

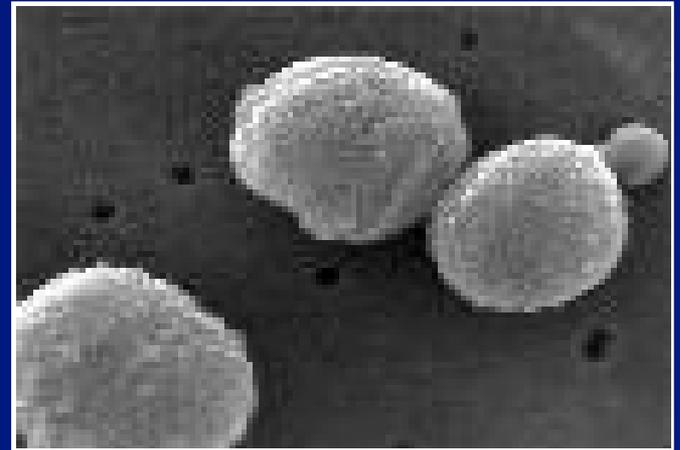
Pneumococcal Disease and Pneumococcal Vaccines

National Center for Immunization and Respiratory Diseases
Immunization Services Division



Streptococcus pneumoniae

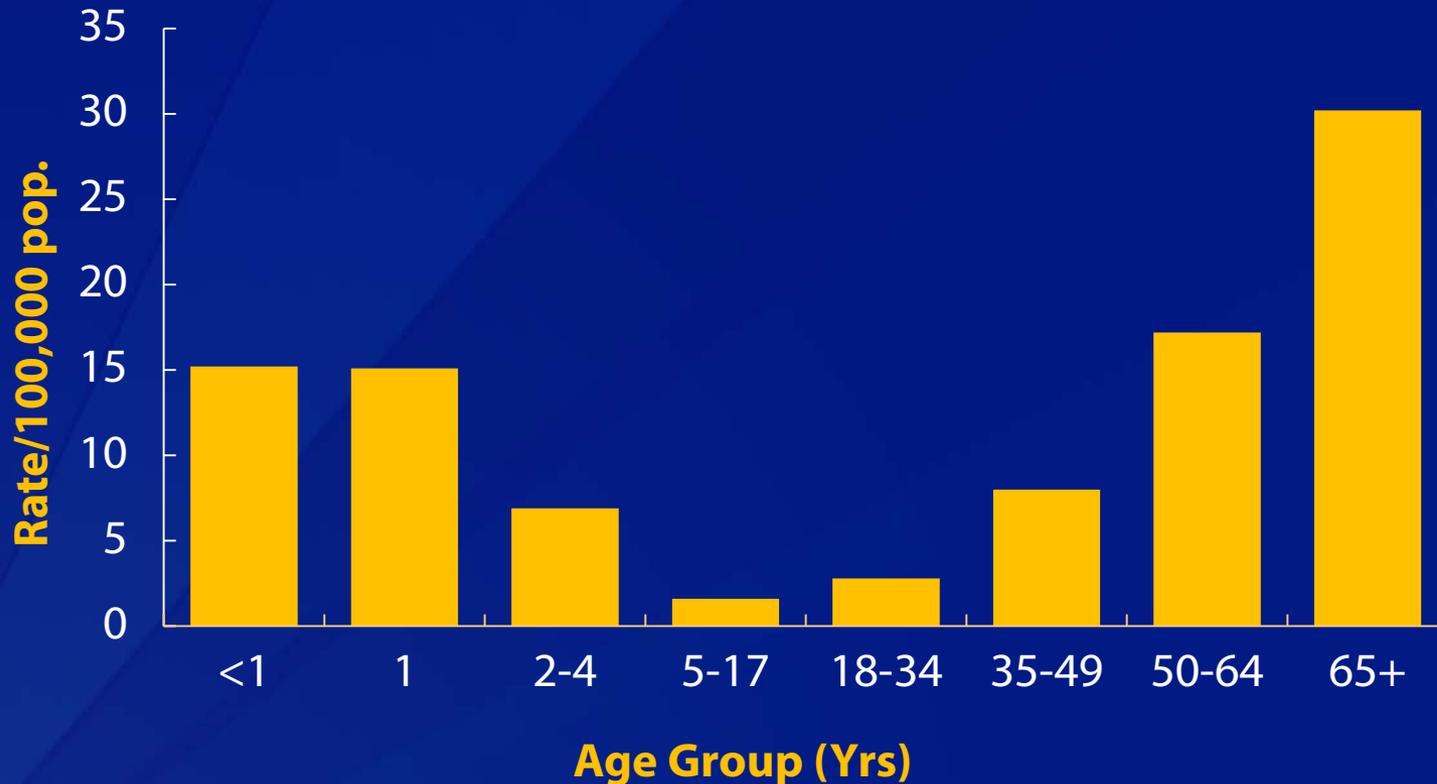
- ❑ Gram-positive bacteria
- ❑ 92 known serotypes
- ❑ Polysaccharide capsule important virulence factor
- ❑ Type-specific antibody is protective
- ❑ Limited cross-reactivity



