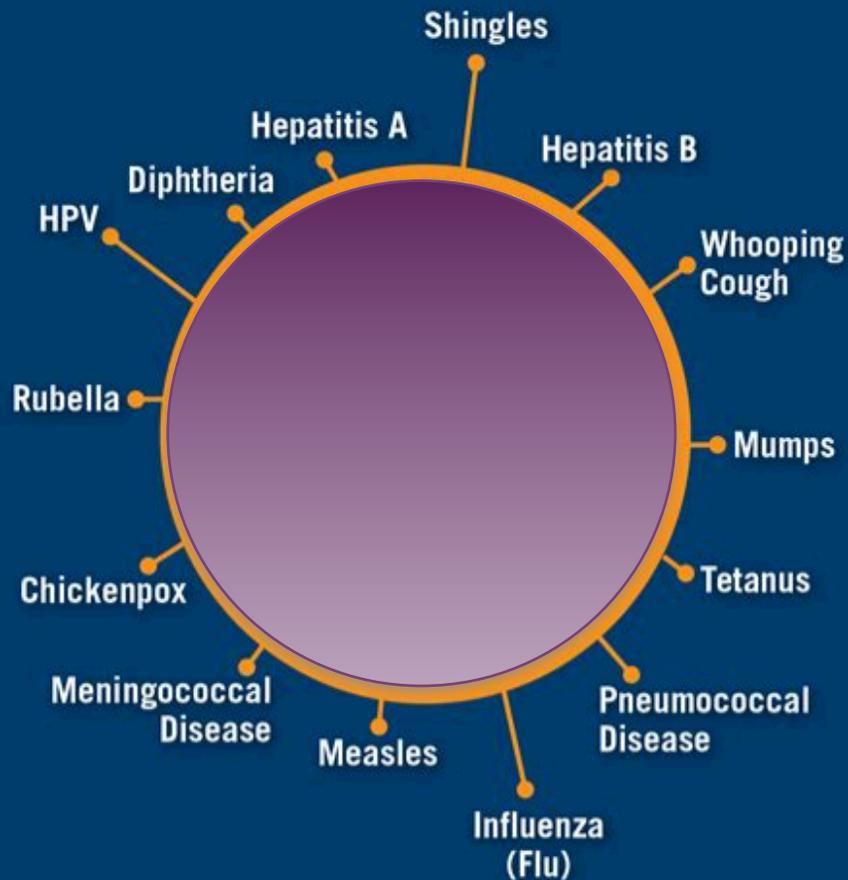


# Vaccines For Adults Living with HIV

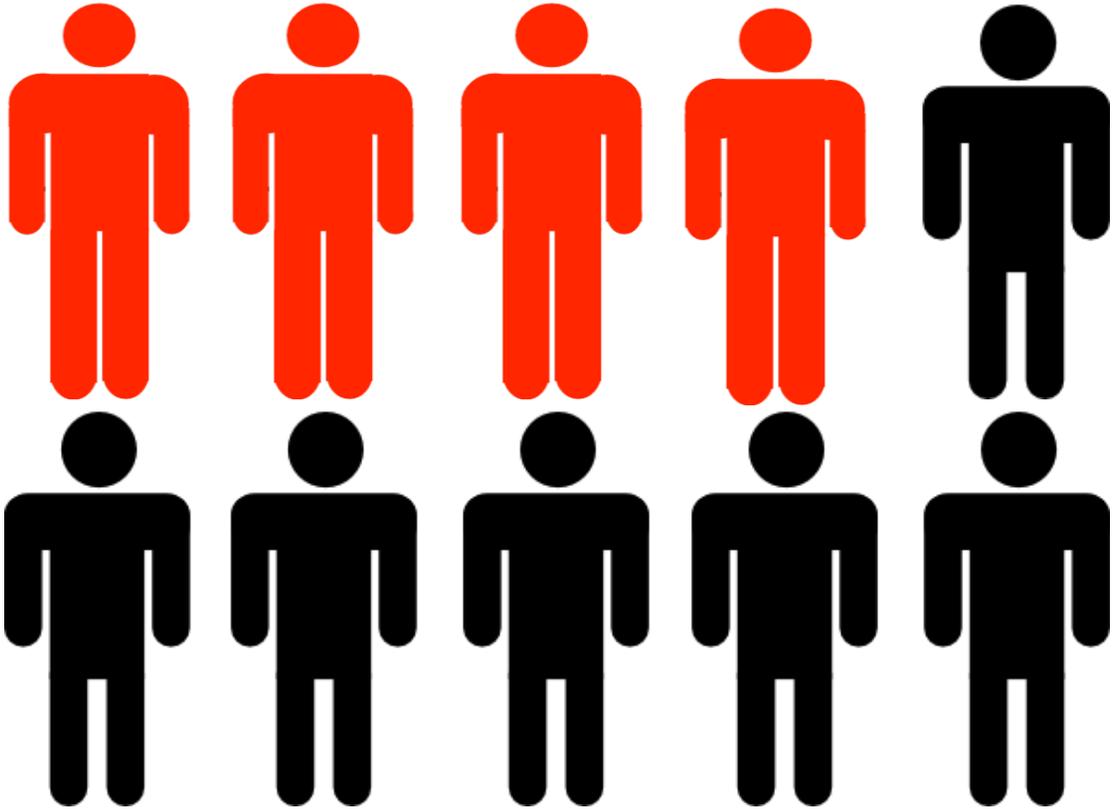


## Recommendations & Thoughts

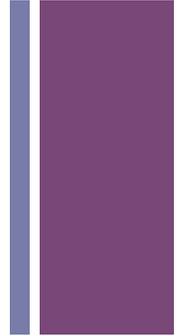
Puja Van Epps, MD  
Assistant Professor of Medicine  
Director, Outpatient Infectious Diseases Clinic  
Louis Stokes Cleveland VA Medical Center



On average, less than 4 in 10 adults living with HIV in the US get the flu vaccine, well below the 70% goal set for Healthy People 2020



# + Objectives



- To review immunization recommendations put forth by the CDC's Advisory Committee on Immunization Practices (ACIP) for adults living with HIV.
- To discuss immunizations in the HIV infected traveller.



Inactivated vaccines  
with broad  
recommendations

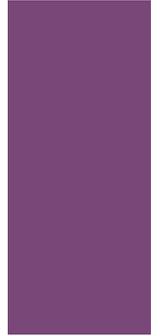


Inactivated vaccines  
with age/risk factor  
specific  
recommendations



Live Vaccines

# + Guidelines and concepts



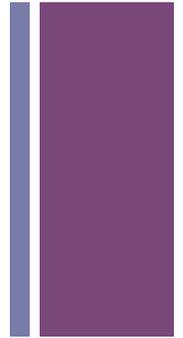
<b>High level Immunosuppression</b>	<b>Low level Immunosuppression</b>
<ul style="list-style-type: none"><li>• HIV infection with a CD4 T count &lt;200 cells/mm<sup>3</sup></li></ul>	<ul style="list-style-type: none"><li>• Asymptomatic HIV-infected patients with CD4 counts of 200–499 cells/mm<sup>3</sup></li></ul>

1. The Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents
2. The 2013 IDSA Practice Guidelines for Vaccination of the Immunocompromised Host
3. ACIP Immunization Guidelines



Inactivated  
vaccines with  
broad  
recommendation  
s

# + Case 1

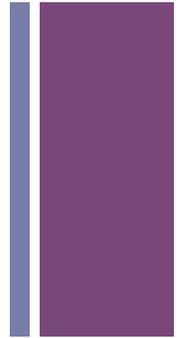


A 54 year old man with HIV presents for routine follow up in November. His most recent viral load was undetectable and CD4 count was 346 cells/mm<sup>3</sup>. You are counseling the patient regarding influenza vaccination.

