



# Immunizations to Consider in Adult HIV Patients

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# Objectives

- Discuss the current immunization recommendations by the CDC Advisory Committee on Immunization Practices (ACIP) for adult HIV patients
- Discuss upcoming changes in the immunization schedule
- Review data supporting the use of meningococcal and pneumococcal vaccines
- Examine the use of Herpes zoster vaccine in HIV patients
- Describe Medicare and Medicaid coverage of immunizations

# Vaccines: issues to consider

- Prevention of mortality and morbidity
- Vaccine schedule
- Injected, spray, oral
- Live attenuated, inactivated
- Immune response/CD4
- Costs, insurance

# The compromised host

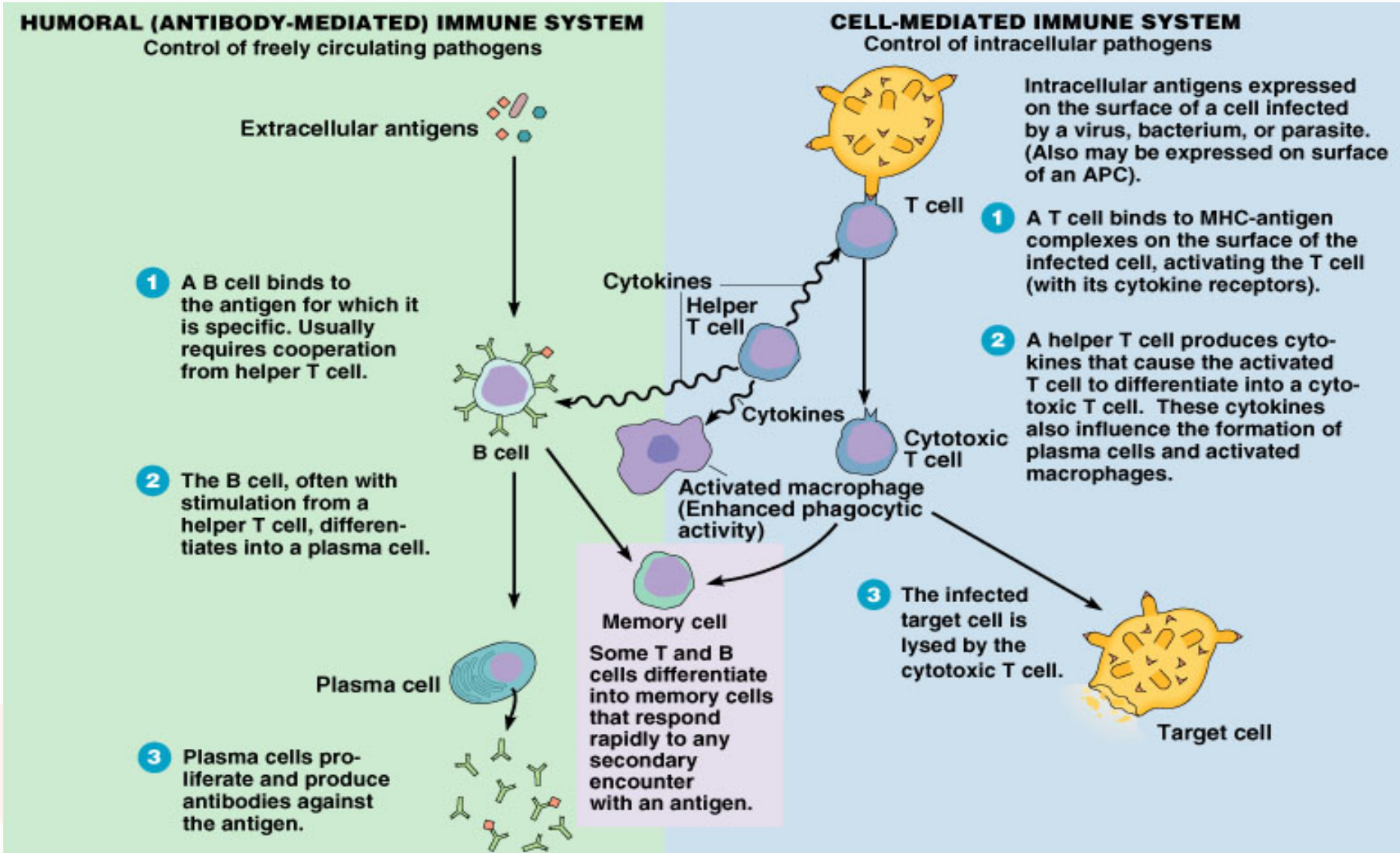
- Defects in cell mediated immunity
- B cell dysfunction
- Suboptimal humoral immune response



# Immune Response

	Humoral-Mediated Immunity	Cell-Mediated Immunity
Mechanism	Antibody-mediated	Cell-mediated
Cell Type	B Lymphocytes	T Lymphocytes
Mode of action	Antibodies circulating in serum	Direct cell-to-cell contact or secreted soluble products (e.g. cytokines)
Purpose	Primary defense against extracellular pathogens: extracellular bacteria, circulating virus	Primary defense against intracellular pathogens: viruses and fungi, intracellular bacteria, (also tumor antigens, and graft rejection)

<http://media-cache-ec0.pinimg.com/736x/13/23/7d/13237d40691d713e082a65898f45556b.jpg>



[http://classes.midlandstech.edu/carterp/Courses/bio225/chap17/17-19\\_Duality\\_1.jpg](http://classes.midlandstech.edu/carterp/Courses/bio225/chap17/17-19_Duality_1.jpg)

## Classification of Vaccines

- Live attenuated
  - viral
  - bacterial
- Inactivated

### Inactivated Vaccines

- Whole
  - viruses
  - bacteria
- Fractional
  - protein-based
    - toxoid
    - subunit
  - polysaccharide-based
    - pure
    - conjugate

<https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/prinvac.pdf>



# Vaccine Types

## **Live, attenuated vaccines (LAV):**

Contains a weakened but live form of a disease-causing microbe that can trigger an immune response. The attenuated (weakened) microbe typically does not cause the disease.

