



# CLINICAL GUIDELINES PROGRAM

NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE | HIV · HCV · SUBSTANCE USE · LGBT HEALTH

## Immunizations for Adults With HIV

*Medical Care Criteria Committee, December 2019, reviewed and updated February 2021*

### Contents

<b>Purpose</b> .....	<b>2</b>
<b>Considerations and Contraindications</b> .....	<b>2</b>
<b>Haemophilus Influenzae Type B Conjugate (Hib)</b> .....	<b>4</b>
<b>Hepatitis A Virus (HAV)</b> .....	<b>4</b>
<b>Hepatitis B Virus (HBV)</b> .....	<b>5</b>
<b>Human Papillomavirus (HPV)</b> .....	<b>6</b>
<b>Influenza</b> .....	<b>7</b>
<b>Measles, Mumps, Rubella (MMR)</b> .....	<b>8</b>
<b>Meningococcal Serotype Non-B (MenACWY)</b> .....	<b>9</b>
<b>Meningococcal Serotype B (MenB)</b> .....	<b>9</b>
<b>Pneumococcal</b> .....	<b>10</b>
<b>Tetanus, Diphtheria, and Pertussis (Tdap) and Tetanus-Diphtheria (Td)</b> .....	<b>11</b>
<b>Varicella</b> .....	<b>12</b>
<b>Zoster</b> .....	<b>12</b>
<b>Summary of Recommended Vaccines for Adults With HIV</b> .....	<b>14</b>
<b>References</b> .....	<b>17</b>



# Immunizations for Adults With HIV

## RECOMMENDATION

### Immunizations

- Clinicians should follow the recommendations for routine vaccination of adults with HIV issued by the Centers for Disease Control and Prevention, the National Institutes of Health, the HIV Medicine Association, and the Infectious Disease Society of America, as presented here. (A2)

## Purpose

This compendium of immunization recommendations for adults (≥18 years) with HIV was compiled by the New York State (NYS) Department of Health (DOH) AIDS Institute (AI) to assist clinical practitioners in NYS who provide primary care to adults with HIV. The goal is to present in one easy-to-use document all of the routine vaccinations recommended for adults with HIV by the Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), HIV Medicine Association (HIVMA) [AIDSinfo 2019], and the Infectious Disease Society of America [Rubin, et al. 2014]. The European AIDS Clinical Society guidelines were also consulted [EACS 2019]. Where a recommendation differs from these source documents, the NYSDOH AI rationale is provided. This document integrates current evidence-based clinical recommendations into the healthcare-related implementation strategies of the *Ending the Epidemic initiative*, which seeks to end the AIDS epidemic in NYS by the end of 2020.

Immunizations against infectious diseases are a particularly important component of care for individuals with HIV. Immunodeficiency reduces natural defenses to vaccine-preventable diseases in people with HIV and places them at increased risk for disease and for severe disease [Crum-Cianflone and Wallace 2014; Rubin, et al. 2014]. However, there is concern that patients with HIV-associated immunodeficiency may not be able to mount and maintain an appropriate immune response to vaccines and may be harmed by live virus vaccines. The strength of the immune response may be lower in patients with more advanced HIV, especially among those with CD4 counts <200 cells/mm<sup>3</sup> and/or HIV viral load >200 copies/mL, and shorter in duration than in adults without HIV [Crum-Cianflone and Wallace 2014]. Immunogenicity, vaccine response monitoring, and requirements for additional booster doses for patients with HIV are discussed on pages for individual vaccines.

**Development of this document:** This reference was compiled by the NYSDOH AI Clinical Guidelines Program, which is a collaborative effort between the NYSDOH AI Office of the Medical Director and the Johns Hopkins University School of Medicine, Division of Infectious Diseases.

The goal of the Clinical Guidelines Program, established in 1986, is to develop and disseminate evidence-based, state-of-the-art clinical practice guidelines to improve the quality of care throughout NYS for people with HIV, hepatitis C virus infections, or sexually transmitted infections; people with substance use issues; and members of the LGBTQ community. NYSDOH AI guidelines are developed by committees of clinical experts through a consensus-driven process.