**Which one of the following is TRUE regarding recommendations for influenza vaccination in persons with HIV infection?**

- A. Single-dose inactivated influenza vaccine is recommended annually for all persons with HIV infection
- B. Persons with HIV infection who have a CD4 count less than 350 cells/mm<sup>3</sup> require a two-dose regimen annually to achieve adequate immunity to influenza
- C. Either the inactivated influenza vaccine or the live-attenuated intranasal vaccine is recommended annually
- D. The live-attenuated intranasal vaccine is the preferred vaccine for persons with HIV infection if they have a CD4 count greater than 350 cells/mm<sup>3</sup>

# + Case 1

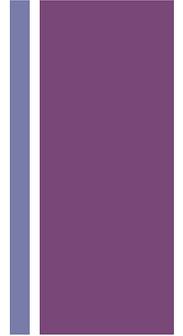


A 54 year old man with HIV presents for routine follow up in November. His most recent viral load was undetectable and CD4 count was 346 cells/mm<sup>3</sup>. You are counseling the patient regarding influenza vaccination.

**Which one of the following is TRUE regarding recommendations for influenza vaccination in persons with HIV infection?**

- A. Single-dose inactivated influenza vaccine is recommended annually for all persons with HIV infection**
- B. Persons with HIV infection who have a CD4 count less than 350 cells/mm<sup>3</sup> require a two-dose regimen annually to achieve adequate immunity to influenza
- C. Either the inactivated influenza vaccine or the live-attenuated intranasal vaccine is recommended annually
- D. The live-attenuated intranasal vaccine is the preferred vaccine for persons with HIV infection if they have a CD4 count greater than 350 cells/mm<sup>3</sup>

# + Risk of Influenza



- People living with HIV (PLWH) have an elevated risk of severe infection and complications from influenza<sup>1</sup>
- Pregnant women with HIV are at particular risk for severe disease<sup>2</sup>
- ART is associated with a reduction in hospitalizations due to influenza<sup>3</sup>
- Yet, PLWH remain at an elevated risk for influenza and related complications compared to general population<sup>4</sup>

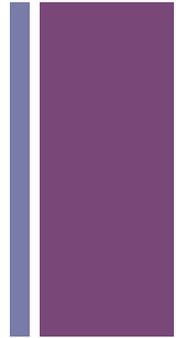
1. Vaccine. 2016;34:5649–55

2. Arch Intern Med. 2001;161:441–6

3. [Clin Infect Dis.](#) 2015 Oct 1;61(7):1063-70.

4. Clin Infect Dis.2011;52:219–27.

# + Efficacy of Flu Vaccines



- Effectiveness may be reduced compared with HIV-uninfected persons, especially in persons with low CD4 counts and HIV viremia<sup>1,2,3</sup>
- A meta-analysis (n =1562) demonstrated that vaccination among PLWH reduces laboratory-confirmed influenza with a pooled efficacy of 85% (95% CI 22–97%)<sup>4</sup>
- A randomized trial among pregnant women with HIV noted a vaccine efficacy of 58%<sup>5</sup>
- A retrospective study among PLWH in the US showed that those who received influenza vaccine early in the season were more likely to develop influenza than those vaccinated later in the season<sup>6</sup>

1. Clin Infect Dis. 2011;52:138–46.

2. AIDS. 2010;24:2187–92.

3. J Acquir Immune Defic Syndr. 2011;58:e99–102.

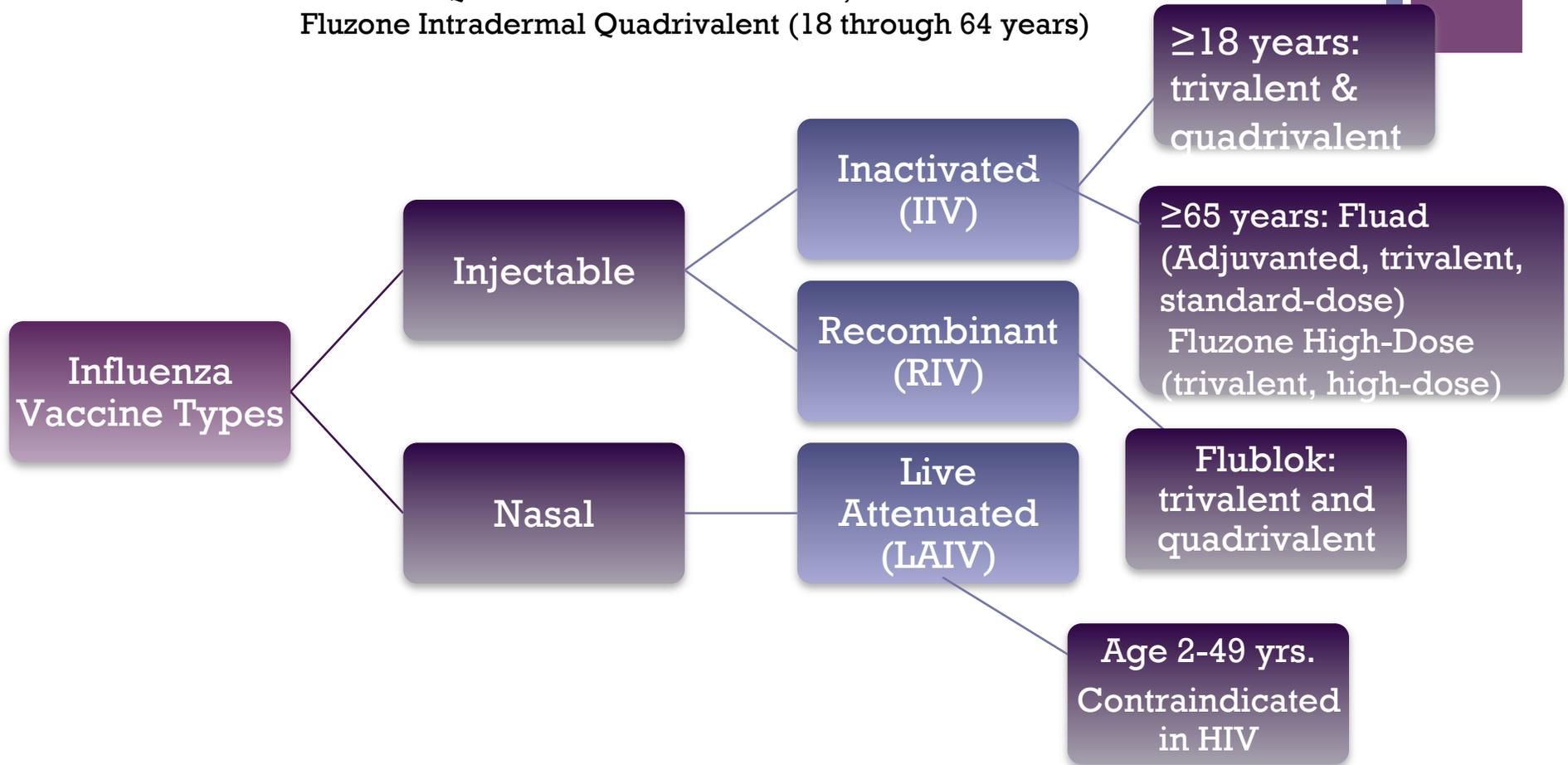
4. Vaccine. 2014;32:5585–92.