## **Inactivated vaccines:**

Made from microbes that have been killed with chemicals, heat, or radiation. There is no risk that an inactivated vaccine can cause disease from infection.

# Inactivated Polysaccharide Vaccines: pure and conjugate

## **Pure Polysaccharide:**

Subunit vaccine composed of chains of sugar molecules that make up the surface capsule of certain bacteria

## **Conjugate Polysaccharide:**

Polysaccharide is chemically combined with a protein molecule (antigen/toxoid) to increase potency

## Polysaccharide Vaccines

### Pure polysaccharide

- pneumococcal
- meningococcal
- *Salmonella Typhi* (Vi)

### Conjugate polysaccharide

- *Haemophilus influenzae* type b (Hib)
- pneumococcal
- meningococcal

<https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/prinvac.pdf>

# Live Vaccines

Bacteria	Viruses
Tuberculosis (BCG)	Oral Polio Vaccine (OPV)
	Measles
	Yellow Fever
	Varicella/Herpes Zoster
	<del>Live attenuated flu vaccine (LAIV)</del>

# CDC Recommended Immunizations for Adult HIV Patients

- Hepatitis B
- Influenza
- Pneumococcal
- Tetanus, diphtheria, and pertussis (Tdap)
- Human papillomavirus (HPV)
- (Meningococcal)

# HIV: Contraindicated if CD4 <200

- Varicella
- Zoster
- Measles, Mumps, Rubella (MMR)

# CDC 2016: Recommended Adult Immunization schedule

Indication ▶	Vaccine ▼	Pregnancy	Immuno-compromising conditions (excluding HIV infection) <sup>4,6,7,8,13</sup>	★ HIV infection CD4+ count (cells/μL) <sup>4,6,7,8,13</sup>		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, on hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia and persistent complement component deficiencies <sup>4,11,12</sup>	Chronic liver disease	Diabetes	Healthcare personnel
				<200	≥200							
Influenza <sup>2,*</sup>												1 dose annually
Td/Tdap <sup>3,*</sup>		1 dose Tdap each pregnancy										Substitute Tdap for Td once, then Td booster every 10 yrs
Varicella <sup>4,*</sup>			Contraindicated									2 doses
HPV Female <sup>5,*</sup>					3 doses through age 26 yrs							3 doses through age 26 yrs
HPV Male <sup>5,*</sup>					3 doses through age 26 yrs							3 doses through age 21 yrs
Zoster <sup>6</sup>			Contraindicated									1 dose
MMR <sup>7,*</sup>			Contraindicated									1 or 2 doses depending on indication
PCV13 <sup>8,*</sup>							1 dose					
PPSV23 <sup>8</sup>							1, 2, or 3 doses depending on indication					
Hepatitis A <sup>9,*</sup>							2 or 3 doses depending on vaccine					
Hepatitis B <sup>10,*</sup>								3 doses				
MenACWY or MPSV4 <sup>11,*</sup>								1 or more doses depending on indication				
MenB <sup>11</sup>								2 or 3 doses depending on vaccine				
Hib <sup>14,*</sup>			3 doses post-HSCT recipients only					1 dose				

[http://www.immunize.org/shop/views/adultsched\\_pg2.pdf](http://www.immunize.org/shop/views/adultsched_pg2.pdf)

# CDC: 2016 Recommended Immunizations for Adults: By Health Condition

	Flu <i>Influenza</i>	Td/Tdap Tetanus, diphtheria, pertussis	Shingles <i>Zoster</i>	Pneumococcal		Meningococcal		MMR Measles, mumps, rubella	HPV <i>Human papillomavirus</i>		Chickenpox <i>Varicella</i>	Hepatitis A	Hepatitis B	Hib <i>Haemophilus influenzae type b</i>
				PCV13	PPSV23	MenACWY or MPSV4	MenB		for women	for men				
Pregnancy	Green	Green	Light Purple	Light Yellow	Blue	Blue	Light Yellow	Light Purple	Light Yellow	Light Yellow	Light Purple	Blue	Blue	Light Yellow
Weakened Immune System	Green	Green	Light Purple	Green	Green	Blue	Blue	Light Purple	Green	Green	Light Purple	Blue	Blue	Green
HIV: CD4 count less than 200	Green	Green	Light Purple	Green	Green	Blue	Blue	Light Purple	Green	Green	Light Purple	Blue	Blue	Blue
HIV: CD4 count 200 or greater	Green	Green	Light Purple	Green	Green	Blue	Blue	Green	Green	Green	Light Purple	Blue	Blue	Blue
Kidney disease or poor kidney function	Green	Green	Light Purple	Green	Green	Blue	Blue	Green	Green	Green	Light Purple	Blue	Blue	Blue
Asplenia (if you do not have a spleen or if it does not work well)	Green	Green	Light Purple	Green	Green	Blue	Blue	Green	Green	Green	Light Purple	Blue	Blue	Green
Heart disease Chronic lung disease Chronic alcoholism	Green	Green	Light Purple	Green	Green	Blue	Blue	Green	Green	Green	Light Purple	Blue	Blue	Blue
Diabetes (Type 1 or Type 2)	Green	Green	Light Purple	Green	Green	Blue	Blue	Green	Green	Green	Light Purple	Blue	Blue	Blue
Chronic Liver Disease	Green	Green	Light Purple	Green	Green	Blue	Blue	Green	Green	Green	Light Purple	Blue	Blue	Blue