Pneumococcal Disease

- ❑ **Second most common cause of vaccine-preventable death in the U.S.**
- ❑ **Major clinical syndromes**
 - Pneumonia
 - Bacteremia
 - Meningitis

Invasive Pneumococcal Disease Incidence by Age Group – 2013*



*CDC Active Bacterial Core surveillance 2009 report:
www.cdc.gov/abcs/reports-findings/survreports/spneu13.html

Risk Factors for Invasive Pneumococcal Disease

- ❑ **Functional or anatomic asplenia, including sickle-cell disease**
- ❑ **Altered immunocompetence**
- ❑ **Underlying medical conditions, including chronic renal disease, nephrotic syndrome, and CSF leak**
- ❑ **Cigarette smoking (adults 19 years and older)**
- ❑ **Cochlear implant**

Pneumococcal Disease Epidemiology

- ❑ **Reservoir** Human carriers
- ❑ **Transmission** Respiratory and autoinoculation
- ❑ **Temporal pattern** Winter and early spring
- ❑ **Communicability** Unknown; probably as long as organism in respiratory secretions

Pneumococcal Vaccines

- ❑ **1977** 14-valent polysaccharide vaccine licensed
- ❑ **1983** 23-valent polysaccharide vaccine licensed (PPSV23)
- ❑ **2000** 7-valent polysaccharide conjugate vaccine licensed (PCV7)
- ❑ **2010** 13-valent polysaccharide conjugate vaccine licensed (PCV13)

Pneumococcal Polysaccharide Vaccine (PPSV23) Characteristics

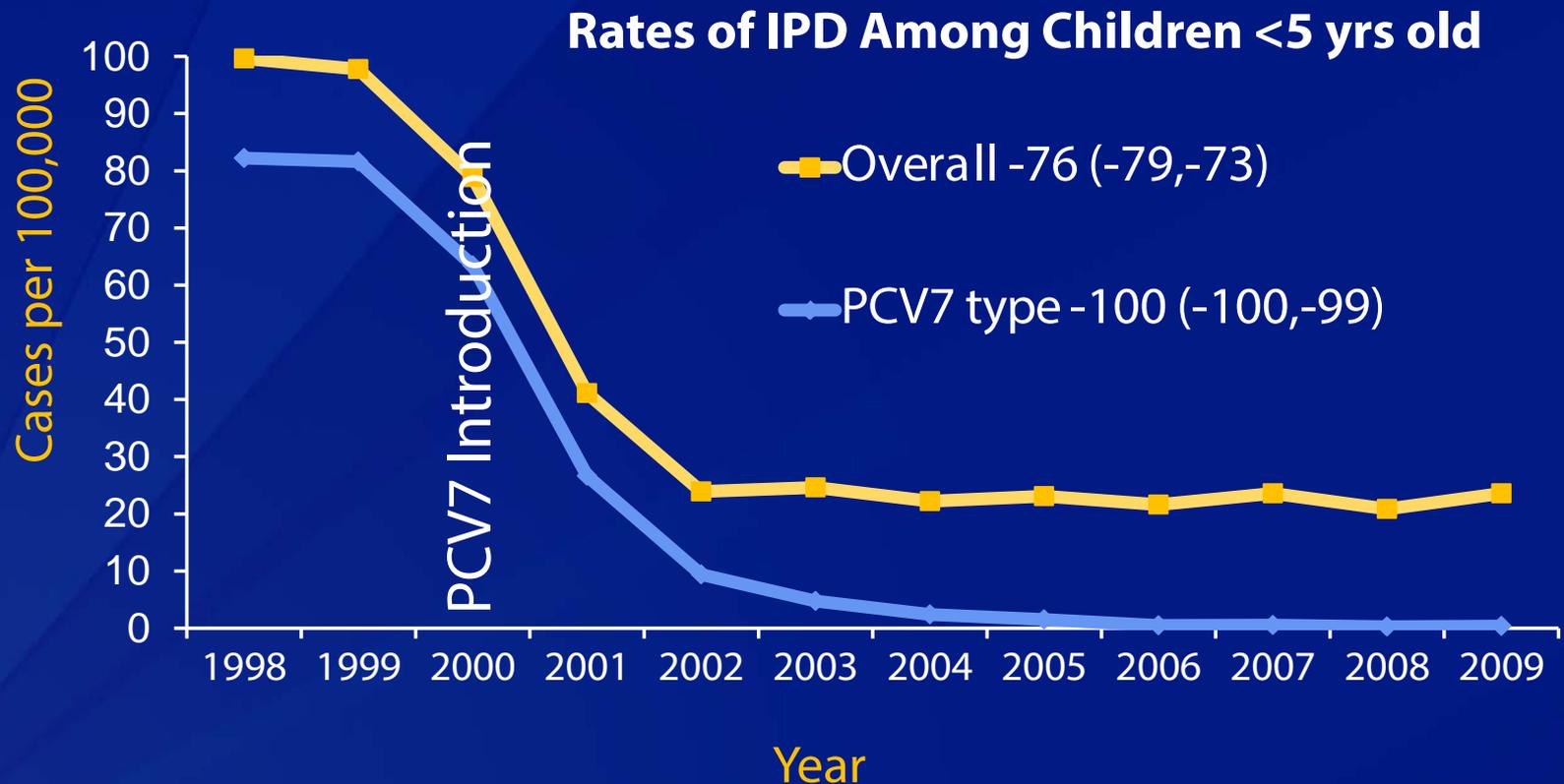
- ❑ Purified capsular polysaccharide antigen from 23 types of pneumococcus**
- ❑ Not effective in children younger than 2 years**

