



UPDATE ON

Adult Immunization Strategies

*Understanding the Current
Recommendations*



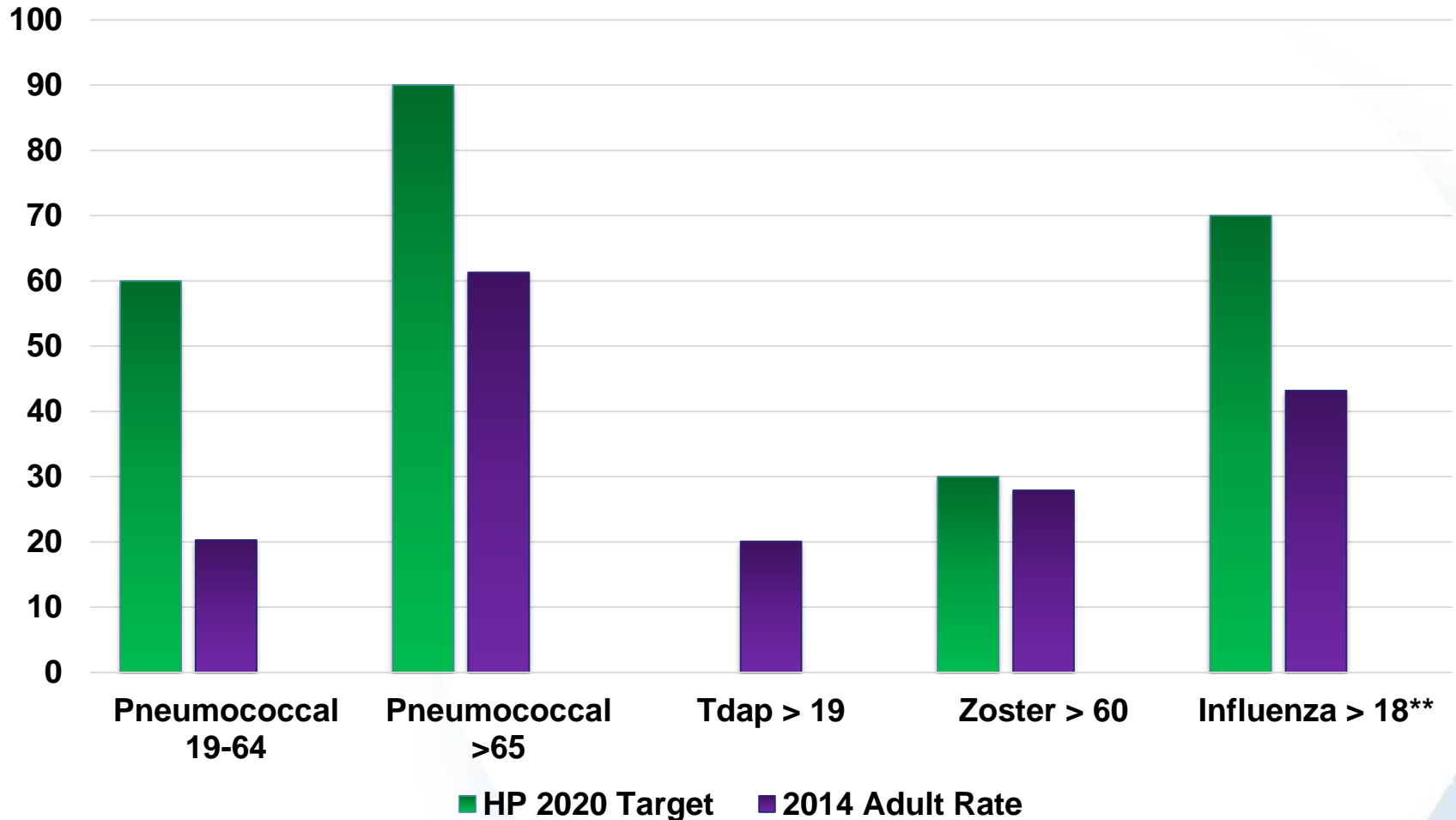
Call-to-Action: Recognizing the Burden of Vaccine- Preventable Diseases

Burden of Vaccine-Preventable Diseases

Each Year

- 200,000 hospitalizations due to influenza
 - As many as 36,000 deaths
- 29,100 cases of invasive pneumococcal disease
 - Approximately 3,300 deaths
- 1.25 million people suffer from chronic HBV infection
- Over 1 million people develop shingles
- 17,000 cancers in women and 9,000 cancers in men are caused by HPV.
 - >4,000 cervical cancer deaths

Adult Immunization Coverage, US



MMWR. Feb 5, 2016. <http://www.cdc.gov/mmwr/volumes/65/ss/ss6501a1.htm>

Healthy People 2020 Objectives on Immunization and Infectious Disease. www.Healthypeople.gov/2020/.

“Prevent all the disease you can, and then treat the rest.”

Michael Hogue

Registries: Not Just for Kids!





Pneumococcal Disease

Patient Case: Jane Williams

64-year-old patient with a history of renal transplant 5 years ago, taking anti-rejection therapy. History of diabetes and hypertension, both now controlled on medication therapy. Jane is enrolled in a pharmacist-run medication management program in your large group practice. Her immunization history shows influenza vaccine last December at your clinic, and Tdap vaccine in 2013. There is no documentation or recollection of pneumococcal vaccine of any kind. Which pneumococcal vaccine, if any, should she receive today?

1. None.
2. Pneumococcal Polysaccharide Vaccine-23 (PPSV-23)
3. Pneumococcal Conjugate Vaccine-13 (PCV-13)
4. Both PPSV-23 and PCV-13 today

Jane Williams

You are seeing Jane today in your family medicine clinic for a routine check up. Given the previous case, which professionals COULD have immunized her already – but apparently did not?