<https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-schedule-easy-read.pdf>



# CDC: 2016 Recommended Immunizations for Adults: By Age

Age Group	Flu <i>Influenza</i>	Td/Tdap Tetanus, diphtheria, pertussis	Shingles Zoster ★	Pneumococcal		Meningococcal		MMR Measles, mumps, rubella ★	HPV Human papillomavirus ★		Chickenpox Varicella	Hepatitis A	Hepatitis B	Hib <i>Haemophilus influenzae type b</i>
				PCV13	PPSV23	MenACWY or MPSV4	MenB		for women	for men				
19 - 21 years	Green	Green	Yellow	Blue	Blue	Blue	Blue	Green	Green	Green	Blue	Blue	Blue	
22 - 26 years	Green	Green	Yellow	Blue	Blue	Blue	Blue	Green	Blue	Green	Blue	Blue	Blue	
27 - 49 years	Green	Green	Yellow	Blue	Blue	Blue	Blue	Green	Yellow	Green	Blue	Blue	Blue	
50 - 59 years	Green	Green	Yellow	Blue	Blue	Blue	Blue	Green	Yellow	Green	Blue	Blue	Blue	
60 - 64 years	Green	Green	Green	Blue	Blue	Blue	Blue	Yellow	Yellow	Green	Blue	Blue	Blue	
65+ year	Green	Green	Green	Green	Green	Blue	Blue	Yellow	Yellow	Green	Blue	Blue	Blue	

<https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-schedule-easy-read.pdf>

# 2017: Schedule Updates

- \*Schedule will contain more information on adults with immune-compromising medical conditions
- Age groups 27 to 49 and 50 to 59 years combined into one block.
- Column for MSM has been relocated to alert healthcare providers to look at high-risk populations

# 2017 Updates

- Varicella and zoster vaccinations: details added for at-risk populations (healthcare workers, HIV).
- HPV vaccination: details added on vaccinating adults with immunocompromising conditions and the MSM population.
- Incorporated June 2016 recommendation for routine vaccination of all HIV-infected adults with a two-dose primary ACWY meningococcal series with revaccination every 5 years.

# Meningococcal update

- Five serogroups of meningococcus bacteria (A, B, C, W, Y)
- In the USA: serogroups B, C, and Y most common
- In HIV patients: serogroups A,C, W, Y most common
- HIV infection confers an additional 5- to 24-fold risk of meningococcal disease compared to uninfected persons
- Lower CD4 and higher viral load increase risk
- Different vaccines depending on age, risk factors

<https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm>

# Available Vaccines

## 1) Meningococcal conjugate vaccine:

- ★ - **MenACWY** (Menactra<sup>®</sup> or Menveo<sup>®</sup>): quadrivalent (A, C, W, Y)
- **Hib-MenCY-TT** (MenHibrix<sup>®</sup>): bivalent (C, Y), *H.influenzae* (type B)

## 2) Meningococcal polysaccharide vaccines:

- **MPSV4** (Menomune<sup>®</sup>): quadrivalent (A, C, W, Y)

## Serogroup B meningococcal vaccine

- **MenB** (Bexsero<sup>®</sup> or Trumenba<sup>®</sup>): monovalent (B)

# CDC 2016: Recommended Adult Immunization schedule

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[http://www.immunize.org/shop/views/adultsched\\_pg2.pdf](http://www.immunize.org/shop/views/adultsched_pg2.pdf)

# Footnote: 2016

There is no recommendation for MenB revaccination at this time. MenB vaccine may be administered concomitantly with MenACWY vaccine but at a different anatomic site, if feasible.

HIV infection is not an indication for routine vaccination with MenACWY or MenB vaccine; if an HIV-infected person of any age is to be vaccinated, administer 2 doses of MenACWY vaccine at least 2 months apart.

[http://www.immunize.org/shop/views/adultsched\\_pg2.pdf](http://www.immunize.org/shop/views/adultsched_pg2.pdf)

# Morbidity and Mortality Weekly Report (*MMWR*)

[CDC](#) > [MMWR](#)

## Recommendations for Use of Meningococcal Conjugate Vaccines in HIV-Infected Persons – A Immunization Practices, 2016

*Weekly* / November 4, 2016 / 65(43):1189–1194



Jessica R. MacNeil, MPH<sup>1</sup>; Lorry G. Rubin, MD<sup>2</sup>; Monica Patton, MD<sup>1</sup>; Ismael R. Ortega-Sanchez, PhD<sup>3</sup>; Stacey W. Martin, MS<sup>1</sup> ([View author affiliations](#))

[View suggested citation](#)

At its June 2016 meeting, the Advisory Committee on Immunization Practices (ACIP) recommended routine use of meningococcal conjugate vaccine (serogroups A, C, W, and Y; including MenACWY-D [Menactra, Sanofi Pasteur] or MenACWY-CRM [Menveo, GlaxoSmithKline]) for persons aged  $\geq 2$  months with human immunodeficiency virus (HIV) infection. ACIP has previously recommended routine vaccination of persons aged  $\geq 2$  months who have certain medical conditions that increase risk for meningococcal disease (1), including persons who have persistent (e.g., genetic) deficiencies in the complement pathway (e.g., C3, properdin, Factor D, Factor H, or C5–C9); persons receiving eculizumab (Soliris, Alexion