5. N Engl J Med. 2014;371:918–31.

6. HIV Med. 2016;17:601–4.

# + Vaccine Options

Flucelvax Quadrivalent standard-dose, cell culture-based  
Fluzone Intradermal Quadrivalent (18 through 64 years)



# + Recommendations

**All PLWH should receive a single dose influenza vaccine annually**

- **Recommended Vaccines:** Inactivated influenza vaccine (trivalent or quadrivalent) or recombinant influenza vaccine(trivalent)
- **Contraindicated Vaccine:** Live attenuated influenza vaccine
- **Persons with Egg Allergy:** Recombinant influenza vaccine, which does not use an egg-based culture system
- **≥65 years:** Standard-dose inactivated influenza vaccine, adjuvanted inactivated influenza vaccine, or high-dose inactivated influenza vaccine

# + Potential strategies to boost immune response

## High Dose

- ❑ The use of a HD vaccine which contains 60 mcg of antigen per strain vs. 15 mcg was evaluated among 190 HIV-infected adults.<sup>1</sup>
- ❑ Seroprotection rates were greater in the HD group for H1N1 (96% vs. 87%,  $p = 0.03$ ) and influenza B (91% vs. 80%,  $p = 0.03$ ) and similar for H3N2 (96% vs. 92%,  $p = 0.30$ ) strains.

## Adjuvant

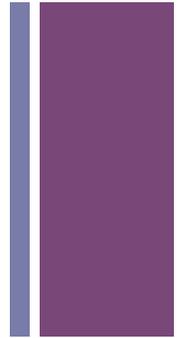
- ❑ The use of adjuvanted vaccines (e.g. AS03) can boost immune responses in HIV.<sup>2</sup>
- ❑ Flud, an adjuvanted vaccine recommended for persons  $\geq 65$  years, has not been studied or approved specifically for adults with HIV.

## Two-doses

- ❑ In one study, the administration of a second dose of influenza vaccine significantly increased seroprotective responses (from 68% to 92% after the second dose)<sup>3</sup>
- ❑ The study utilized an adjuvant plus vaccine

1. Vaccine. 2016;34:3141–8.  
2. Clin Trials. 2012;13:23–32.  
3. AIDS. 2009;2013(27):87–93.

## + Case 2

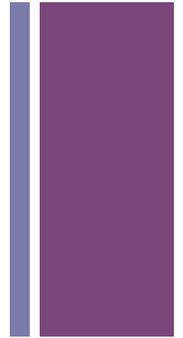


A 31-year-old man is newly diagnosed with HIV infection and initial labs show a CD4 count of 150 cells/mm<sup>3</sup> and an HIV RNA of 350,000 copies/mL. A baseline genotype shows no mutations and he is started on antiretroviral therapy. He has never received any doses of a pneumococcal vaccine.

**What would you recommend regarding the pneumococcal conjugate 13 (PCV13) and pneumococcal polysaccharide vaccine (PPSV23) vaccine series?**

- A. Administer the first dose of the pneumococcal vaccine series now
- B. Defer the first dose of the pneumococcal vaccine series until the patient has an undetectable plasma HIV RNA level
- C. Defer the first dose of the pneumococcal vaccine series until the patient has an undetectable plasma HIV RNA level and a CD4 count greater than 200 cells/mm<sup>3</sup>

## + Case 2

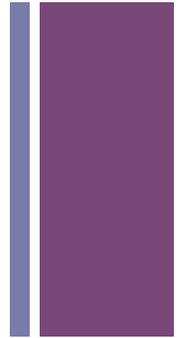


A 31-year-old man is newly diagnosed with HIV infection and initial labs show a CD4 count of 150 cells/mm<sup>3</sup> and an HIV RNA of 350,000 copies/mL. A baseline genotype shows no mutations and he is started on antiretroviral therapy. He has never received any doses of a pneumococcal vaccine.

**What would you recommend regarding the pneumococcal conjugate 13 (PCV13) and pneumococcal polysaccharide vaccine (PPSV23) vaccine series?**

- A. Administer the first dose of the pneumococcal vaccine series now**
- B. Defer the first dose of the pneumococcal vaccine series until the patient has an undetectable plasma HIV RNA level
- C. Defer the first dose of the pneumococcal vaccine series until the patient has an undetectable plasma HIV RNA level and a CD4 count greater than 200 cells/mm<sup>3</sup>

# + Burden of Pneumococcal Disease



- Risk of Pneumococcal disease during the early epidemic was 20- to 40-fold higher than general population<sup>1,2</sup>
- Due to widespread use of ART and herd immunity, over the last decade, the risk of Pneumococcal disease has declined in PLWH<sup>3,4</sup>
- Still a 7-fold increased risk compared to general population remains<sup>5</sup>

1. J Infect Dis. 1990;162:1012-7.

2. AIDS. 2012;26:87-94.

3. Vaccine. 2007 Mar 22;25(13):2420-7.

4. Ann Intern Med. 2006 Jan 3;144(1):1-9.

5. AIDS Patient Care STDS. 2016 Oct;30(10):463-470.

# + Efficacy of Pneumococcal Vaccines

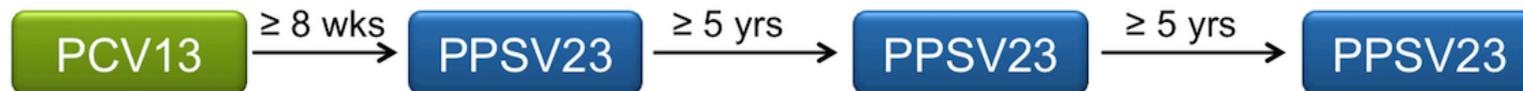
- Very modest clinical benefit from 23-valent pneumococcal polysaccharide vaccine (PPSV23) in reducing rates of pneumococcal infections in PLWH<sup>1</sup>
- Immunologic response to PPSV23 is impaired in persons with CD4 counts < 200 cells/mm<sup>3</sup>; CD4 count above 500 cells/mm<sup>3</sup> have optimal response<sup>2,3</sup>
- There are no published clinical efficacy data for 13-valent pneumococcal conjugate vaccine (PCV13) in PLWH
- A randomized control trial using two doses of PCV7 given 1 month apart in 496 adults (88% with HIV infection) in Malawi demonstrated a vaccine efficacy of 74% in preventing invasive pneumococcal disease<sup>4</sup>
- No data exist regarding the efficacy of the combined PCV13 plus PPSV23 vaccine regimen as recommended for persons with HIV infection in the US<sup>5</sup>

Clin Infect Dis. 2003 Aug 1;37(3):438-47.  
Clin Infect Dis. 2001 Mar 1;32(5):794-800.  
N Engl J Med. 2010 Mar 4;362(9):812-22.  
Vaccine. 2000 Nov 22;19(7-8):886-94.