- 1. Transplant Clinic Nurse/NP/PharmD/MD**
- 2. Pharmacist in Med Management Clinic**
- 3. Pharmacist who provides her Rxs**
- 4. Nurse in your clinic when she received the flu shot**
- 5. All of the above**

Making Prevention a Priority



Patient Case: Jon Williams

Jon, Jane's husband, is 63 years old with a history of diabetes mellitus which is recent onset and well controlled with metformin + lifestyle modification. He is in your family medicine practice today for an annual physical exam. There is no record of Jon having received any immunizations since he last received a Td vaccine 15 years ago following an injury. What pneumococcal vaccine, if any, should Jon receive today?

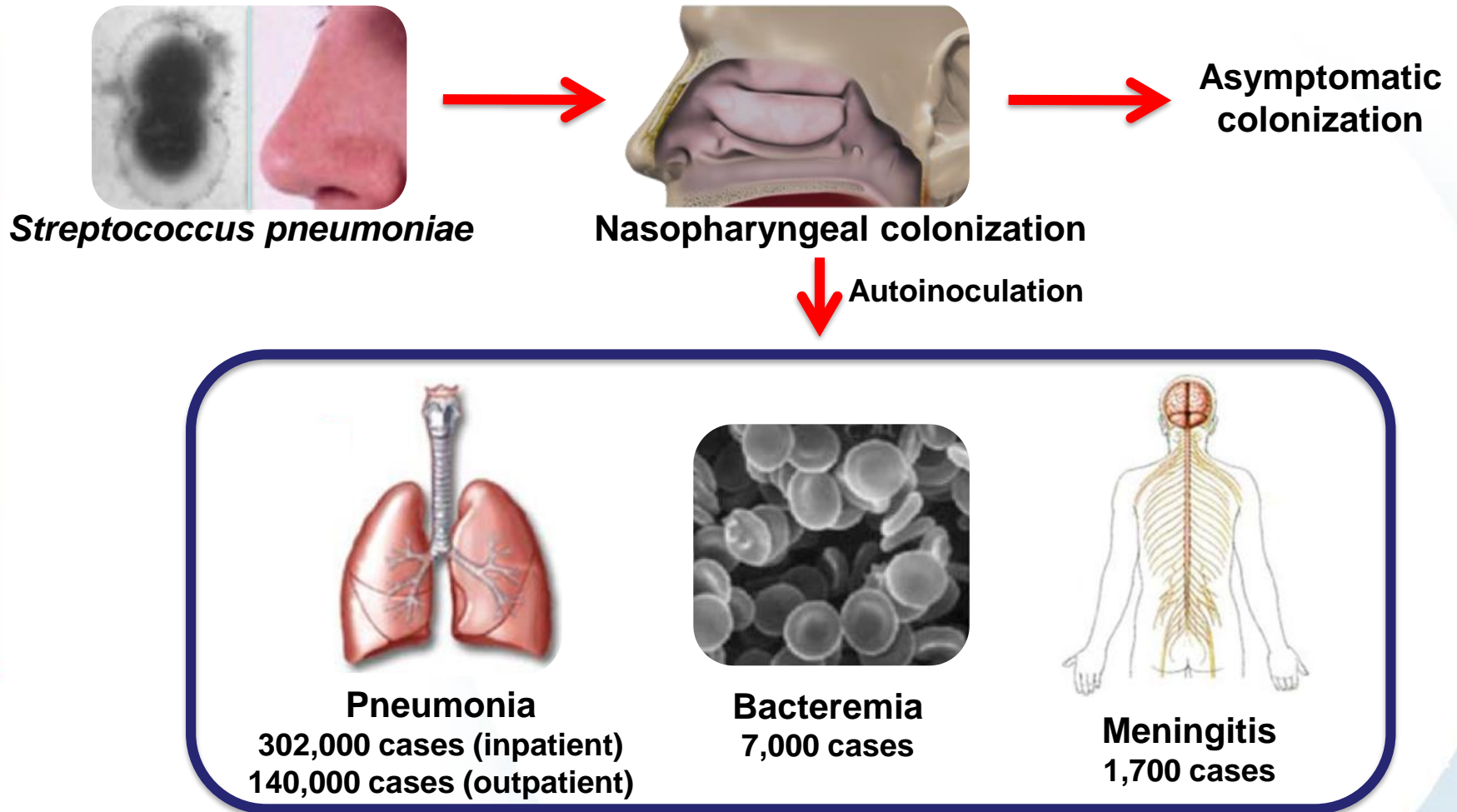
1. NO pneumococcal immunization
2. PCV13
3. PPSV23
4. PPSV23 today and PCV13 in 1 year
5. PCV13 today and PPSV23 in 1 year

Patient Case: David Summers

David, Jane's father, is 86 years old and in perfect health. Other than osteoarthritis, he has no chronic conditions. He gets his flu shot every year. No one has ever asked him about a "pneumonia shot". Which of the following is an accurate pneumococcal vaccine schedule for David?

- 1. PCV13 now, and done.**
- 2. PPSV23 now, and done.**
- 3. PCV13 now, and PPSV23 in one year**
- 4. PPSV23 now, and PCV 13 in one year**
- 5. PCV 13 now, PPSV 23 in one year, and repeat PPSV23 in 5 years**

Pneumococcal Disease Pathogenesis and Burden in Adults Aged ≥ 50 Years



1. Henriques-Normark B, et al. *Cold Spring Harb Perspect Med.* 2013;3:a010215.
2. Huang SS, et al. *Vaccine.* 2011;29:3398–3412.