[www.cdc.gov/](http://www.cdc.gov/)

<https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm>



# Updated Recommendations:

- June 22, 2016: ACIP recommends use of meningococcal conjugate vaccine amongst HIV patients >2 months
- Two doses 8 weeks apart, with booster every 5 years until age 70
- Evaluated meningococcal disease epidemiology against cost effectiveness of a vaccination schedule
- Based on immunogenicity data from two studies

<https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm>

# The study

- Open label trial: 324 HIV infected individuals (11-24 yrs) received one dose at entry
- After 24 weeks, based on CD4% >15%, randomized to receive another dose
- Those with CD4% <15% all received a second dose

<https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm>

- Measured antibodies against each serogroup at weeks 4, 24, 28, 72 (predefined titer 1:128)
- Response based on CD4% (serogroup C)

	4 weeks	28 weeks	72 weeks
CD4 >15% (1 dose)	65%	31%	21%
CD4 >15% (2 doses)	59%	64%	35%
CD4 <15% (2 doses)	22%	22%	6%

# Safety

- Adverse events assessed for 6 weeks after each dose; inversely related to entry CD4%
- 5% reported a serious adverse event (AE)- one AE judged to be related to MenACWY

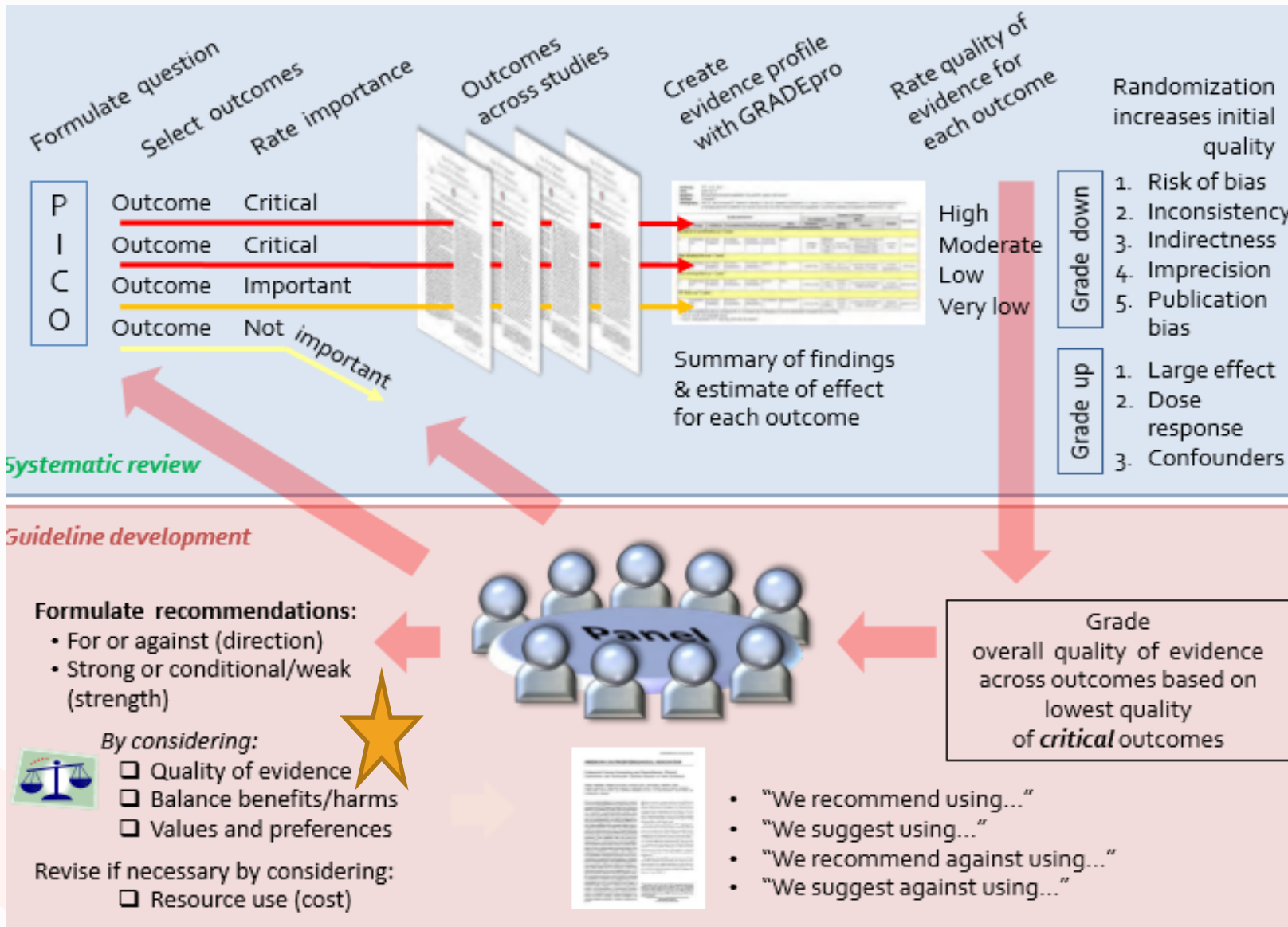
**Summary of evidence for meningococcal conjugate vaccination of HIV-infected persons aged  $\geq 2$  months using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)\* framework — United States**

