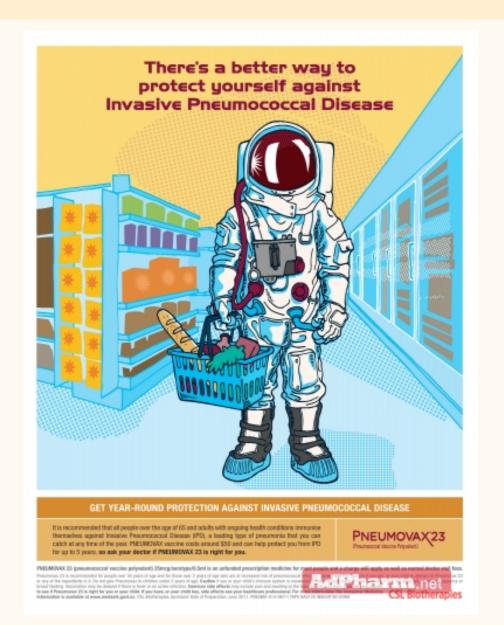
PPSV 23

Received PPSV23 at age 65 or older

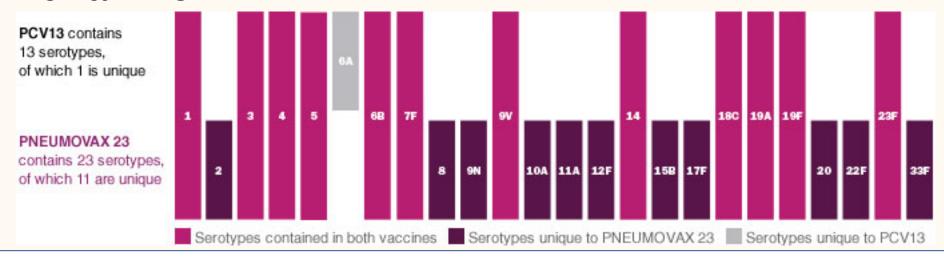
1 year

PCV **13**





Pneumovax 23



14 Year Retrospective Study (1978 to 1992) showed:

57% overall efficacy against invasive infection in patients \geq 6 years old

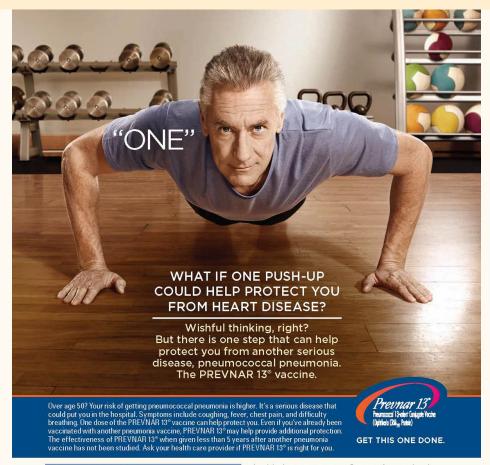
75% efficacy against invasive infections in patients \geq 65 years old

Used to prevent septicemia associated with *S. pneumoniae* pneumonia

NO T-Cell Response, thus, NO B-cell memory formation Effectiveness of PPV in patients \geq 65 years old declines significantly within 5 years of vaccination



But if you're 50 or older, there is one step you can take to help prevent pneumococcal pneumonia.



INDICATIONS FOR PREVNAR 13

- Prevnar 13º is a vaccine approved for adults 50 years of age and older for the prevention of pneumococcal pneumonia and invasive disease caused by 13 Streptococcus pneumoniae strains (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). This indication is based upon immune responses to the vaccine
- Prevnar 13° is not 100% effective and will only help protect against the 13 strains included in the vaccine
- Effectiveness when given less than 5 years after a pneumococcal polysaccharide vaccine is not known

IMPORTANT SAFETY INFORMATION

- Prevnar 13° should not be given to anyone with a history of severe allergic reaction to any component of Prevnar 13° or any diphtheria toxoid—containing vaccine
- Adults with weakened immune systems (eg, HIV infection, leukemia) may have a reduced immune response

- In adults, immune responses to Prevnar 13° were reduced when given with injected seasonal flu vaccine
- In adults, the common side effects were pain, redness, or swelling at the injection site, limitation of arm movement, fatigue, headache, muscle pain, joint pain, decreased appetite, chills, or rash
- Ask your health care provider about the risks and benefits of Prevnar 13°. Only a health care provider can decide if Prevnar 13° is right for you

You are encouraged to report negative side effects of vaccines to the US Food and Drug Administration (FDA) and Centers for Disease Control and Prevention (CDC). Visit www.vaers.hhs.gov or call 1-800-822-7967.