Pneumococcal Disease

PNEUMOCOCCAL DISEASE:

Sinusitis
Otitis media
Pneumonia

USA 4,000,000 cases/year
445,000 hosp. admits/year
22,000 deaths/year

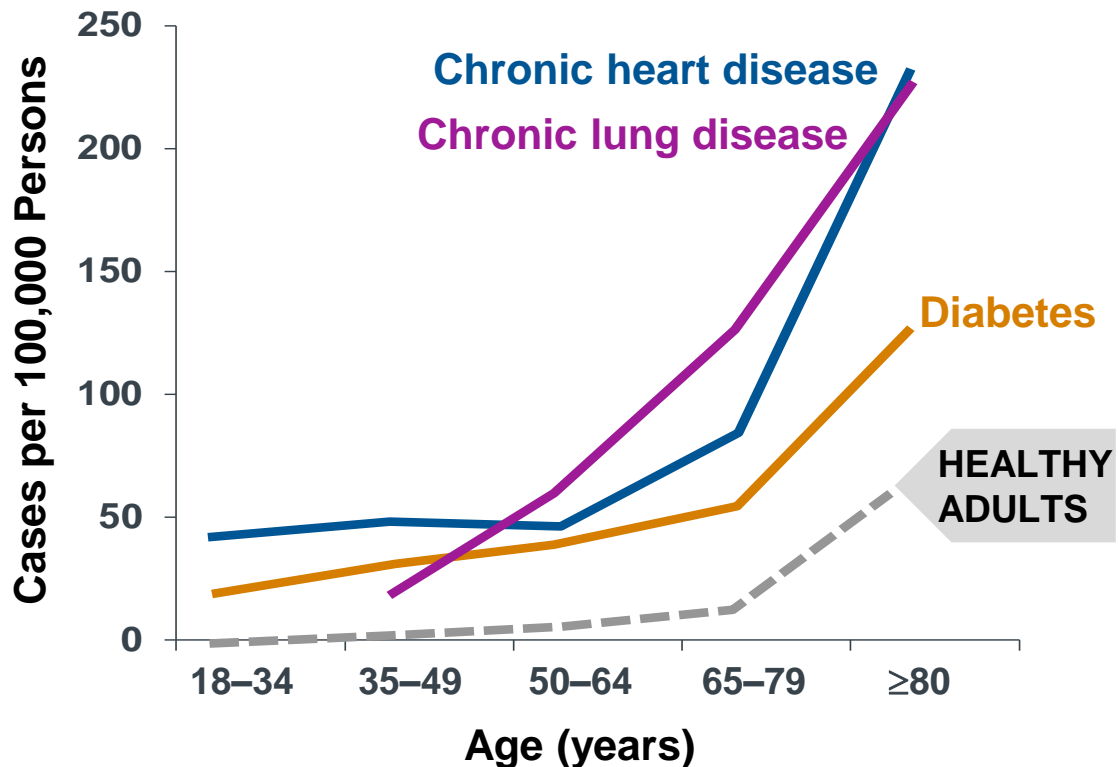
INVASIVE PNEUMOCOCCAL DISEASE (IPD):

Bacteremia
Meningitis
Sepsis

USA:

- 29,100 cases (9.1/100,000)
 - 3250 deaths
- <5 yr: 8.7/100,000
- ≥65: 24.8/100,000

The Incidence of Pneumococcal Disease Increases With Age and Certain Chronic Conditions



Diabetes mellitus

3X the risk of IPD compared to healthy adults

Chronic heart disease

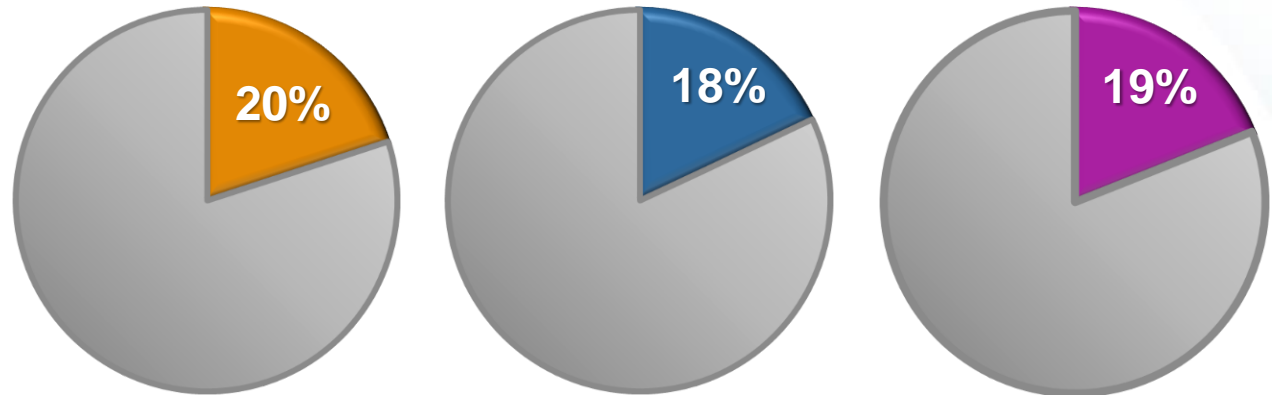
6X the risk of IPD compared to healthy adults

Chronic lung disease

6X the risk of IPD compared to healthy adults

Many Adults With Pneumococcal Disease Have Underlying Medical Conditions

Frequency of Certain Chronic Conditions Among Adults With IPD — United States^a



Age group	Diabetes mellitus	Chronic heart disease	Chronic lung disease
18–49 years (n=1,037)	10%	4%	4%
50–64 years (n=1,123)	22%	12%	21%
≥65 years (n=1,178)	25%	37%	31%

IPD, invasive pneumococcal disease.

^aBased on 2009 Active Bacterial Core surveillance data. N=3,338 cases in adults aged ≥18 years. The Active Bacterial Core surveillance areas represented approximately 22 million adults aged ≥18 years in 2009.

Muhammad RD, et al. *Clin Infect Dis.* 2013;56:e59–e67.

Pneumococcal Vaccination

Key Principles

1. Never give PCV-13 and PPSV-23 together at the same visit.
2. Whenever both are indicated, it is best to give PCV-13 first, and follow with PPSV-23 at the appropriate interval.
3. If either vaccine is inadvertently given earlier than the recommended interval, do NOT repeat the dose.