Harms	Grade
Serious adverse events (after any dose)	4

<https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm>

# GRADE

- **Grading of Recommendations, Assessment, Development and Evaluations (GRADE)**
- CDC vaccine recommendations are developed using this evidence-based method
- A systematic, explicit, transparent approach to making judgements about quality of evidence and strength of recommendations
- Widely seen as the most effective method of linking evidence-quality evaluations to clinical recommendations



<https://www.cdc.gov/vaccines/acip/recs/grade/downloads/guide-dev-grade.pdf>

- MenACWY can be given with PCV13
- No data for the use of MPSV4 in HIV patients
- Pregnancy should not preclude vaccination with MenACWY
- Compared with no vaccination, approximately 122 cases and 23 deaths can be prevented
- 385 quality-adjusted life years (QALYs) saved at mean cost of \$732,000 per QALY

<https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm>

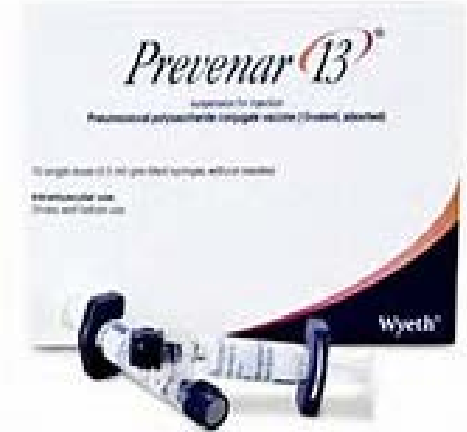
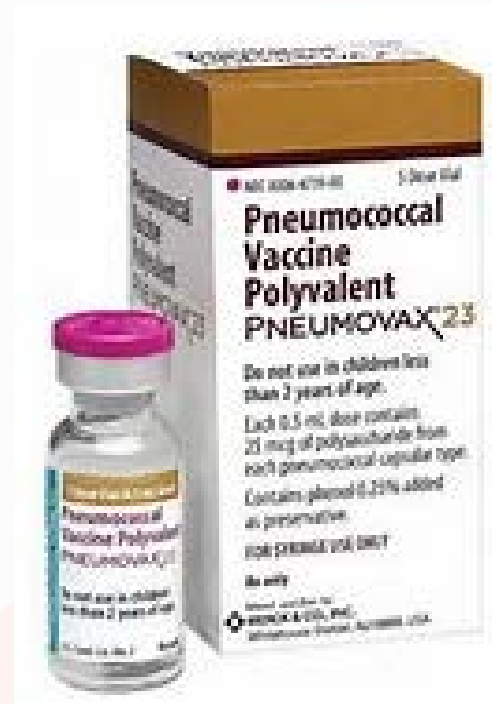
# Pneumococcal vaccine

Invasive pneumococcal disease remains a source of significant morbidity and mortality amongst HIV-infected individuals

Incidence of bacterial pneumonia is higher in HIV-infected individuals than in those who are not HIV infected

Recurrent pneumonia (2 or more episodes within a 1-year period) is an AIDS-defining condition

Rates of pneumococcal bacteremia remains 35-fold higher than in age-matched HIV-uninfected persons



<https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/327/bacterial-respiratory>



# Pneumococcal vaccinations

- **Pneumococcal polysaccharide vaccine**

- PPSV23

- Pneumovax 23<sup>®</sup>

- **13-valent pneumococcal conjugate vaccine**

- PCV13

- Prevnar 13<sup>®</sup>

- PCV13 and PPSV23 are covered by Medicare Part B

# Current Recommendations

- Those who have never received any pneumococcal vaccine should receive a single dose of PCV13 regardless of CD4 count (**AI**)
- Those with CD4  $\geq 200$  cells/mm<sup>3</sup> should then receive a dose of PPV23 at least 8 weeks later (**AII**)
- Those with CD4  $< 200$  cells/mm<sup>3</sup> can receive PPSV23 eight weeks after PCV13 (**CIII**), however, it may be preferable to defer until CD4 increases to  $> 200$  cells/mm<sup>3</sup> (**BIII**)

<https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/327/bacterial-respiratory>

# Pneumococcal Vaccination schedule



1 year

PPSV23 → → → PCV13

# ACIP study analysis: (PCV13, PPSV23)

- Evidence of benefits, harms, values and preferences, and cost-effectiveness were reviewed in accordance with GRADE methods
- Both vaccines were evaluated using data for HIV-infected adults
- Studies with 7-valent pneumococcal conjugate vaccine (PCV7) used as a proxy when no PCV13 studies were available
- Randomized controlled trials (RCT), direct observations studies
- PCV13 (RCTs), PPSV23 (1 RCT and 9 observational studies with conflicting data)

<https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html>

# Outcomes Reviewed

- Prevention of death
- Invasive pneumococcal disease (IPD)
- Pneumococcal pneumonia
- Hospitalizations due to pneumococcal disease
- Vaccine-induced immunogenicity
- Adverse events

<https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html>

# PCV13

Table 1. Benefits: 13-valent Pneumococcal Conjugate Vaccine in immunocompromised adults