# + Recommendations

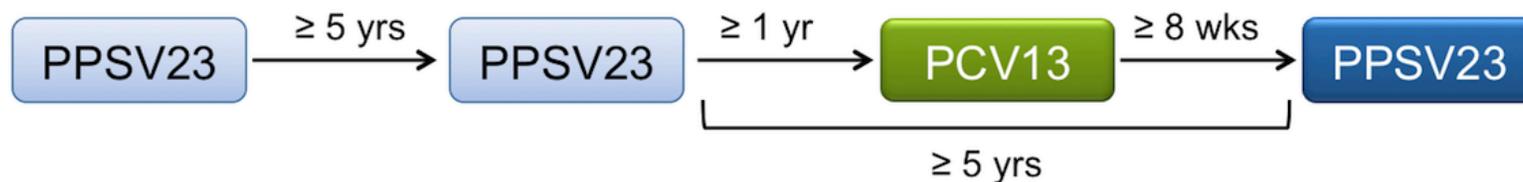
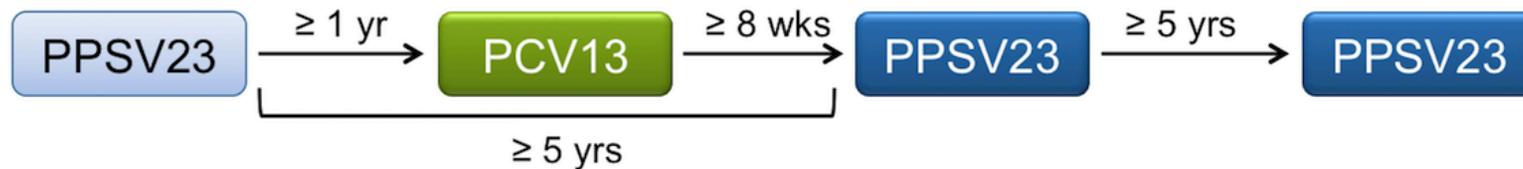
## Pneumococcal Vaccine-Naïve Adults

≥ Age 65



## PPSV23-Immunized Adults

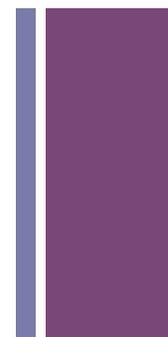
≥ Age 65



<https://www.hiv.uw.edu/go/basic-primary-care/immunizations>

CDC Immunization guidelines for HIV, [https://aidsinfo.nih.gov/contentfiles/lvguidelines/adult\\_OI.pdf](https://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_OI.pdf)  
2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:309–18.

# + Case 3



A 51-year-old man presents to establish care after diagnosis of HIV one week ago. He also received a diagnosis of chronic Hepatitis C recently. There are no records of prior immunization to Hepatitis B. Hepatitis B serology shows a positive core antibody, negative surface antigen and negative surface antibody.

**Which one of the following best describes the recommendation regarding hepatitis B (HBV) immunization for persons with HIV infection?**

- A. HBV vaccination is not recommended for persons with HIV infection due to the risk of HBV-antigen stimulated HIV activation
- B. HBV vaccination is recommended only for persons with HIV and hepatitis C coinfection
- C. HBV vaccination is recommended only for persons with HIV infection and cirrhosis
- D. HBV vaccination is recommended for all persons with HIV-infection who lack immunity
- E. HBV vaccination is not recommended for persons isolated core antibody

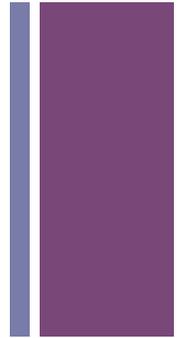
# + Case

A 51-year-old man presents to establish care after diagnosis of HIV one week ago. He also received a diagnosis of chronic Hepatitis C recently. There are no records of prior immunization to Hepatitis B. Hepatitis B serology shows a positive core antibody, negative surface antigen and negative surface antibody.

**Which one of the following best describes the recommendation regarding hepatitis B (HBV) immunization for persons with HIV infection?**

- A. HBV vaccination is not recommended for persons with HIV infection due to the risk of HBV-antigen stimulated HIV activation
- B. HBV vaccination is recommended only for persons with HIV and hepatitis C coinfection
- C. HBV vaccination is recommended only for persons with HIV infection and cirrhosis
- D. **HBV vaccination is recommended for all persons with HIV-infection who lack immunity**
- E. HBV vaccination is not recommended for persons isolated core antibody

# + Hepatitis B



- **RISK:** PLWH have an increased risk of acquiring hepatitis B infection due to shared routes of transmission<sup>1</sup>
- **MORBIDITY:** Co-infected persons have an increased likelihood of establishing chronic HBV, accelerated progression of liver disease, and significantly higher rates of liver-related mortality compared with HIV-uninfected individuals<sup>2</sup>
- **VACCINE RESPONSE:** Hepatitis B vaccine response rates are significantly lower ranging from 18 to 71% (compared to 60 to 80% in persons without HIV infection)<sup>3</sup>
- **FACTORS ASSOCIATED WITH LOW RESPONSES:** A recent or nadir CD4 count less than 200 cells/mm<sup>3</sup>, detectable HIV RNA levels, and coinfection with hepatitis C virus<sup>4</sup>
- **STRATEGIES:** Double dose (40 mcg of the hepatitis B surface antigen [HBsAg] instead of 20 mcg), increased number of doses (four instead of three), and using intradermal rather than intramuscular dosing<sup>5,6,7</sup>

1.Lancet. 2002 Dec 14;360(9349):1921-6

2.Int J STD AIDS. 2009 Sep;20(9):595-600; 3.Lancet Infect Dis. 2012 Dec;12(12):966-76.

4.Int J STD AIDS. 1996 Nov-Dec;7(7):490-4; 5 JAMA. 2011 Apr 13;305(14):1432-40.

6.MMWR December 8, 2006 / 55(RR16);1-25; 7.Vaccine. 2000 Jan 18;18(13):1161-5

# + Recommendations

**PLWH who do not have active HBV or evidence of immunity to HBV should be vaccinated with a hepatitis B vaccine**

Pre-vaccine screening should include HBsAg, anti-HBs, and anti-HBc

- **HBsAg+**: active infection, no vaccine
- **Anti-HBs+ and anti-HBc+**: immune from prior infection, no vaccine
- **Anti-HBs+**: immune from vaccination (with a titer greater than 10 IU/mL), no vaccine
- **Anti-HBc+** (isolated core): this pattern may signify a false positive result, exposure in the distant past with waning anti-HBs, or occult HBV infection. Check a HBV DNA and if negative administer a complete hepatitis B vaccine series to those with isolated hepatitis B core antibody

MMWR Morb Mortal Wkly Rep. 2017 Feb 10;66(5):136-138.  
Clin Infect Dis. 2014 Feb;58(3):309-18.

<https://www.aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/344/hbv>

# + Hepatitis B

**Vaccination is recommended at entry into care for all PLWH who lack immunity**

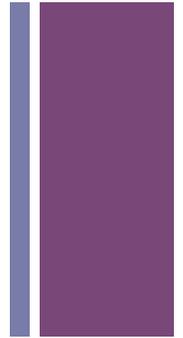
No specific guidelines as to timing of vaccination relative to CD4 count or HIV RNA status.