Pneumococcal Vaccines

- **PPSV23**

- Purified capsular polysaccharide → ‘traditional’ PNC vaccine
- Contains 23 types—cause ~88% bacteremic pneumococcal disease
- 60%–70% effectiveness vs. invasive disease
 - Challenge to assess prevention of PNC pneumonia.
- Immunity lasts at least 5 years following 1 dose
- FDA-approved for all persons ≥2 years at increased risk for pneumococcal disease
- Local reactions – only common adverse event

- **PCV13**

- Conjugate vaccine – results in higher antibody titers
- Replaced PCV7 for childhood immunization [6 wk–6 yr] in 2010
- 2011 FDA-approved for adults >50 years: prevent pneumonia, IPD
 - Based on immunogenicity and safety studies
- 2012 ACIP recommends PCV: IPD prevention, highest-risk adults
 - Highest risk based on anatomic and immunocompromised
 - Best practice: give BEFORE PPSV23
- 2014 ACIP recommends PCV/PPS combination strategy in aged 65+
- Local reactions – only common adverse event

In 2013, 38% of IPD among adults aged ≥65 years was caused by serotypes unique to PPSV23

CDC. *MMWR Morb Mortal Wkly Rep.* 2012;61(21):394-395.

CDC. *MMWR Morb Mortal Wkly Rep.* 2014;63(37):822-5.

PPSV23 Vaccine Effectiveness

- What is the evidence in preventing IPD and pneumonia?
 - Meta-analysis including 18 RCTs (64,852 participants)

Event	No. of RCTs	Event with Vaccine (n/N)	Event with Control (n/N)	OR (95% CI)
IPD	11	15/18634	63/17855	0.26 (0.14 to 0.45)
IPD (vaccine types only)	5	14/13889	140/17334	0.18 (0.10 to 0.31)
Pneumonia (all causes)	16	978/22643	1547/25091	0.72 (0.56 to 0.93)
Definitive pneumococcal pneumonia	10	15/18132	60/17351	0.26 (0.15 to 0.46)
Definitive pneumococcal pneumonia (vaccine types only)	4	3/15583	30/14978	0.13 (0.05 to 0.38)

Protective vaccine efficacy for definitive pneumococcal pneumonia : 74% (95% CI, 54%–85%)

PCV13 Adult Vaccine Effectiveness

CAPiTA

- Placebo-controlled RCT PCV13 unimmunized adults 65+ years
 - Netherlands
 - No routine pneumococcal vaccine in adults
 - PCV7 in Dutch infants since 6/2006 -> PCV10 in March 2011
- 84,000+ participants PCV13 vs. Placebo
 - Enrolled 9/2008–1/2010, follow-up thru 8/2013
- Outcomes:
 - **Primary: Reduced 1st bacteremic CAP with vaccine-type PNC (42%)**
 - **Secondary: Reduced 1st nonbacteremic CAP (45%)**
 - **Secondary: Reduced Invasive PNC over 75%**
- Serologic and urinary Ag used to identify PNC infection
- DID NOT address sequential PCV13/PPSV23 immunization

Strategies for Sequential Use of Conjugate and Polysaccharide Vaccine Use in Adults

- Conjugate vaccine: more immunogenicity (higher antibody levels) and can have booster effect
 - 13 serogroups (accounts for approximately 50% of invasive cases of pneumococcal disease)
- Polysaccharide vaccine: less immunogenicity and NO booster effect
 - But has 23 serogroups (accounts for approximately 89% of invasive cases)
- Give conjugate first, followed by polysaccharide for potentially optimal effect
- If polysaccharide given initially, wait one year to administer the conjugate vaccine

Pneumococcal Immunization I

PPSV23 ALONE for INCREASED RISK

All cigarette smokers ≥ 19 years to 64 years

Chronic conditions ≥ 19 years to 64 years:

Diabetes

Lung disease: asthma, COPD

Cardiovascular disease

Liver disease, alcoholism

Kidney disease

(except ESRD, nephrotic syndrome –
HIGHEST risk)

- **REVACCINATION ONCE** after age 65 [PLUS 5 years after initial dose] for those vaccinated prior to age 65
- **Adults 65 years and older: now in highest risk group. Follow different recommendations.**

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5934a3.htm>

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6140a4.htm>

Pneumococcal Immunization IIa

SEQUENTIAL PCV13 + PPSV23: **HIGHEST RISK**

Immunocompromised (≥ 19 YEARS OF AGE):

1. Disease:

- Cancer: solid tumors, hematologic malignancies, myeloma, etc.
- HIV
- INHERITED and OTHER immune deficiency (CVID, etc.)
- End-stage kidney disease (ESRD), nephrotic syndrome

2. Iatrogenic:

- MEDS: Steroids (20+ mg/d), biologic immunomodulators, others
- TRANSPLANTS: solid organ, bone marrow, stem cell

3. Asplenia:

- ANATOMIC: splenectomy (best if immunized prior to)
- FUNCTIONAL: hemoglobinopathy, sickle cell, other

Anatomic (≥ 19 YEARS OF AGE):

- CSF leak, cochlear implant, splenectomy

Sequence: PCV13, then ≥ 8 weeks PPSV23, then 5 years later PPSV23

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6140a4.htm>

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6337a4.htm>

Pneumococcal Immunization IIb

SEQUENTIAL PCV13 + PPSV23: **HIGHEST RISK**

Age: ≥ 65 years of age

Sequence: PCV13 then 1 year later PPSV23 (CDC Preferred Sequencing)

Caveat: IF patient has already received PPSV23 on or after age 65, then:

- Single dose of PCV13 at least 1 year after the PPSV23 dose

Additional Information:

- Patients over age 65 who received one or more doses of PPSV23 PRIOR to age 65 should still receive one dose each of PCV13 and PPSV23 AFTER age 65.
 - Post-65 dose of PCV13 must be 1 year after pre-65 dose of PPSV23
 - Post-65 dose of PPSV23 must be 1 year after post-65 dose of PCV13 AND must be 5 years after pre-65 dose of PPSV23.