Pneumococcal Conjugate Vaccine (PCV13) Characteristics

- ❑ Contains 13 serotypes of *S. pneumoniae* conjugated to nontoxic diphtheria CRM₁₉₇ carrier protein**
- ❑ Approval based on demonstration of immunologic noninferiority to PCV7 rather than clinical efficacy**

PCV7 Introduction Among U.S. Children and its Impact on Invasive Pneumococcal Disease

- PCV7 introduced into routine schedule 2000



Moore, IDSA, 2009 and CDC, unpublished data

Pneumococcal Conjugate Vaccine (PCV13) in Children

- In 2008, 61% of invasive pneumococcal disease cases among children younger than 5 years were attributable to the serotypes included in PCV13**

Pneumococcal Conjugate Vaccine (PCV13) in Adults

- ❑ In 2013, 20%-25% of invasive pneumococcal disease cases among adults 65 years old and older were attributable to PCV13 serotypes**
- ❑ 10 percent of community-acquired pneumonia in adults due to PCV13 serotypes (Pfizer urine studies)**

Estimating Cases Potentially Preventable Annually among Adults 65 Years or Older

Outcome (PCV13 type)	2015 20% reduction due to herd effects* PCV13 direct effects** Coverage 10% (5%-30%)	2019 86% reduction due to herd effects* PCV13 direct effects** Coverage 30% (20%-60%)
IPD	160 (80-480)	80 (50-170)
Inpatient CAP	2,030 (1,020-6,090)	1,070 (700 -2,130)
Outpatient CAP	2,970 (1,480-8,900)	1,560 (1,040 – 3,120)
Total CAP	5,000 (2,500-14,990)	2,630 (1,740 – 5,250)

*Based on post-PCV7 reductions observed between 2003 and 2009

**Assume PCV13 VE =75% (IPD) and 45% (CAP)

Pneumococcal Polysaccharide Vaccine (PPSV23) Immunogenicity/Effectiveness

- Most estimates range between 60%-70% effective against invasive disease among immunocompetent older persons and adults with underlying illnesses**
- Effectiveness among immunocompromised or very old persons not demonstrated**

Pneumococcal Conjugate Vaccine (PCV13) Immunogenicity/Efficacy

- Highly immunogenic in infants and young children, including those with high-risk medical conditions**
- PCV7 was 97% effective against invasive disease caused by vaccine serotypes (presumably PCV13 as well)**

New Evidence Supporting PCV13 use among Adults, CAPiTA Results

Study/Population	Endpoint	Vaccine Efficacy (95% CI)
CAPiTA ~85,000 Adults 65+ Netherlands	PCV13-serotype IPD	75% (41%, 91%)
	PCV13-serotype nonbacteremic pneumonia	45% (14%, 65%)



MMWRTM

Morbidity and Mortality Weekly Report

www.cdc.gov/mmwr

Recommendations and Reports

December 10, 2010 / Vol. 59 / No. RR-11

Prevention of Pneumococcal Disease Among Infants and Children – Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

PCV13 Licensure

- ❑ **PCV13 is approved by the Food and Drug Administration for:**
 - Children 6 weeks through 17 years of age
 - Adults 50 years of age and older
- ❑ **ACIP recommended use of PCV13 for immunocompromised persons 6 years and older (2012, 2013)**
- ❑ **ACIP recommended use of PCV13 for all adults 65 years or older in 2014**