Outcome	No. subjects (# studies)	Incidence in unvaccinated (cases/100,000)	Incidence in vaccinated unvaccinated (cases/100,000)	Vaccine efficacy (95% CI)	unvaccinated (cases/100,000) <sup>d</sup>	Number needed to vaccinate
Invasive Pneumococcal Disease <sup>a</sup>	496 (1 RCT, HIV+ adults, Malawi)[2]	64 <sup>c</sup>	17 <sup>d</sup>	74% (30, 90) <sup>b</sup>	47 <sup>d</sup>	2128 <sup>d</sup>

<https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html>

# PCV13

Table 5. Considerations for Formulating Recommendations: 13-valent Pneumococcal Conjugate Vaccine in immunocompromised adults

Key factors	Comments
Evidence type for benefits and harms	Indirectness & lack of evidence for 3 of 4 critical disease outcomes
Balance between benefits and harms	Benefits outweigh harms. Very high burden of disease in immunocompromised adults
Value	ACIP pneumococcal work group consensus regarding the importance of preventing critical pneumococcal outcomes
Cost-effectiveness	Uncertainty regarding costs/benefits relative to PPSV23

<https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html>



# PPSV23

Table 7. Summary of Evidence: 23-valent Pneumococcal Polysaccharide Vaccine in immunocompromised adults

Comparison	Outcome	Study design (# studies)	Findings	Evidence type	Overall Evidence type <sup>a</sup>
<b>PPSV23 vs. Placebo</b>	Death	RCT (1)	Inconclusive data on efficacy against mortality	3	3/4
<b>PPSV23 vs. Placebo or No vaccination</b>	IPD <sup>b</sup>	RCT (1) Observational (6)	Negative efficacy among highly immunosuppressed adults; effectiveness against all IPD 49% (34%, 61%) from observational studies	3/4	3/4
<b>PPSV23 vs. Placebo or No vaccination</b>	All-cause pneumonia	RCT (1) Observational (5)	Negative efficacy among highly immunosuppressed adults; effectiveness of 31% (27%, 36%) from observational studies	3/4	3/4
<b>PPSV23</b>	Systemic adverse events	Post-licensure surveillance	PPSV23 appears safe for use among adults with HIV	3	3/4

<https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html>

# PPSV23

Table 8. Considerations for Formulating Recommendations: 23-valent Pneumococcal Polysaccharide Vaccine in immunocompromised adults

Key factors	Comments
<b>Evidence type for benefits and harms</b>	Inconsistent evidence for all-cause pneumonia; limited data from RCT not generalizable to the US HIV+ population
<b>Balance between benefits and harms</b>	Some uncertainty about benefits. Vaccine appears to be safe in this population
<b>Value</b>	ACIP pneumococcal work group consensus regarding the importance of preventing critical pneumococcal outcomes
<b>Cost-effectiveness</b>	Cost-effectiveness in the general adult population demonstrated; uncertainty around the assumptions utilized in cost-effectiveness analysis



Summary: Benefits are likely greater than harms. High values were placed on prevention of the morbidity and mortality of pneumococcal infection among immunocompromised adults. (*recommendation category B; evidence type 3/4*)

<https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html>

# ACIP Conclusions

- Half of IPD in immunocompromised adults caused by serotypes included in PCV13 immunization; an additional 21% caused by serotypes included in PPSV23 immunization
- Antibody response is non-inferior or superior when PCV13 is given before PPSV23 compared to PPSV23 administration before PCV13
- Compared to giving PPSV23 first as an initial dose, there is a significant increase in antibody (non-inferior to superior response) when PPSV23 is given eight weeks after PCV13

<https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html>

# Final Recommendations

- For adults previously immunized with PPSV23, waiting at least 1 year after PPSV23 before giving a dose of PCV13 may provide a better immune response (expert opinion)
- **GRADE** (Grading of Recommendations, Assessment, Development and Evaluation) process led to the conclusion that both PCV13 and PPSV23 are effective in this group & that benefits likely outweigh harms

<https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html>

# Zoster

Risk of varicella reactivation as herpes zoster is increased in persons over age 50

Those with HIV have up to a 10-fold higher risk compared with HIV-uninfected persons, even with effective use of ART



# Zoster Vaccine (Zostavax<sup>®</sup>)

- Approved by the FDA (May, 2006) for those >50 yrs
- Recommended by CDC (single dose) for those >60 yrs
- Reduces incidence of shingles by around 51%
- Reduces severity and duration of pain by around 67%
- ACIP guidelines do not require documented history of primary varicella/zoster, nor evidence of varicella antibody prior to vaccination

<https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6333a3.htm>

# Herpes Zoster vaccine safe and effective in HIV positive people

1 April 2012. Related: Conference reports, Vaccines and microbicides, CROI 19 (Retrovirus) 2012.

## Simon Collins, HIV i-Base

Encouraging results were presented from the ACTG A5247 study on the use of two doses of a live varicella zoster virus (VZV) vaccine (Zostavax, Merck) in almost 400 HIV positive people who were VZV positive or who had herpes zoster (HZ)/shingles outbreak at least one year before study entry, and who were virally suppressed on stable ART. [1]

The incidence and severity of HZ and post herpetic neuralgia (PHN) is higher in HIV positive people and early use of early acyclovir treatment is not always effective. As susceptibility to HZ increases with reduced age-related immune function, a protective vaccine response already demonstrated in HIV negative people > 60 years [2] would be particularly important for HIV positive people.