Millions of Adults at Increased Risk Remain Unvaccinated¹⁻⁴

What percentage of the **~73 million unvaccinated US adults¹**
fall into these risk categories?

All adults aged ≥ 65
years

~39%

Adults aged ≥ 19 years who are
immunocompetent with certain
chronic conditions such as:

~67%

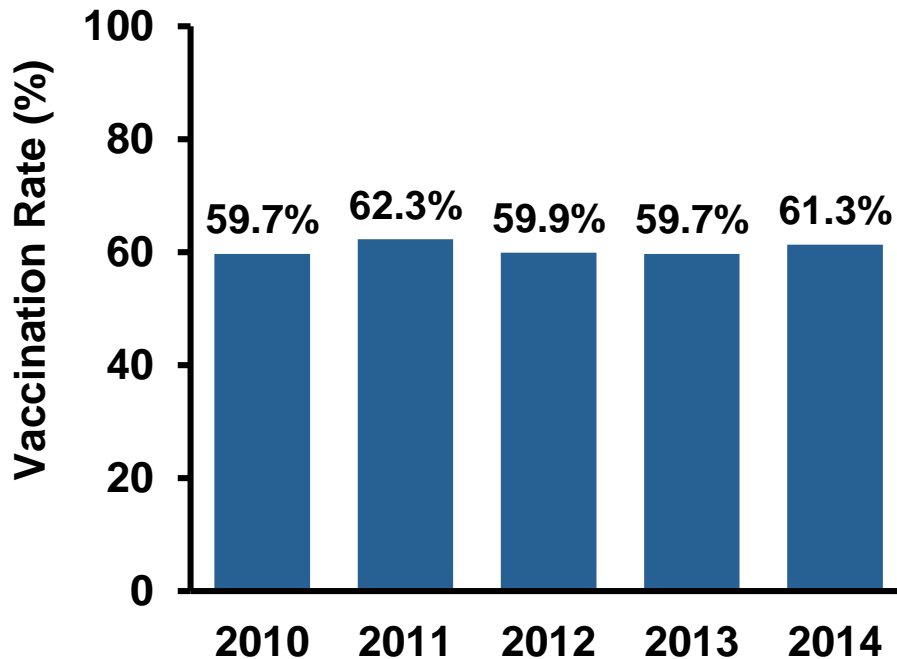
Adults aged ≥ 19 years with
immunocompromising conditions or
certain other conditions:

~14%

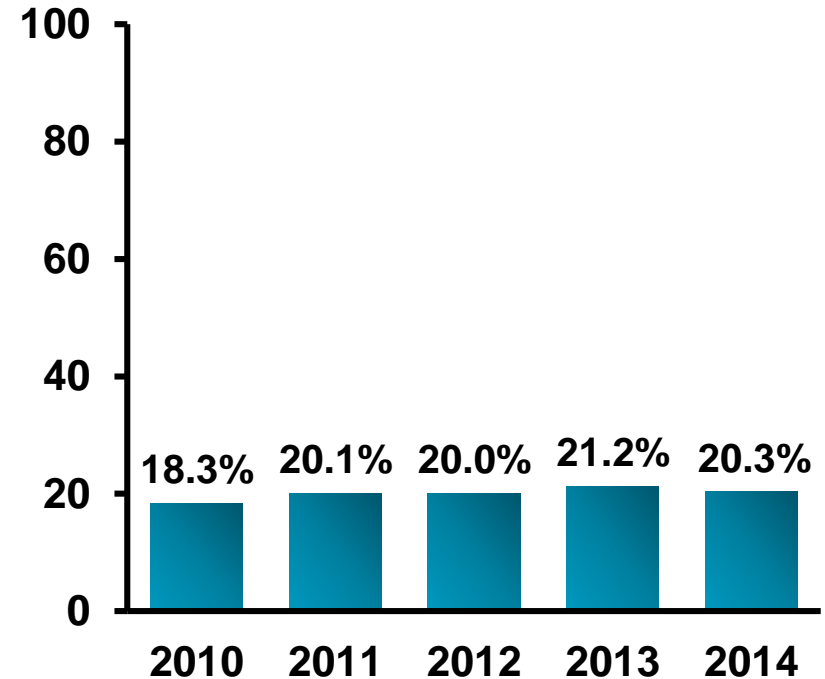
1. National Foundation for Infectious Diseases (NFID). Pneumococcal disease: hard to say it, easy to get vaccinated. adultvaccination.org/professional-resources/public-health-toolkit/pneumo-fact-sheet-hcp.pdf.
2. Centers for Disease Control and Prevention (CDC). *MMWR Recomm Rep*. 2012;61:816–819.
3. Lu P, et al. *Am J Epidemiol*. 2012;175:827–837.
4. Shea KM, et al. *Open Forum Infect Dis*. Spring 2014;1:1–9.
5. *MMWR*. Feb 5, 2016. <http://www.cdc.gov/mmwr/volumes/65/ss/ss6501a1.htm>

CDC Says Adult Vaccination Rates Are “Unacceptably Low”¹

Pneumococcal Vaccination Rates — United States, 2010–2014



Adults aged ≥ 65 years^{2,3}



High-risk adults aged < 65 years^{2,3,a}

^aAdults with certain underlying medical conditions defined as high risk per the CDC’s Advisory Committee on Immunization Practices.

1. Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep.* 2013;62(4):66–72.
2. National Center for Health Statistics. *Health, United States, 2012: With Special Feature on Emergency Care.* Hyattsville, MD. 2013. cdc.gov/nchs/data/hus/hus12.pdf.
3. CDC. *MMWR Morb Mortal Wkly Rep.* 2016;65(1):1-36.