PCV13 IN CHILDREN

ACIP Recommendations for PCV13

- ❑ **Routine vaccination recommendation the same as for PCV7 (children 2-59 months)**
 - 4 doses at 2, 4, 6, and 12 to 15 months
 - Fewer doses if series started at 7 months of age or older
- ❑ **Children who have received 1 or more doses of PCV7 should complete the immunization series with PCV13**

Pneumococcal Conjugate Vaccine Schedule for Unvaccinated Older Children-Primary Series

Age at First Dose	# of Doses	Booster
7-11 months	2 doses	Yes
12-23 months	2 doses*	No
24-59 months	1 dose	No
24-71 months, medical conditions**	2 doses*	No

*Separated by at least 8 weeks; see *MMWR* 2010;59(RR-11):1–19

**Chronic heart, lung disease, diabetes, CSF leak, cochlear implant, sickle cell disease, other hemoglobinopathies, functional or anatomic asplenia, HIV infection, immunocompromising conditions

ACIP Recommendations for PCV13 Supplemental Dose

- ❑ **A single supplemental dose of PCV13 is recommended for children who have received a complete age-appropriate series of PCV7:**
 - Healthy children 14 through 59 months
 - Children 14 through 71 months with an underlying medical condition (including those who have already received a dose of PPSV)

ACIP Recommendations for PCV13 Children

- ❑ Children aged 24–71 months with underlying medical conditions who received an incomplete schedule of PCV7 should receive 2 doses of PCV13 (8 weeks apart)**

ACIP Recommendations for PCV13 Dose

- ❑ **A dose of PCV13 should be administered to children 6 through 18 years of age who are at increased risk for invasive pneumococcal disease* (and no prior PCV13 doses)**
 - Functional or anatomic asplenia, including sickle cell disease
 - HIV infection and other immunocompromising conditions
 - Cochlear implant
 - CSF leak