<http://i-base.info/htb/16280>

# ACTG A5247: CROI 2012

- Two doses of Zostavax given to 395 HIV positive patients
- Randomized 3:1 to active or placebo arms
- Stratified by CD4 count: 200-349 vs >350
- Median age 49
- 75% were VZV positive, 33% had a shingles outbreak one year prior to study entry
- All were virally suppressed on ART

<https://www.poz.com/article/hiv-zostavax-shingles-22067-3905>



# The Study

- Vaccinations: Day 0 and at week 6
- Immune responses evaluated at weeks 2, 6, 8, 12, and 24
- Primary endpoints were: 1) Safety 2) efficacy (change in VZV titer at 6 weeks)

<https://www.poz.com/article/hiv-zostavax-shingles-22067-3905>

# Study Outcomes

- No significant differences between active and placebo groups regarding safety
- Mean fold-rise in VZV antibody titer increased by 1.75 ZV vs 1.09 placebo from baseline to week 6 ( $p < 0.001$ )
- This remained similar at week 12 (indicating no change from the second dose)
- Patients with higher CD4 count ( $>350$ ) had higher antibody titer over time ( $p = 0.024$ )

<https://www.poz.com/article/hiv-zostavax-shingles-22067-3905>

# Safety

- Injection site reactions more frequent in the active group (42% vs 12 %,  $p < 0.01$ ).
- VZV-like rashes seen in 3 active and 2 placebo patients (PCR showing negative or non-vaccine-strain results).

<https://www.poz.com/article/hiv-zostavax-shingles-22067-3905>

- Study not conducted long enough to determine whether Zostavax actually reduces the risk of outbreaks compared with placebo.

# HIV and Zostavax<sup>®</sup>

- No specific recommendations for HIV-infected patients
- Live attenuated vaccine → contraindicated with CD4 <200 (potency is 14x that of varicella vaccine)
- For HIV infected patients who do not have a history of primary varicella/evidence of antibody protection, consider vaccinating with varicella vaccine
- Consider for HIV infected patients with CD4 >200, with evidence of varicella immunity

# Acyclovir vs Zostavax<sup>®</sup>

## Preventing Recurrence

The efficacy of long-term antiviral prophylaxis to prevent herpes zoster recurrences in HIV-seropositive persons has not been evaluated and is not routinely recommended.

An attenuated virus vaccine for prevention of herpes zoster is FDA-approved for use in immunocompetent persons aged  $\geq 50$  years, but is recommended for use beginning at age 60 years by the Advisory Committee on Immunization Practices (ACIP). The zoster vaccine is contraindicated in persons with CD4 cell counts  $< 200$  cells/ $\mu$ L.

<https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/341/vzv>

# Unanswered Questions

Assuming a CD4 >200:

- Should Zostavax<sup>®</sup> be given to all HIV patients?
- Just those over 60?
- Just those over 50?
- Those with viral suppression only?
- Over a certain CD4 threshold ie CD4 >200 vs >350?
- Zostavax<sup>®</sup> only above a certain number of recurrent episodes?

# Immunizations and Insurance



# Medicare

## Part B

- Influenza vaccine
- PCV13, PPSV23 (second dose 11 months apart)
- Hepatitis B (medium-high risk)

## Part D

- all other commercially available vaccines (not covered by Part B)

# Part D

- Starting in 2008 all Part D plan formularies must contain all commercially available vaccines
- The negotiated price for a Part D vaccine includes: vaccine ingredient cost, dispensing fee, sales tax, vaccine administration fee
- Part D plans have the discretion to implement either a single vaccine administration fee for all vaccines or multiple administration fees

<https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/downloads/SE0727.pdf>

# Part D

- Beneficiary pays the physician and then submits a claim to his or her Part D plan for reimbursement **up to the plan's allowable charge.**
- In the absence of communication with the plan prior to vaccine administration, the amount the physician charges may be different from the plan's allowable charge, and a differential may remain that **the beneficiary will be responsible for paying.**

<https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/downloads/SE0727.pdf>

# Part D: more information on CMS website

Variance in provider type, and product administration →  
Providers/Patients should contact Part D plans regarding  
specific vaccine fees

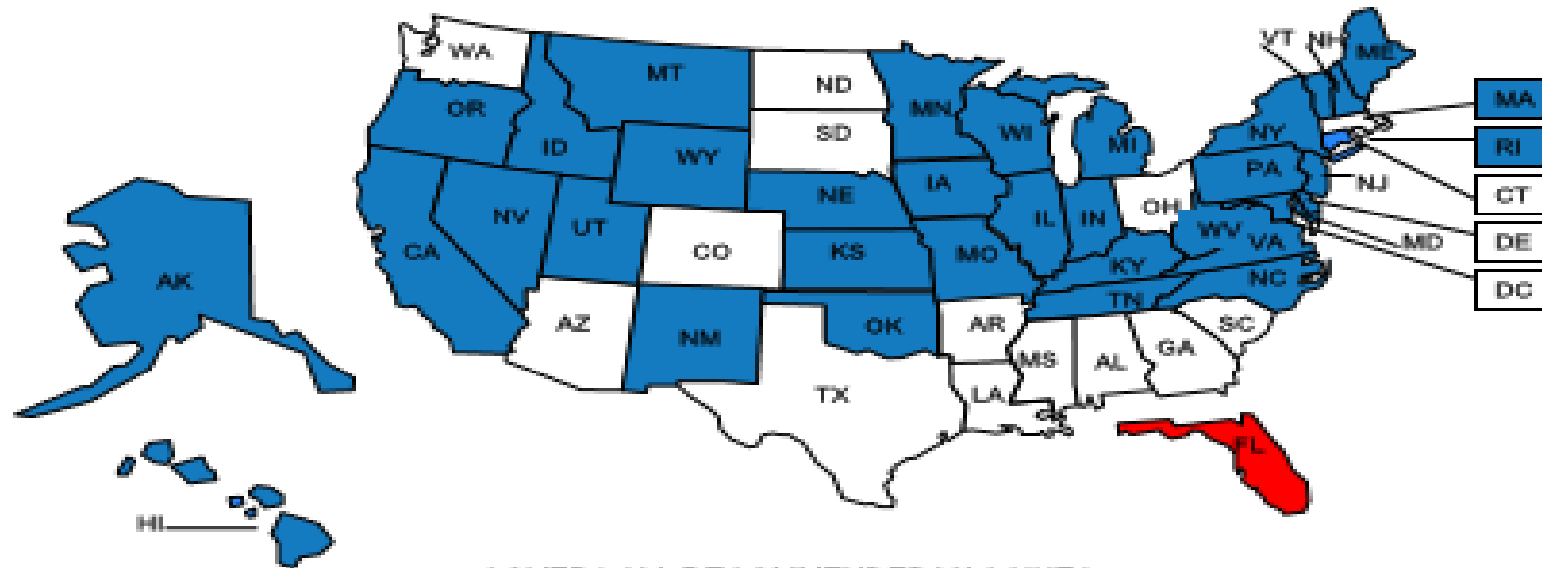
<http://www.cms.gov/Medicare/Prescription-DrugCoverage/PrescriptionDrugCovGenIn/index.html>