Call to Action:

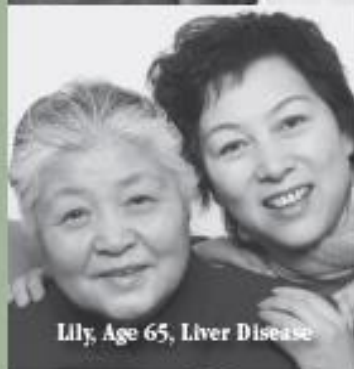
Preventing Pneumococcal Disease in US Adults with Chronic Conditions



Diane, Age 50, Heart Disease



Michael, Age 30, Asthma



Lily, Age 65, Liver Disease



Joseph, Age 55, Diabetes

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National
Foundation for
Infectious
Diseases

January 2015

Indications for PCV13 and PPSV23 Administration for Adults Age 19 Years* and Older by Risk Group

Source: Centers for Disease Control and Prevention (CDC)¹

Risk Group	Underlying Medical Condition	PCV13	PPSV23	
		Recommended	Recommended	Revaccination 5 years After First Dose
Immunocompetent persons	Chronic heart disease [†]		✓	
	Chronic lung disease [§]		✓	
	Diabetes mellitus		✓	
	Cerebrospinal fluid leak	✓	✓	
	Cochlear implant	✓	✓	
	Alcoholism		✓	
	Chronic liver disease, cirrhosis		✓	
	Cigarette smoking		✓	
Persons with functional or anatomic asplenia	Sickle cell disease/other hemaglobinopathy	✓	✓	✓
	Congenital or acquired asplenia	✓	✓	✓
Immunocompromised persons	Congenital or acquired immunodeficiency [¶]	✓	✓	✓
	Human immunodeficiency virus infection	✓	✓	✓
	Chronic renal failure	✓	✓	✓
	Nephrotic syndrome	✓	✓	✓
	Leukemia	✓	✓	✓
	Lymphoma	✓	✓	✓
	Hodgkin disease	✓	✓	✓
	Generalized malignancy	✓	✓	✓
	Iatrogenic immunosuppression ^{**}	✓	✓	✓
	Solid organ transplant	✓	✓	✓
	Multiple myeloma	✓	✓	✓

* All adults age 65 years and older should receive a dose of PPSV23, regardless of previous pneumococcal vaccination history.

† Including congestive heart failure and cardiomyopathies, excluding hypertension.

§ 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.



Herpes Zoster

Herpes Zoster (Shingles)



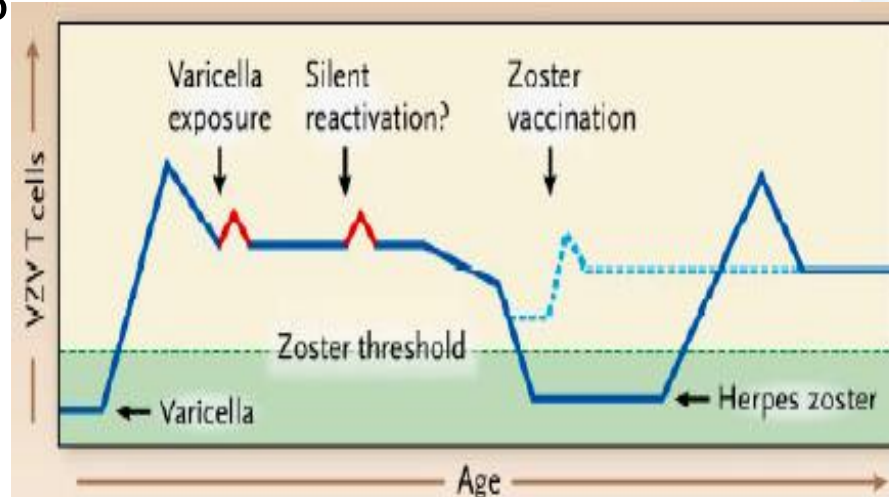
Patient Case: Don Acton

A healthy 66-year-old man returns for his wellness visit. He smokes 2 cigarettes a week and had an episode of shingles 8 months ago. He received high-dose influenza vaccine from his local pharmacy in September and pneumococcal vaccine 1 year ago. Which of the following is the most correct regarding zoster immunization for Don?

- 1. No Zoster vaccination; he had previous shingles**
- 2. No Zoster vaccination today; can't be co-administered with PPSV23**
- 3. Zoster vaccine today**
- 4. Zoster vaccine today and booster vaccination in 5–10 years**

Zoster

- Most who have varicella have Ab for life
 - Zoster occurs when cell-mediated immunity (CMI) surveillance declines
 - Reactivation or varicella exposure re-stimulates CMI
 - Cycle can repeat multiple times
- Lifetime risk of Zoster ~33%
 - By age 85: risk ~50%
 - PHN= most common AE
 - Up to 1/3 patients with Zoster
 - More common
 - >70 years with Zoster
 - Immunocompromised
- Vaccination stimulates CMI



PHN, postherpetic neuralgia.

Arvin A. *N Engl J Med.* 2005;352:2266-77.

Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5705a1.htm>

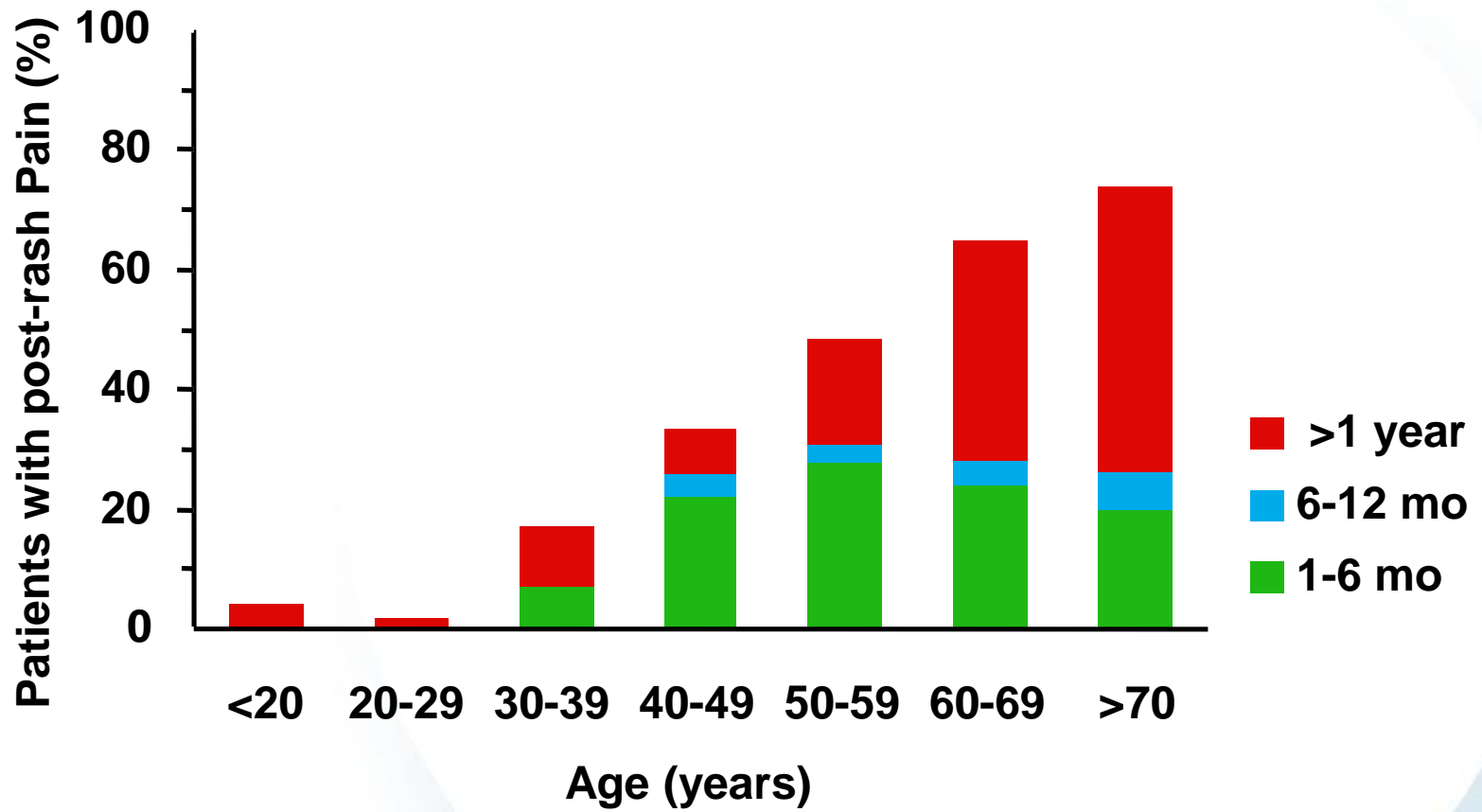
Zoster Pathophysiology

- Reactivation of a latent Varicella zoster virus
 - Promptly or decades after chickenpox
- Trigger factors
 - Reduced immunocompetence
 - Trauma
 - Normal aging
- Estimated 1 million cases annually in the US
- Adults at greatest risk:
 - Immunocompromised conditions (e.g., malignancy, HIV)
 - Taking immunosuppressive medications (e.g., steroids, rheumatoid arthritis meds)

Complications of Zoster

- **Scarring and keloid formation; secondary skin infection of skin lesions**
- **Visceral zoster and encephalitis**
- **Corneal damage and blindness**
- **Pneumonia (viral or bacterial)**
- **Postherpetic neuralgia (PHN)**
 - Pain in the dermatome of rash after rash heals
 - Criteria: 90 (or 120) days after rash onset
 - Pain can last months to years
 - As people get older, more likely to develop PHN and the pain is more likely to be severe

Duration of Pain after Rash Heals Increases With Age



Zoster

Vaccine Efficacy Trial:

- 38,546 Veterans Median age: 69 years
 - 60–69 years: 20,747 [Efficacy greatest in this group]
 - ≥70 years: 17,799 (46%)
 - ≥80 years: ~2,500 (6.5%)
 - Excluded: Immunocompromised, prior zoster, <60 yrs.
- Vaccine group had [vs. placebo]:
 - 51% fewer episodes of zoster
 - Less severe disease
 - 66% less postherpetic neuralgia
- No significant safety issues were identified

Zoster



- Vaccinate **HEALTHY** adults 60+ years old
- ACIP: *NOT IMMUNOCOMPROMISED*
 - FDA-approved from age 50 differs from ACIP recommendation
 - Regardless of prior Zoster [arbitrary CDC opinion: wait 1 year]
 - No need to test/vaccinate vs. varicella first
- Contraindications
 - Pregnancy
 - Anaphylactic hypersensitivity to neomycin, gelatin
 - No need to defer for ‘at-risk contacts’– transmission risk low
 - No need to defer if recent transfusion, Ab-containing products
- Adverse events
 - Occasional mild varicella-like rash at vaccine site
- Frozen vaccine: Give w/in 60 minutes, 0.65 mL SQ deltoid
- Duration of protection: At least 4 years. No booster.