- ❑ **Regardless of previous history of PCV7 or PPSV vaccine**

*Off-label recommendation, ACIP vote, February 20, 2013

PCV13 USE IN ADULTS

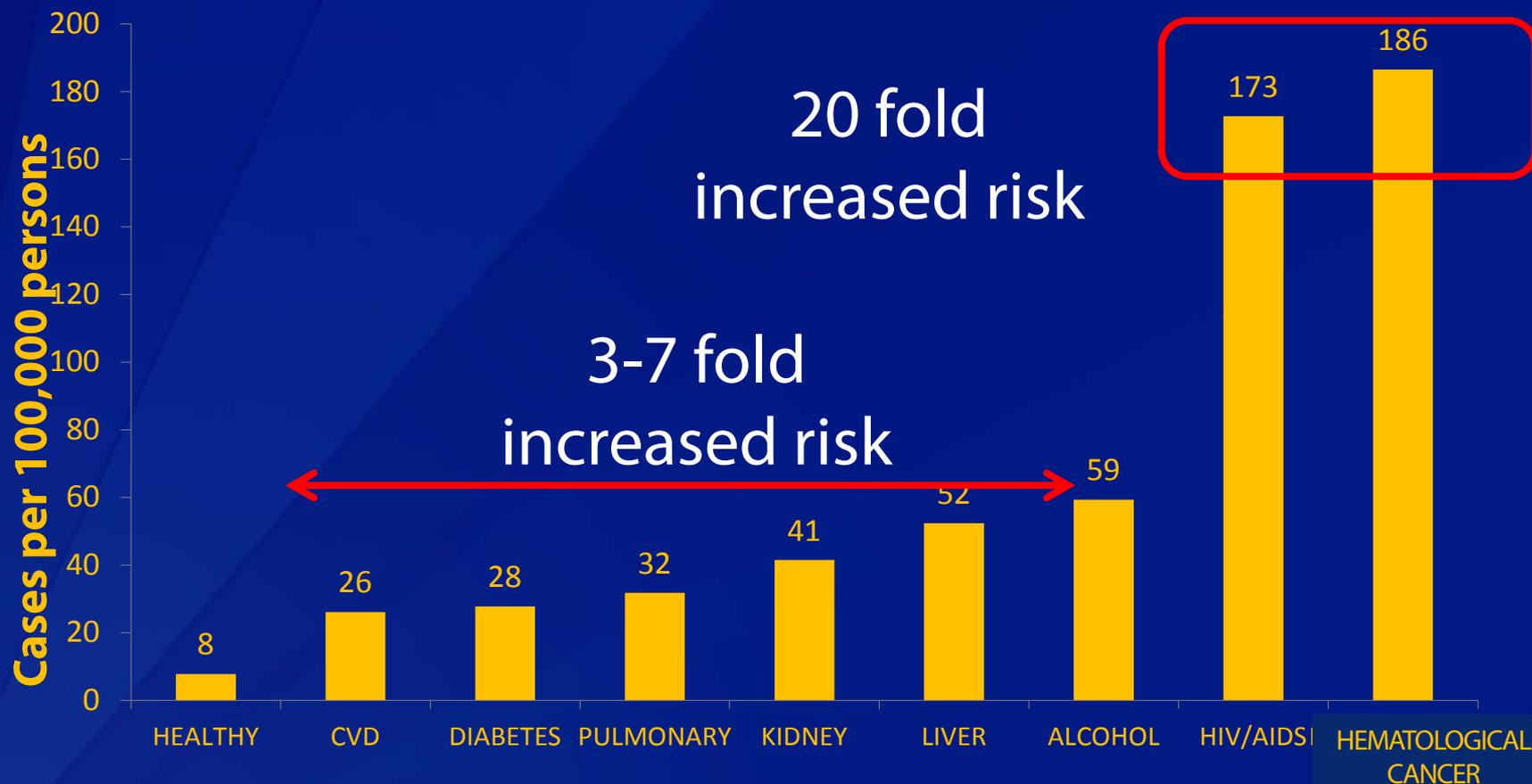
PCV13 for Adults

- ❑ **Licensed for use among adults >50 years old on 12/30/11**
- ❑ **FDA approved under the Accelerated Approval Pathway**
- ❑ **Based on noninferior immunogenicity compared to PPSV23**
- ❑ **Postapproval condition of licensure:**
 - Randomized controlled trial of PCV13 against pneumococcal pneumonia among adults ≥ 65 years old in the Netherlands

PCV13 for Adults (2014)

- ❑ ACIP now recommends PCV13 for adults 65 years old and older**
- ❑ Some adults have received PCV13 already**

Incidence of IPD in Adults Aged 18-64 Years with Selected Underlying Conditions, United States, 2009



Unpublished data, Active Bacterial Core surveillance, 2009

PCV13 for Immunocompromised Adults*

- ❑ **Adults 19 years of age or older with:**
 - Immunocompromising conditions
 - Functional or anatomic asplenia
 - CSF leaks
 - Cochlear implants

- ❑ Those who have not previously received PCV13 or PPSV23 should receive a single dose of PCV13 followed by a dose of PPSV23 at least 8 weeks later, with a booster dose of PPSV23 5 or more years later

**MMWR*. October 12, 2012 ; 61(40):816-819

PPSV23 USE IN CHILDREN AND ADULTS

Pneumococcal Polysaccharide Vaccine Recommendations

- Persons 2 years and older with normal immune systems who have chronic illness**

Cardiovascular of pulmonary disease (asthma if 19 years old or older)	Smoking (19 years old or older)
Diabetes	CSF leak
Liver disease	Cochlear implant
Alcoholism	

- Persons in environments or settings with increased risk**

Pneumococcal Polysaccharide Vaccine Recommendations

- ❑ **Persons 2 years and older who are immunocompromised (due to disease or treatment)**
 - Asplenia (functional or anatomic)
 - Chronic renal failure
 - Nephrotic syndrome
 - Hodgkin disease
 - Lymphoma and leukemia
 - Multiple myeloma
 - Organ transplant
 - HIV infection

Pneumococcal Polysaccharide Vaccine Revaccination

- ❑ Routine revaccination of immunocompetent persons is not recommended**
- ❑ Revaccination recommended for persons 2-64 years of age who are at highest risk of serious pneumococcal infection**

Pneumococcal Polysaccharide Vaccine

Candidates for Revaccination

- ❑ **5-year interval (2-64 years) with additional dose after 65th birthday, 5 years after previous dose:**
 - Functional or anatomic asplenia (including sickle cell disease)
 - Immunosuppression (including HIV infection)
 - Transplant
 - Chronic renal failure
 - Nephrotic syndrome

- ❑ **1 dose is recommended after the 65th birthday, but only 1 dose recommended after 65th birthday**

MMWR 2010;59(No.34):1102-5 and 2010;59(RR-11)

Administering PCV13 and PPSV23 Vaccines

General Rules

- ❑ **PCV13 and PPSV23 should not be administered during the same clinic visit**
 - Either vaccine may be administered simultaneously with influenza vaccine
- ❑ **Administer PCV13 before PPSV23 whenever possible**

Table 1. Medical conditions or other indications for administration of PCV13 and PPSV23 for adults