## Standard dosing schedule



- **Alternative schedules:** 4-dose (0, 7, and 21 to 30 days, and 6 months; High dose (40 mcg vs. 20 mcg)
- **OI Prophylaxis Guidelines:** Standard or 4 dose schedule; ACIP: no specific guidelines for HIV; IDSA: consider high dose
- **Post vaccination titers:** Antibody titer of at least 10 mIU/mL to hepatitis B surface antigen (anti-HBs) 1 to 2 months after completing the final dose is considered protective

# + Tetanus Diphtheria and Pertussis (Tdap)



- PLWH should receive Tdap and Td per the same schedule as those without HIV infection
- **No Prior Tdap:** One-time dose of Tdap, followed by a Td booster every 10 years
- **Prior Td:** Tdap regardless of the interval since Td was last administered
- **Tdap for Pregnant Women:** Tdap during every pregnancy preferably during gestational weeks 27–36, regardless of the prior history of Tdap

# + Meningococcal

- PLWH have an estimated 5 to 13-fold higher risk of developing meningococcal disease than general population (low CD4 count or high viral load appear to be at greatest risk)
- Local outbreaks of meningococcal meningitis have been reported among MSM in the US

Serogroup types in 62 cases of meningococcal disease in PLWH

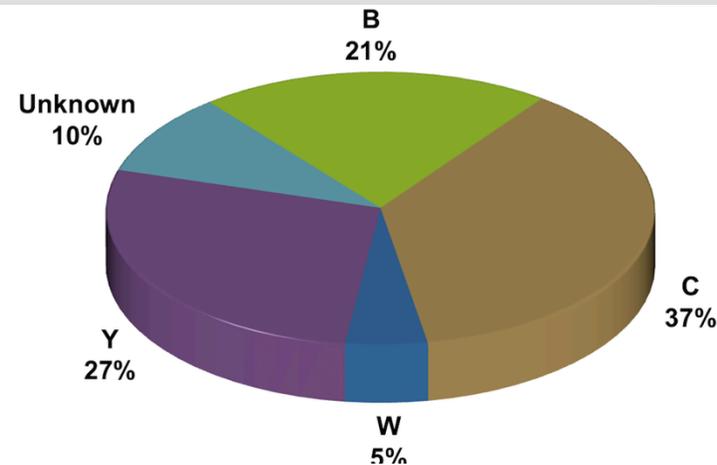
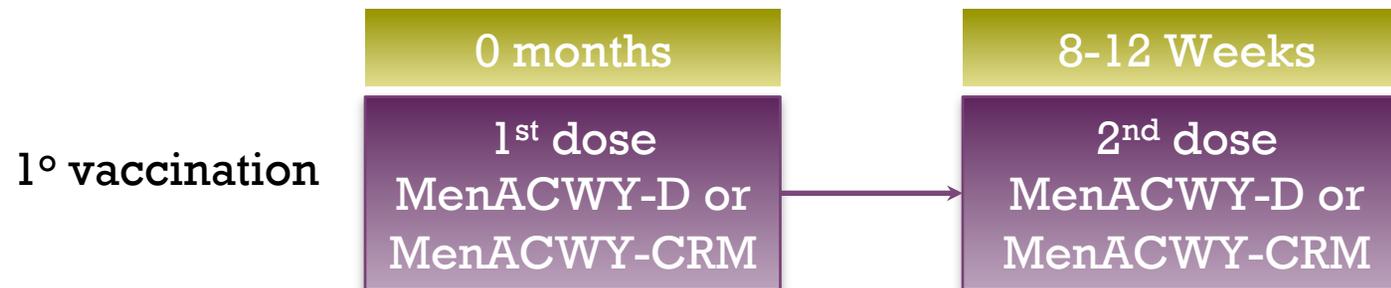


TABLE. Number of reported cases of meningococcal disease among men who have sex with men, by serogroup and reporting jurisdiction — United States, January 2012–June 2015

Jurisdiction	Total	Serogroup					HIV-positive*	Died†
		C	B	W	Y	Unknown		
New York City	23	22 (96)	1 (4)	0—	0—	0—	15 (65)	6 (26)
Los Angeles County	14	10 (71)	3 (21)	0—	1 (7)	0—	5 (42)	5 (36)
Chicago	11	11 (100)	0—	0—	0—	0—	5 (50)	3 (27)
Other <sup>§</sup>	26	19 (73)	1 (4)	2 (8)	2 (8)	2 (8)	12 (67)	10 (38)
<b>Total</b>	<b>74</b>	<b>62 (84)</b>	<b>5 (1)</b>	<b>2 (3)</b>	<b>3 (4)</b>	<b>2 (3)</b>	<b>37 (59)</b>	<b>24 (32)</b>

# + Recommendations

Routine administration of meningococcal conjugate vaccine (serogroups A, C, W, Y) for all PLWH

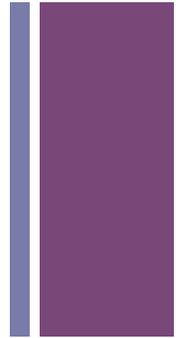


## Booster dose

**<7 years at previous dose:** Additional dose of MenACWY-D or MenACWY-CRM 3 years after primary series; boosters should be repeated every 5 years thereafter

**≥7 years at previous dose** Additional dose of MenACWY-D or MenACWY-CRM 5 years after primary series; boosters should be repeated every 5 years thereafter

# + Recommendations



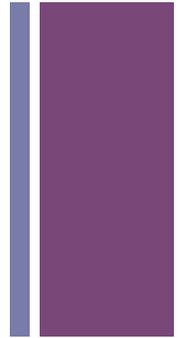
- **MenACWY** is preferred for use in adults aged 55 and younger
- It is also preferred for adults aged 56 years and older who were either previously vaccinated with MenACWY and are recommended for revaccination, or in whom multiple doses are anticipated
- **Conjugate Meningococcal B Vaccine:** Routine administration of conjugate meningococcal B vaccine is not recommended for persons with HIV infection.



Inactivated  
vaccines with  
age/risk factor  
specific  
recommendation

S

# + Case 4

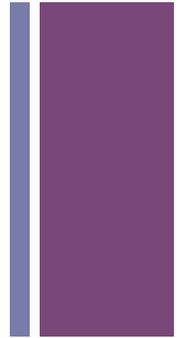


A 26-year-old man with newly diagnosed HIV presents to establish care. He reports 3 male and 2 female sexual partners in the past 6 months.

## **Would you recommend HPV vaccine for this patient?**

- A. Yes, all males with HIV infection are eligible for the vaccine, regardless of age
- B. Yes, males with HIV infection aged 9 through 26 should receive the vaccine
- C. No, the patient has already been sexually active and is therefore unlikely to benefit
- D. No, HPV vaccines are not approved for use in males
- E. Not yet, he needs to be screened for HPV first to see if the vaccine would be useful

# + Case 4

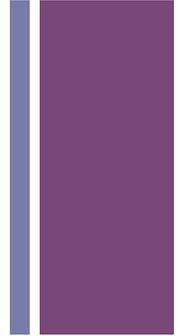


A 26-year-old man with newly diagnosed HIV presents to establish care. He reports 3 male and 2 female sexual partners in the past 6 months.

**Would you recommend HPV vaccine for this patient?**

- A. Yes, all males with HIV infection are eligible for the vaccine, regardless of age
- B. Yes, males with HIV infection aged 9 through 26 should receive the vaccine
- C. No, the patient has already been sexually active and is therefore unlikely to benefit
- D. No, HPV vaccines are not approved for use in males
- E. Not yet, he needs to be screened for HPV first to see if the vaccine would be useful

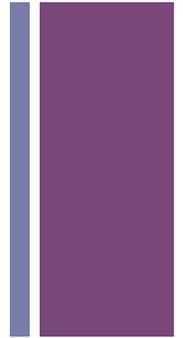
# + Burden of HPV



- PLWH have a disproportionately heavy burden of HPV disease compared to general population
- Abnormal cervical cytology is nearly 11 times more common in women with HIV
- Men with HIV have a 30-fold increased risk of anal cancer
- Despite ART, the incidence of anal cancer among men and the incidence of cervical cancer among women have not declined in recent years

Clin Infect Dis. 2014 Jan;58(1):e1-34.  
AIDS. 2014 Jan 14;28(2):215-22.  
Arch Intern Med. 2010 Aug 9;170(15):1337-45.  
Curr HIV Res. 2010 Oct;8(7):493-7

# + Efficacy



- Highly effective in PLWH:
  - seroconversion rates of 92.3 to 100% among women aged 16 to 23 (quadrivalent)
  - seroconversion rates of 95% in men age 18 and older (quadrivalent)
- Most adults with HIV infection have not received HPV vaccine and most are older than the age recommended for use of these vaccines

# + HPV

## VACCINE OPTIONS

- In the United States, the 9-valent (9vHPV) vaccine is the only HPV vaccine currently manufactured
- The 9v vaccine includes the serotypes 6, 11, 16, and 18 and 5 additional cancer-causing HPV types (31, 33, 45, 52, and 58)
- The HPV types 16, 18 account for approximately 66% of cases of cervical cancer, HPV types 6 and 11 account for approximately 90% of genital warts
- The HPV vaccines are prepared from recombinant noninfectious virus-like particles and are considered safe for immunocompromised
- The 9-valent vaccine is FDA-approved for use in females and males for ages 9 through 26.