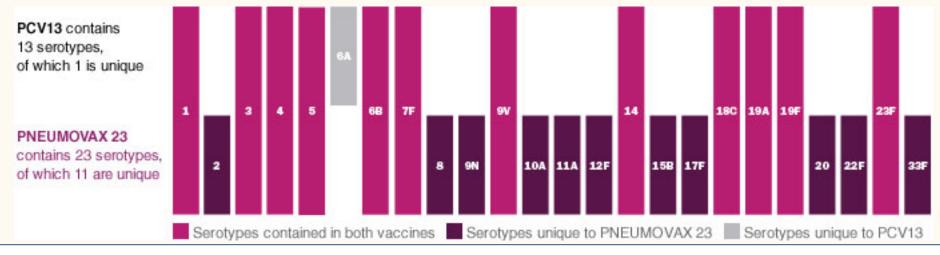
Please see Important Facts for Prevnar 13° on the following page.



PREVNAR 13 is a registered trademark of Wyeth LLC. Manufactured by Wyeth Pharmaceuticals Inc. Marketed by Pfizer Inc. PSA669703-01 ©2014 Pfizer Inc. All rights reserved. September 2014



Prevnar 13



Community-Acquired Pneumonia Immunization Trial (CAPITA) 5 Years | 84,496 adults aged \geq 65 years

- 31% overall efficacy of PCV protecting against S. pneumoniae
- Strategy to achieve higher immunogenicity: administered one dose of PCV13 to those previously vaccinated with PPSV23!

UPDATE: Indicated for adults 18 years of age and older for the prevention of pneumococcal pneumonia and invasive pneumonia caused by the 13 strains in Prevnar 13.

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



Age 65 Years or Older

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

No history of pneumococcal vaccine

PCV 13 Prevnar 13°

1 year

(8 weeks for groups B & C as defined below)

PPSV 23 Pneumovax® 23

Received PPSV23 before age 65

1 year

PCV 13

1 year

(8 weeks for groups B & C as defined below) **and 5 years** after prior dose of PPSV23

PPSV 23

Received PPSV23 at age 65 or older

1 year

PCV **13**



Thank You, Orange County Immunization Coalition!

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References

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- Harrison's Principles of Internal Medicine: Chapter 217: Varicella-Zoster Virus Infections
- CDC: Shingles Surveillance CDC: Shingles Clinical Overview National and State-Specific Shingles Vaccination Among Adults Aged > 60 Years
- Vaccination of Special Populations: Protecting the Vulnerable
- Preventing Shingles and it's Complications in Older Persons
- Determining the Optimal Vaccination Schedule for HZV: a CE Analysis
- The role of the T cell in age-related inflammation
- Efficacy, Safety, and Tolerability of Herpes Zoster Vaccine in Persons Aged 50–59 Years
- In Adults ≥ 70 years of age, an adjuvant herpes zoster subunit vaccine reduced herpes zoster at a mean 3.7 years
- Efficacy of Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older
- Immunogenicity and safety of an adjuvant herpes zoster subunit candidate vaccine in adults ≥ 50 years of age with a prior history of herpes zoster: A phase III, non-randomized, open-label clinical trial
- Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults
- · Efficacy and Safety of Investigational Herpes Zoster Subunit Vaccine Candidate in Adults 70 Years of Age and Older
- Primary Efficacy Results for Investigational Adjuvanted Herpes Zoster Vaccine Candidate in Adults 50 Years of Age and Older From a Phase III Study
- Availability of the GlaxoSmithKline Adjuvanted Herpes Zoster Subunit Vaccine Candidate
- Long-Term Immunogenicity and Safety of an Investigational Adjuvanted Herpes Zoster Subunit Vaccine Candidate in Adults ≥60 Years of Age
- Adult pneumococcal vaccination: advances, impact, and unmet needs
- Time to follow up when comparing studies of pneumococcal vaccines
- Preventing pneumococcal infections in older adults
- Developing Better Pneumococcal Vaccines for Adults
- Intervals Between PCV13 and PPSV23 Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP)
- Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Years: Recommendations of the Advisory Committee on Immunization Practices (ACIP)
- Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine for Adults with Immunocompromising Conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP)
- Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older United States, 2017

^{*}Links to PDFs availanble upon request.