Medical indication	Underlying medical condition	PCV13 for ≥ 19 years	PPSV23* for 19 through 64 years		PCV13 at ≥ 65 years	PPSV23 at ≥ 65 years
		Recommended	Recommended	Revaccination	Recommended	Recommended
None	None of the below				✓	✓ ≥ 1 year after PCV13
Immunocompetent persons	Alcoholism					
	Chronic heart disease [†]					
	Chronic liver disease				✓	✓
	Chronic lung disease [‡]		✓			
	Cigarette smoking					
	Diabetes mellitus					
	Cochlear implants	✓	✓ ≥ 8 weeks after PCV13		✓ If no previous PCV13 vaccination	✓ ≥ 8 weeks after PCV13 ≥ 5 years after any PPSV23 at < 65 years
CSF leaks						
Persons with functional or anatomic asplenia	Congenital or acquired asplenia		✓ ≥ 8 weeks after PCV13	✓ ≥ 5 years after first dose PPSV23	✓ If no previous PCV13 vaccination	✓ ≥ 8 weeks after PCV13 ≥ 5 years after any PPSV23 at < 65 years
	Sickle cell disease/other hemoglobinopathies	✓				
Immunocompromised persons	Chronic renal failure					
	Congenital or acquired immunodeficiencies [§]					
	Generalized malignancy					
	HIV infection					
	Hodgkin disease		✓	✓	✓	✓
	Iatrogenic immunosuppression [¶]	✓	≥ 8 weeks after PCV13	≥ 5 years after first dose PPSV23	✓ If no previous PCV13 vaccination	✓ ≥ 8 weeks after PCV13 ≥ 5 years after any PPSV23 at < 65 years
	Leukemia					
	Lymphoma					
	Multiple myeloma					
	Nephrotic syndrome					
Solid organ transplant						

*This PPSV23 column only refers to adults 19 through 64 years of age. All adults 65 years of age or older should receive one dose of PPSV23 5 or more years after any prior dose of PPSV23, regardless of previous history of vaccination with pneumococcal vaccine. No additional doses of PPSV23 should be administered following the dose administered at 65 years of age or older.

[†]Including congestive heart failure and cardiomyopathies

[‡]Including chronic obstructive pulmonary disease, emphysema, and asthma

[§]Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease)

[¶]Diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy

PCV13 and PPSV23 for Adults 19 – 64 Years

Immunocompromised, asplenic (sickle cell, hemoglobinopathy), CSF leaks, cochlear implants who are **pneumococcal-naive**

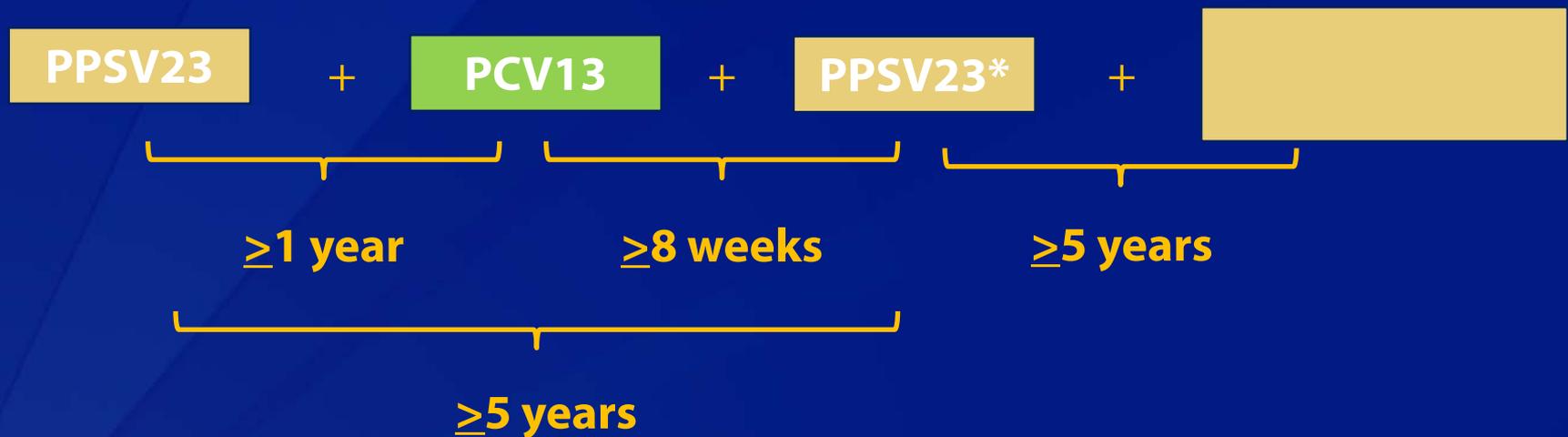


*Second PPSV23 dose before age 65 years NOT recommended for adults with CSF leaks or those with cochlear implants

*ACIP off-label recommendation for PCV13 for adults 19 through 49 years of age

PCV13 and PPSV23 for Adults 19 – 64 Years

Immunocompromised, asplenic (sickle cell, hemoglobinopathy), CSF leaks, cochlear implants
who have previously received PPSV23