# + Recommendations

The ACIP recommends HPV vaccine routinely for females and males with HIV infection through age 26, starting at age 11

Regardless of Past sexual history, HPV or Pap smear testing, or history of genital warts



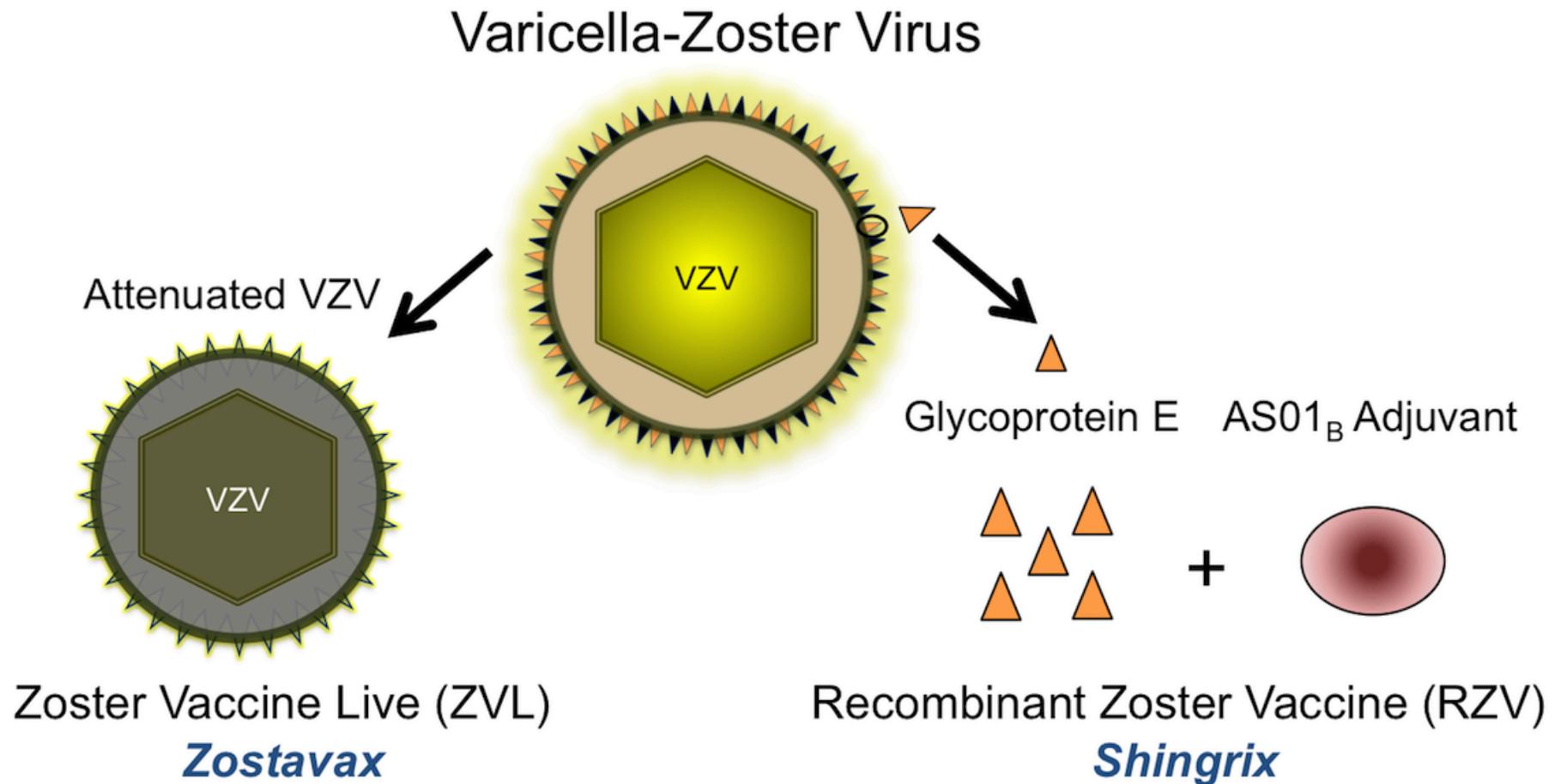
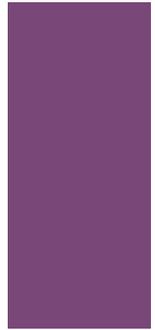
- There are no recommendations for the use of the HPV vaccine in women or men older than age 26
- The ACIP recommends against administering HPV vaccine to pregnant women

# + Shingles (Herpes Zoster/HZ)

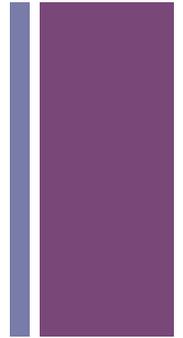
## RISK

- The incidence of HZ among PLWH is 15-fold higher than among age-matched immunocompetent adults
- Risk is highest, especially of severe disease, in persons with a CD4 count less than 200 cells/mm<sup>3</sup>
- Widespread use of antiretroviral therapy has led to decline in the incidence of HZ among PLWH

# + Vaccines to prevent Shingles



# + Zoster Vaccine Live (ZVL)



- Licensed by FDA in 2006 for use in  $\geq 50$  year old adults
- Live-attenuated Oka-strain VZV ( $\geq 14X$  titer in Varivax)
- ACIP recommends for adults  $\geq 60$  years old
- Contraindicated for PLWH with CD4 counts  $< 200$ , no specific recommendations for CD4 count  $> 200$
- Safe and immunogenic in adults with CD4 counts  $> 200$  and viral load  $< 75$  copies/mL (Benson C et al. Abstract #96. CROI 2012). Not powered for outcomes.
- Per ACIP there is insufficient data for the use of zoster vaccine in HIV infected persons with CD4 counts  $> 200$ . It is contraindicated for CD4  $< 200$

+

# New Recombinant Zoster Vaccine (Shingrix/RZV)

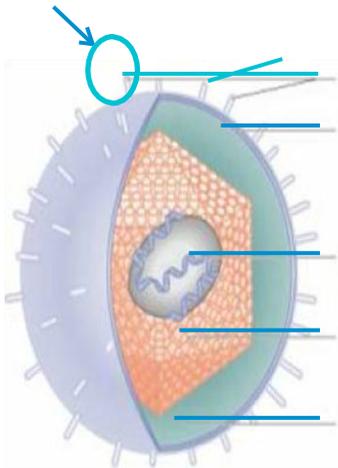
Adjuvanted Recombinant VZV subunit vaccine