The NYSDOH AI [Medical Care Criteria Committee](#) is charged with developing evidence-based clinical recommendations for clinicians in NYS who treat adults with HIV. The recommendations in this document, with the exception of one, are the same as those of the CDC/NIH/HIVMA guidelines. This document also discusses published literature related to specific vaccines and the rationale for recommendations for which there is no consensus among the referenced guidelines, no evidence specific to patients with HIV, or new data have been published.

## Considerations and Contraindications

The tables and accompanying discussion in this section compile recommendations from the Centers for Disease Control and Prevention (CDC), National Institutes of Health, and HIV Medicine Association guidelines on immunization of adults with HIV

who are not pregnant, along with vaccination schedules, clinical comments, and sources. The only recommendation in this guideline that was developed by the HIV Clinical Guidelines Program Medical Care Criteria Committee is in the section on zoster vaccination. Table 20 compiles all immunization recommendations into one printable table.

Inactivated vaccines are generally considered safe, although data are insufficient to rule out rare adverse effects [Rubin, et al. 2014; Ezeanolue, et al. 2019]. Live, attenuated vaccines are contraindicated for patients with CD4 counts <200 cells/mm<sup>3</sup>, because of the risk of severe reactions in individuals who are immunosuppressed [Davis, et al. 1977; CDC 1985; Redfield, et al. 1987; CDC 1996]. For patients with HIV and CD4 counts ≥200 cells/mm<sup>3</sup>, inactivated forms of vaccines such as those for polio, influenza, typhoid, and zoster are preferred over the live vaccine options. Live, attenuated vaccines should be administered only when an inactivated version does not exist and the risk of the disease clearly outweighs the theoretical risk of vaccination.

→ KEY POINTS: USE OF LIVE, ATTENUATED VACCINES

- **Patients with CD4 count <200 cells/mm<sup>3</sup>:** The following live, attenuated vaccines are **contraindicated:** Bacillus Calmette-Guérin; measles, mumps, rubella; oral typhoid; rotavirus\*; varicella; yellow fever; zoster.
- **Patients with CD4 count ≥200 cells/mm<sup>3</sup>:** Use live, attenuated vaccines only if an inactivated alternative is not available *and* the risk of disease is greater than the risk of vaccination.

**\*Patient education:** Patients with HIV should avoid handling diapers of infants vaccinated for rotavirus in the previous 4 weeks, and all household members should wash their hands after changing diapers of an infant recently vaccinated for rotavirus.

Transient increases in viral load and decreases in CD4 cell count caused by immune system activation have been described after vaccination in patients with HIV in some older studies [Rey, et al. 2000; Kolber, et al. 2002]. The changes are less likely to occur in patients taking antiretroviral therapy (ART) and have not been found to have long-term negative effects [Sullivan, et al. 2000; Rubin, et al. 2014].

→ KEY POINTS

- In people older than 5 years with HIV, effective ART is defined as ART taken for ≥6 months, with a CD4 percentage ≥15% and a CD4 count ≥200 cells/mm<sup>3</sup> for ≥6 months [McLean, et al. 2013].
- Viral suppression is defined as an HIV viral load <200 copies/mL.

Clinicians should advise their patients with HIV that family members, close contacts, and other household members should receive all age-appropriate vaccinations, including an annual influenza vaccine, to reduce the patients’ exposure to vaccine-preventable diseases [Fiore, et al. 2011; Rubin, et al. 2014; Grohskopf, et al. 2019]. Live, attenuated virus vaccines may be safely administered to close contacts of persons with HIV, with specific precautions for varicella and rotavirus vaccines. Transmission of live, attenuated virus after vaccination is rare [Rubin, et al. 2014]. However, patients with HIV who lack varicella immunity are advised to avoid direct contact with persons who develop a rash after varicella or zoster vaccination and should not handle diapers of an infant recently vaccinated for rotavirus [Marin, et al. 2007; Cortese and Parashar 2009; Fiore, et al. 2011; Rubin, et al. 2014].

Tables 7 through 19 (for each vaccine listed) present the recommended immunizations for adults with HIV, followed by discussion of each. For complete vaccination recommendations, see the *CDC Immunization Schedules* and the vaccine manufacturers’ package inserts.