*Second PPSV23 dose before age 65 years NOT recommended for adults with CSF leaks or those with cochlear implants

*ACIP off-label recommendation for PCV13 for adults 19 through 49 years of age

PCV13 and PPSV23 for Adults 65 Years and Older

- ❑ Pneumococcal-naïve or unknown vaccination history
- ❑ Healthy adult



- ❑ If PPSV23 cannot be given at 12 months later, it should be given during the next visit

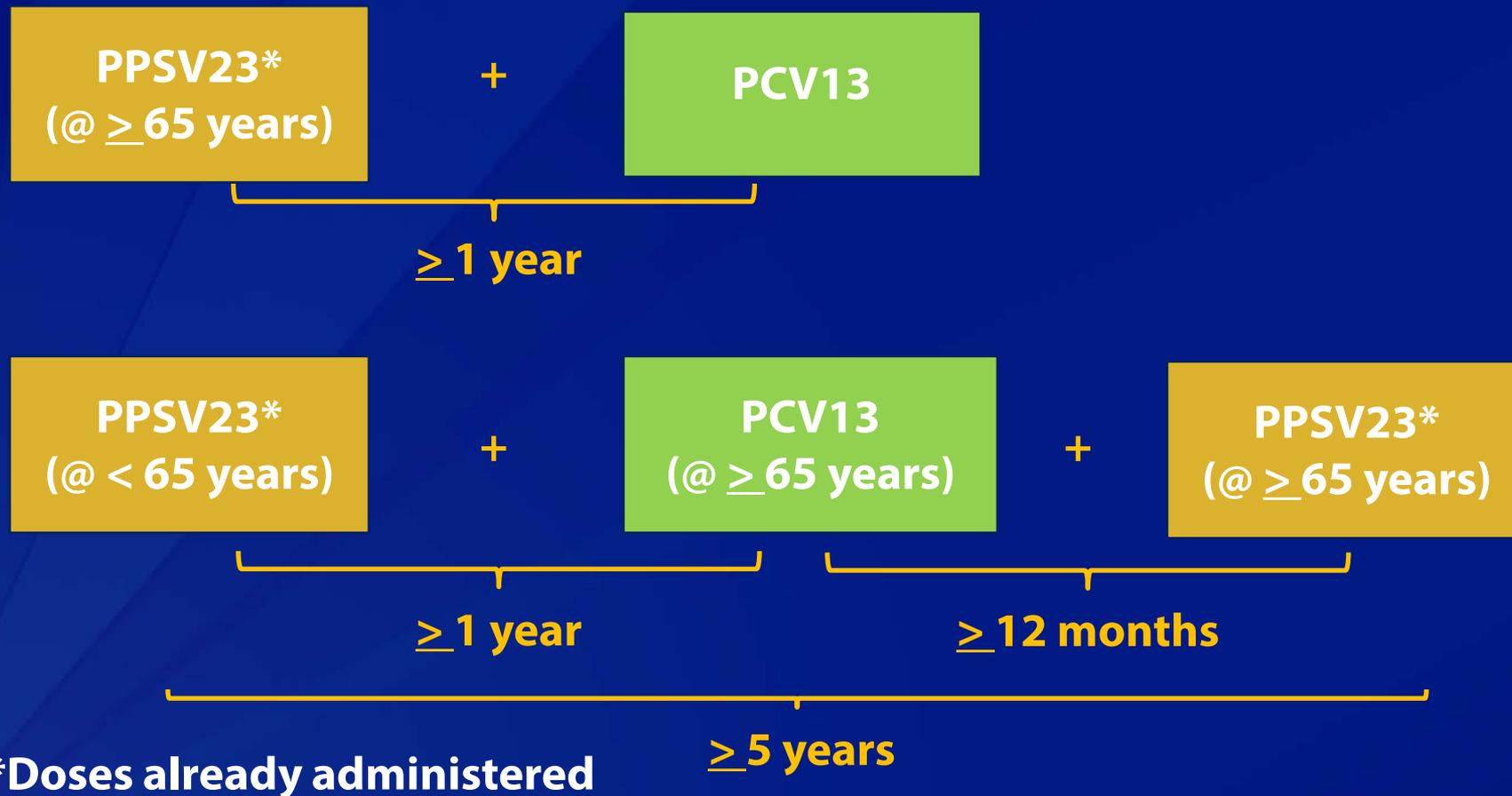
PCV13 and PPSV23 for Adults 65 Years and Older

- ❑ Pneumococcal-naïve or unknown vaccination history
- ❑ High-risk immunocompromised adult