Antigen

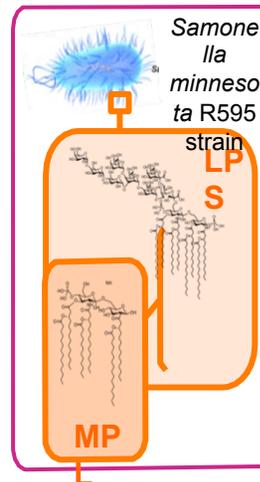
Glycoprotein E (gE) -  
50 µg

Adjuvant System

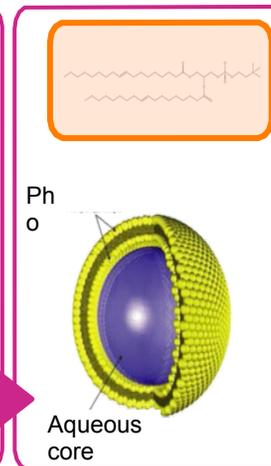
AS01<sub>B</sub> (MPL and QS-21) -  
50 µg each



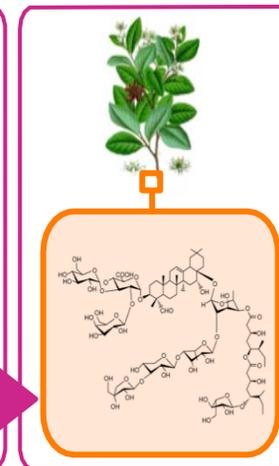
MPL



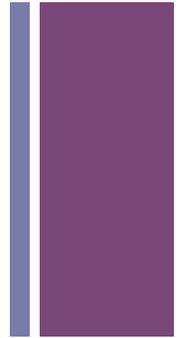
Liposome



Saponin QS-21\*

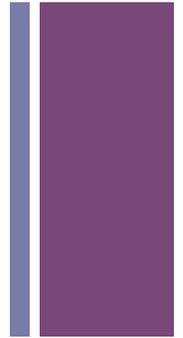


# + General Use Guideline



- RZV is recommended for use in immunocompetent adults aged  $\geq 50$  years
- There is no recommendation for use in PLWH yet, however it is not a live vaccine and recommended by other entities and experts (NY Health Dept. HIV Guidelines)
- Does not require screening for a history of chickenpox (varicella) and can be given in those with prior zoster or ZVL
- ACIP has made a preferential recommendation of RZV over ZVL

# + General Use Guideline



- Two dose series, 2 to 6 months apart
- If the second dose of RZV is given less than 4 weeks after the first, the second dose should be repeated
- The vaccine series need not be restarted if more than 6 months have elapsed since the first dose
- Two doses of the vaccine are necessary regardless of prior history of herpes zoster or prior receipt of ZVL

# Safety and Immunogenicity of an Adjuvanted Herpes Zoster Subunit Candidate Vaccine in HIV-Infected Adults: A Phase 1/2a Randomized, Placebo-Controlled Study

Elchonon M. Berkowitz,<sup>1</sup> Graeme Moyle,<sup>2</sup> Hans-Jürgen Stellbrink,<sup>4</sup> Dirk Schürmann,<sup>5</sup> Stephen Kegg,<sup>3</sup> Matthias Stoll,<sup>6</sup> Mohamed El Idrissi,<sup>7</sup> Lidia Oostvogels,<sup>7</sup> and Thomas C. Heineman<sup>1</sup>; for the Zoster-015 HZ/su Study Group<sup>a</sup>

<sup>1</sup>GlaxoSmithKline Vaccines, King of Prussia, Pennsylvania; <sup>2</sup>Chelsea and Westminster Hospital, and <sup>3</sup>Queen Elizabeth Hospital NHS Trust, The Trafalgar Clinic, London, United Kingdom; <sup>4</sup>Infektionsmedizinisches Centrum Hamburg; <sup>5</sup>Department of Infectious Diseases and Pulmonary Medicine, Charité–Universitätsmedizin Berlin, and <sup>6</sup>Medizinische Hochschule Hannover, Zentrum Innere Medizin, Klinische Immunologie II, Germany; and <sup>7</sup>GlaxoSmithKline Vaccines, Wavre, Belgium

---

**Background.** Human immunodeficiency virus (HIV)–infected individuals are at increased risk of herpes zoster (HZ), even in the antiretroviral therapy (ART) era. Because concerns exist about the use of live-attenuated vaccines in immunocompromised individuals, a subunit vaccine may be an appropriate alternative.

**Methods.** This phase 1/2, randomized, placebo-controlled study evaluated the immunogenicity and safety of an investigational HZ subunit vaccine (HZ/su). Three cohorts of HIV-infected adults aged  $\geq 18$  years were enrolled: 94 ART recipients with a CD4<sup>+</sup> T-cell count of  $\geq 200$  cells/mm<sup>3</sup>, 14 ART recipients with a CD4<sup>+</sup> T-cell count of 50–199 cells/mm<sup>3</sup>, and 15 ART-naive adults with a CD4<sup>+</sup> T-cell count of  $\geq 500$  cells/mm<sup>3</sup>. Subjects received 3 doses of HZ/su (50  $\mu$ g varicella-zoster virus glycoprotein E [gE] combined with AS01<sub>B</sub> adjuvant) or 3 doses of saline at months 0, 2, and 6.

**Results.** One month after dose 3, serum anti-gE antibody concentrations and frequencies of gE-specific CD4<sup>+</sup> T cells were higher following HZ/su vaccination than after receipt of saline ( $P < .0001$ ). Median cell-mediated immune responses peaked after dose 2. Humoral and cell-mediated immune responses persisted until the end of the study (month 18). No vaccination-related serious adverse events were reported. No sustained impact on HIV load or CD4<sup>+</sup> T-cell count was noted following vaccinations.

**Conclusions.** HZ/su was immunogenic and had a clinically acceptable safety profile in HIV-infected adults. **JID 2014**

# + Hepatitis A

## VACCINE OPTIONS

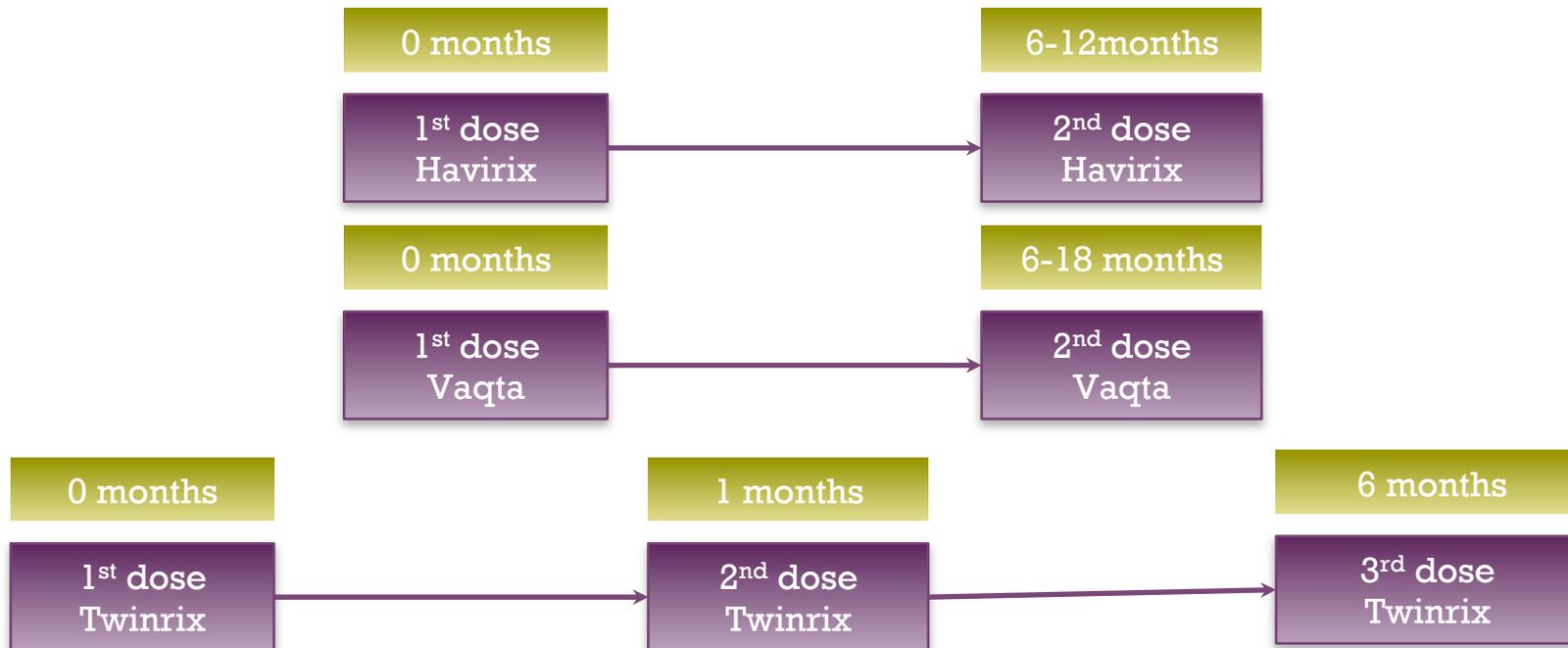
- Inactivated vaccine that can be given either alone (*Havrix* or *Vaqta*) or as part of a combination vaccine (*Twinrix*) that contains both inactivated hepatitis A and recombinant hepatitis B vaccine
- *Twinrix* contains half of *Havrix* dose of hepatitis A antigen
- The two brands of hepatitis A are interchangeable