# Medicaid

- Vaccination services for adults are optional. States determine policy surrounding:
  - Which (if any) vaccines to cover
  - Enrollee copayment
  - Provider reimbursement
  - Settings where vaccines may be administered
- \*All programs except Florida cover at least one vaccine

<https://www.izsummitpartners.org/content/uploads/2016/05/2b-1-Stewart-Medicaid-Adult-Vax-Coverage-and-Reimbursement.pdf>

## States Covering All ACIP Recommended Vaccines 2012 (n=36)



### COVERS ALL RECOMMENDED VACCINES

Alaska, California, Connecticut, Delaware, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New York, North Carolina, Oklahoma, Oregon, Pennsylvania, Rhode Island, Tennessee, Utah, Vermont, Virginia, West Virginia, Wisconsin, Wyoming

State does not cover any vaccines in 2012

<https://www.izsummitpartners.org/content/uploads/2016/05/2b-1-Stewart-Medicaid-Adult-Vax-Coverage-and-Reimbursement.pdf>

VACCINE	SUMMARY OF MEDICAID COVERAGE BY VACCINE 2012
FLU	1 state does not cover (Florida) <ul style="list-style-type: none"> <li>• <b>Most frequently covered vaccine.</b> Most states cover intramuscular preservative &amp; preservative-free</li> </ul>
PNEUMO	3 states do not cover (Florida, Georgia, S. Dakota)
TD/TDAP	4 states do not cover TD (Florida, Georgia, Mississippi, S. Carolina) 5 states do not cover TDAP (DC, Florida, Louisiana, Mississippi, S. Carolina)
HEP. A	4 states do not cover (Alabama, Florida, Louisiana, Mississippi)
HEP. B	2 states do not cover (Florida, Louisiana) <ul style="list-style-type: none"> <li>• <b>Second-most frequently covered vaccine = intramuscular 90746</b></li> </ul>
MMR	5 states do not cover (Florida, Georgia, Louisiana, Mississippi, S. Carolina)
MENING	4 states do not cover (Florida, Louisiana, Mississippi, Texas)
HPV	7 states do not cover (Alabama, Arizona, Arkansas, Florida, N. Dakota, S. Carolina, S. Dakota) <ul style="list-style-type: none"> <li>• 42/51 states cover quadrivalent 90649. 32/51 states cover bivalent 90650. Recommended in 2007</li> </ul>
VARICELLA	8 states do not cover (Arkansas, Florida, Georgia, Louisiana, Mississippi, N. Dakota, S. Carolina, Texas) <ul style="list-style-type: none"> <li>• <b>Second least frequently covered vaccine</b></li> </ul>
ZOSTER	11 states do not cover (Arkansas, Colorado, DC, Florida, Louisiana, Mississippi, N. Dakota, Ohio, S. Carolina, Texas, Washington) <ul style="list-style-type: none"> <li>• <b>Least frequently covered vaccine. Recommended in 2008</b></li> </ul>

<https://www.izsummitpartners.org/content/uploads/2016/05/2b-1-Stewart-Medicaid-Adult-Vax-Coverage-and-Reimbursement.pdf>

# 2016 Medicaid

- Certain vaccines may be available if supplemental insurance is obtained



# Resources

- <https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html>
- <http://hivinsite.ucsf.edu/InSite?page=kb-03-01-08#S4.2X>
- <https://aidsinfo.nih.gov/education-materials/fact-sheets/21/57/hiv-and-immunizations>
- <http://www.hivguidelines.org/clinical-guidelines/hiv-prevention/prevention-of-secondary-disease-preventive-medicine/immunizations/>
- [http://publichealth.gwu.edu/departments/healthpolicy/DHP\\_Publications/pub\\_uploads/dhpPublication\\_5F6FC614-5056-9D20-3D48DB884F5C18C8.pdfm](http://publichealth.gwu.edu/departments/healthpolicy/DHP_Publications/pub_uploads/dhpPublication_5F6FC614-5056-9D20-3D48DB884F5C18C8.pdfm)

# Questions?