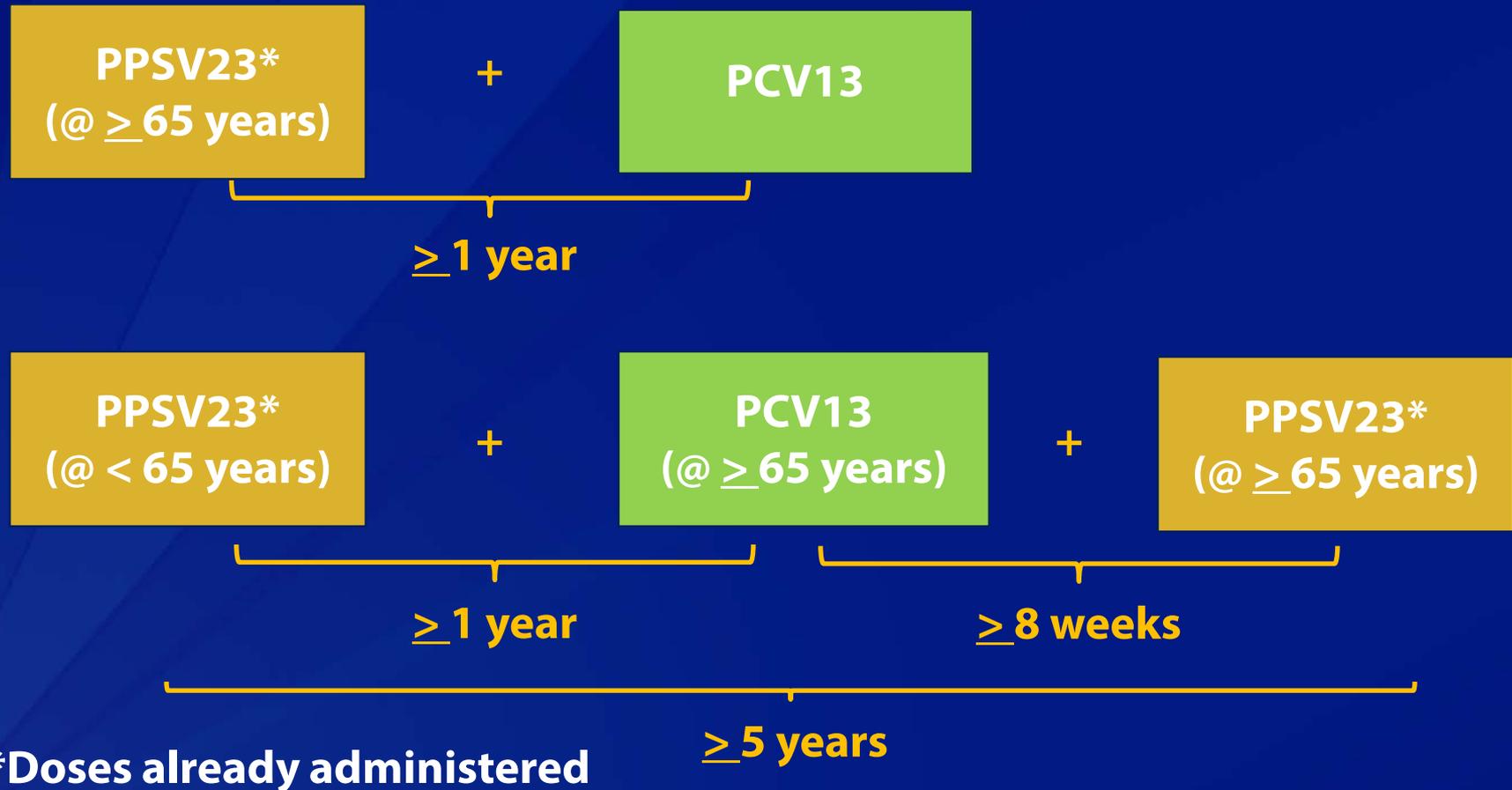
PCV13 and PPSV23 for Adults 65 Years and Older

- ❑ Previously received 1 or more doses of PPSV23
- ❑ Healthy adult



PCV13 and PPSV23 for Adults 65 Years and Older

- ❑ Previously received 1 or more doses of PPSV23
- ❑ High-risk immunocompromised adult



Pneumococcal Vaccines

Contraindications and Precautions

- ❑ Severe allergic reaction to vaccine component or following prior dose of vaccine**
- ❑ Moderate or severe acute illness**

Pneumococcal Vaccines

Adverse Reactions

	PPSV23	PCV
❑ Local reactions	30%-50%	5%-49%
❑ Fever, myalgia	<1%	24-35%
❑ Febrile seizures	---	Rare: 1-14/100,000; with IIV 4 -45/ 100,000
❑ Severe adverse reactions	rare	8% (local)

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Active Bacterial Core Surveillance - www.cdc.gov/abcs/reports-findings/surv-reports.html