# + Hepatitis A

**Vaccination is recommended for all PLWH who are at risk of Hepatitis A infection**

Men who have sex with men; Health care workers; Hemophiliacs; Persons who inject drugs; International travellers; Anyone seeking protection from hepatitis A infection

- **TIMING:** Ideally when (or before) CD4 <200 cells/mm<sup>3</sup> and VL declines





# Live Vaccines

# + Varicella (VZV)

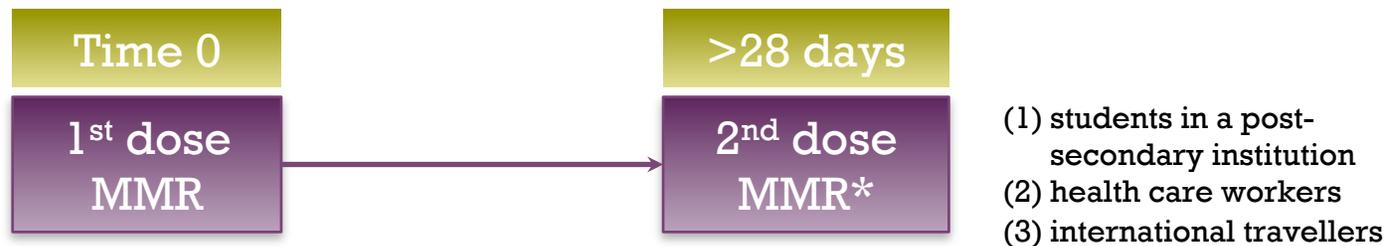
Adults with HIV without evidence of immunity to VZV and CD4 count of 200 cells/mm<sup>3</sup> or greater should receive varicella vaccine



- **CONTRAINDICATIONS:** The varicella vaccine is a live attenuated vaccine and contraindicated in persons with CD4 count less than 200 cells/mm<sup>3</sup>
- The vaccine does not need to be given to those born in the US before 1980
- Zoster vaccine should not be used interchangeably for varicella

# + Measles Mumps & Rubella (MMR)

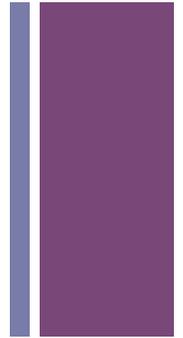
Adults with HIV without evidence of immunity to measles and mumps and CD4 cell count greater than 200 cells/mm<sup>3</sup> should receive a single dose of MMR



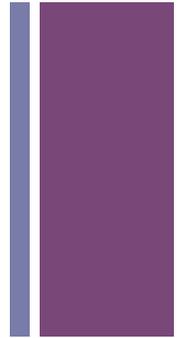
- **CONTRAINDICATIONS:** The MMR vaccine is a live attenuated vaccine and contraindicated in persons with CD4 count less than 200 cells/mm<sup>3</sup>. It is also contraindicated in pregnancy
- Adults born before 1957 in the US are considered immune to measles and mumps

## + Routine vaccines that are contraindicated

- Live Influenza Vaccine (all)
- Quadrivalent MMRV (all)
- MMR (CD4 < 200 cells/mm<sup>3</sup>, pregnant women)
- ZVL (CD4 < 200 cells/mm<sup>3</sup>)
- Varicella (CD4 < 200 cells/mm<sup>3</sup>)



## + Case 5

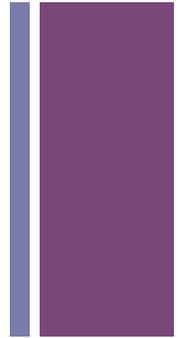


51 year old man with HIV, on ART, virally suppressed with CD4 count of 250 presents for follow up. He is planning a trip to Peru in 1 month. You are advising him on travel vaccination.

**Which of the following vaccines are safe to use in this patient?**

- A. Typhoid, Ty21a, oral
- B. Intranasal influenza
- C. Typhoid, Vi, Injectable
- D. Yellow fever

## + Case 5



51 year old man with HIV, on ART, virally suppressed with CD4 count of 250 presents for follow up. He is planning a trip to Peru in 1 month. You are advising him on travel vaccination.

**Which of the following vaccines are safe to use in this patient?**

- A. Typhoid, Ty21a, oral
- B. Intranasal influenza
- C. Typhoid, Vi, Injectable**
- D. Yellow fever

# + Vaccinations for Travellers with HIV

	CD4>200	CD4<200
<b><u>Live Vaccines</u></b>		
LAIV	X	X
MMR	✓	X
Typhoid, Ty21a	X	X
Varicella	✓	X
Yellow Fever	Precaution	X
<b><u>Inactivated Vaccines</u></b>		
Hep A	✓	✓
Hep B	✓	✓
Influenza	✓	✓
Japanese encephalitis	✓	✓
Meningococcal conjugate	✓	✓
PCV13 ->PPSV23	✓	✓
Rabies	✓	✓
Td/TdaP	✓	✓
Typhoid, Vi	✓	✓

2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:309–18.

# + In Summary

## ALL

Influenza: Annually

Tdap: Once followed by Td booster every 10 years

Pneumococcal: PCV13 (once) ->  
PPSV23 (every 5 years (twice) ->  
PPSV23 after 65

Hepatitis B: 3 dose series

Conjugate Meningococcal ACWY: 2 dose series, booster every 5 years

## Some

HPV: 3 dose series (upto 26 yrs)

Hep A: 2 dose series (MSM, liver dz, travel, HCW, IDU)

MMR and Varicella: lack immunity (CD4 > 200)

Recombinant Zoster Vaccine: 2 dose series (>50yrs)

## Contraindicated

**All PLWH:** MMRV, LIAV, Oral Typhoid

**CD4 < 200:** Varicella, ZVL, Yellow Fever,

MMR

## None

HiB, Conjugate Meningococcal B