Zoster: Special Populations

- Prior to Immune Suppression
 - American College of Rheumatology recommends Zoster vaccine [2008] in age 50+ years
 - Recommend off IS × 4 weeks after vaccine
 - Poster ACR 2014:
 - Zoster vaccine in 57 patients on biologics SQ, IV
 - NO disseminated Zoster
 - Study ongoing...
- HIV
 - No recommendation for vaccination, studies are underway
- On the horizon
 - Revaccination 10 years out (Levin et al JID 2016)
 - Vaccination before age 50 years
 - Subunit vaccine

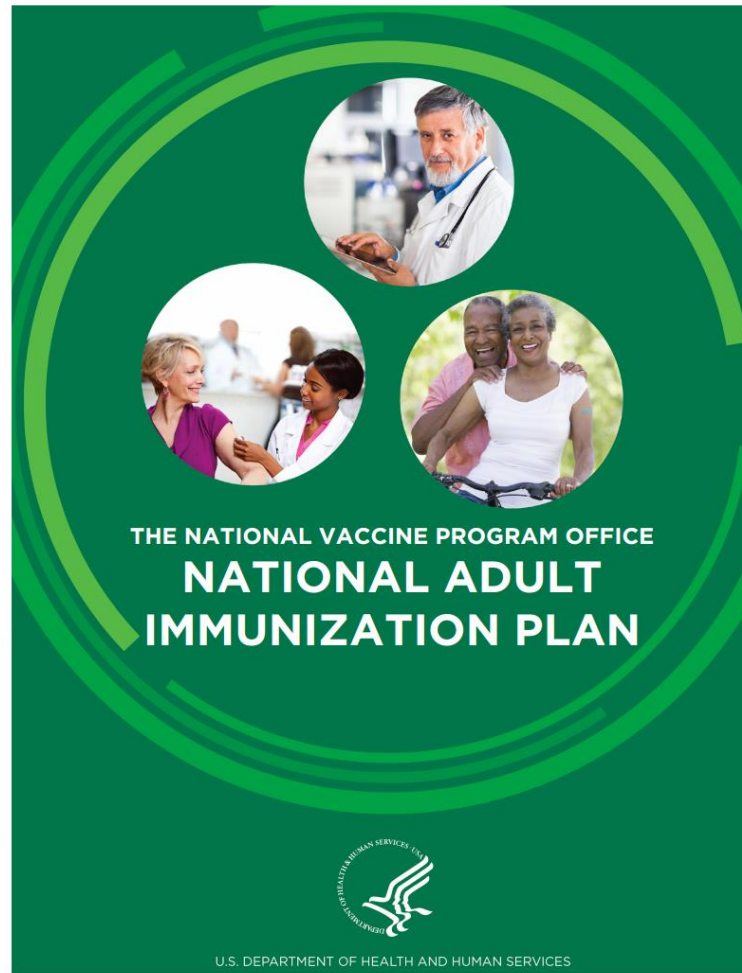
Zoster: Special Consideration

- Simultaneous administration of pneumococcal vaccine
 - One study showed the average titer against varicella zoster virus (VZV) was lower in persons who received zoster and PPSV23 at the same visit compared to persons who received these vaccines 4 weeks apart- this led to FDA recommendation.
 - However, a large study was subsequently conducted that showed that zoster vaccine was equally effective at preventing herpes zoster whether it was administered simultaneously with PPSV23 or 4 weeks earlier
 - CDC continues to recommend that HZV and PPSV23 be administered at the same visit if the person is eligible for both vaccines.



General Practice Recommendations

National Vaccine Advisory Committee (NVAC)



Available at: <http://www.hhs.gov/sites/default/files/nvpo/national-adult-immunization-plan/naip.pdf>

NVAC Goals

The goals are as follows:

Goal 1: Strengthen the adult immunization infrastructure.










Goal 2: Improve access to adult vaccines.

Goal 3: Increase community demand for adult immunizations.

Goal 4: Foster innovation in adult vaccine development and vaccination-related technologies.

Vaccine Storage and Handling

Key Messages:

-  The vaccine cold chain is a temperature-controlled environment used to maintain and distribute vaccines in optimal condition.
-  Monitor the temperature of your storage unit(s) regularly to assure that appropriate conditions are maintained.
-  Take immediate corrective action when a storage unit temperature is outside the recommended range (Troubleshooting).
-  Call the vaccine manufacturer for guidance.
-  If you are a VFC provider or have other vaccines purchased with public funds, contact your immunization program .
-  Vaccine appearance is NOT a reliable indicator that vaccines have been stored under appropriate conditions.
-  Vaccine exposed to inappropriate temperatures that is inadvertently administered generally should be repeated. Contact your immunization program , vaccine manufacturer(s), or both for guidance.

Vaccine Storage & Handling Toolkit

May 2014



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Timing and Spacing of Doses

- Doses inside the minimum interval do not count!
 - 4-day grace period for all minimum intervals except for rabies vaccine
 - Some states have more stringent requirements: follow those if so
 - Note: The previous mentioned exception with pneumococcal vaccines (not included in CDC's General Recommendations)
- Increasing the interval potentially delays complete protection; but never need to restart a series
 - Case in point: HPV vaccine
 - Exception: Oral typhoid vaccine

Combination Vaccines

- Reduce the number of injections
- Potentially improve coverage and compliance
- Potentially reduce costs for both providers and patients
- Downside: Difficult to isolate which antigen may have caused side effect in the event one occurs
- Accurate documentation is a must!

Immunosuppression and Vaccines

- Live vaccines should be administered ≥ 4 weeks prior to planned immunosuppression.
- Inactivated vaccines should be administered ≥ 2 weeks prior to planned immunosuppression.
- Specialists and primary care providers share responsibility for immunizing immunosuppressed patients and their family members.

2013 IDSA Clinical Practice Guideline for
Vaccination of the Immunocompromised Host

Lorry G. Rubin,¹ Myron J. Levin,² Per Ljungman,^{3,4} E. Graham Davies,⁵ Robin Avery,⁶ Marcie Tomblyn,⁷ Athos Bousvaros,⁸ Shireesha Dhanireddy,⁹ Lillian Sung,¹⁰ Harry Keyserling,¹¹ and Insoo Kang¹²

Take Home Points

Per CDC:

ASSESS vaccination status of all patients in every clinical encounter

Strongly **RECOMMEND** vaccines that patients need

ADMINISTER needed vaccines or **REFER** to a provider who can vaccinate

DOCUMENT vaccines received by your patients



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