❖ HOW TO FILE A CLAIM WITH THE VACCINE INJURY COMPENSATION PROGRAM

- Tel: 1-800-338-2382
- Website: [hrsa.gov/vaccinecompensation](https://hrsa.gov/vaccinecompensation)
- Address to file a claim: US Court of Federal Claims, 717 Madison Place, NW, Washington DC 20005

## Haemophilus Influenzae Type B Conjugate (Hib)

Table 7: Hib Vaccine	
Trade Names	Hiberix; ActHIB
Indications	Patients at risk of Hib infection (see <i>CDC: Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States 2018</i> )
Administration	Administer according to the <i>CDC Immunization Schedule</i> for all adults at risk
Revaccination	None
Comments	Not routinely recommended for people with HIV in the absence of other risk factors (see the <i>CDC Immunization Schedule</i> )

**Discussion:** Hib vaccination is not routinely recommended for patients with HIV in the absence of other risk factors, such as anatomic or functional asplenia, sickle cell disease, or hematopoietic stem cell transplant, because there is a low risk of *H. influenzae* type b infection in adults with HIV [Briere, et al. 2014; Rubin, et al. 2014; CDC 2019c]. Data on the safety and efficacy of the Hib vaccine among adults with HIV indicate a strong immune response, similar to that in adults without HIV, except among those with severe immunosuppression [Steinhoff, et al. 1991; Kroon, et al. 1997; Dockrell, et al. 1999; MacLennan, et al. 2016].

## Hepatitis A Virus (HAV)

Table 8: HAV Vaccine	
Trade Names	<ul style="list-style-type: none"> <li>HAV: Havrix; Vaqta</li> <li>HAV inactivated + hepatitis B virus (HBV): Twinrix</li> </ul>
Indications	Patients aged ≥1 year with HIV [CDC 2019a]
Administration	<ul style="list-style-type: none"> <li>Administer according to the <i>CDC Immunization Schedule</i></li> <li>Obtain HAV IgG at least 1 month after final dose of vaccination series to identify nonresponders</li> <li>If immune reconstitution appears likely, then consider deferring until patient’s CD4 count &gt;200 cells/mm<sup>3</sup> [AIDSinfo 2019]</li> </ul>
Revaccination	Nonresponders to primary HAV vaccination series should be revaccinated [Aberg, et al. 2014] and counseled to avoid exposure
Comments	<ul style="list-style-type: none"> <li>See the New York State Department of Health AIDS Institute guideline <i>HAV-HIV Coinfection</i></li> <li>Covered by the <i>Vaccine Injury Compensation Program</i></li> </ul>

**Discussion:** Among patients with HIV, the HAV vaccine is recommended for those at risk of HAV infection or those who wish to reduce their risk of HAV infection [WHO 2017; CDC 2019c].

The reported rate of HAV antibody seroconversion after vaccination ranges from 49% to 96% [Fiore, et al. 2006; Crum-Cianflone and Wallace 2014; Mena, et al. 2015]. A long-term follow-up study reported that more than 85% of individuals who seroconverted after vaccination had a sustained antibody response for 5 to 10 years [Crum-Cianflone, et al. 2011b; Cheng, et al. 2017]. Although immunocompetent individuals with HIV respond to the HAV vaccine nearly as well as individuals without HIV, individuals with lower CD4 cell counts are less likely to acquire protective levels of antibody [Fiore, et al. 2006; Crum-Cianflone and Wallace 2014; Mena, et al. 2015].

If a patient’s CD4 count is <200 cells/mm<sup>3</sup> or the patient has symptomatic HIV, it is preferable to defer vaccination until several months after initiation of antiretroviral therapy to maximize the antibody response to the vaccine [AIDSinfo 2019]. HAV vaccination should not be deferred in patients who are unlikely to achieve an increased CD4 cell count (see NYSDOH AI guideline *HAV-HIV Coinfection*).

Care providers should perform HAV IgG at least 1 month after final dose of vaccination series to identify nonresponders. Nonresponders to HAV vaccination should be revaccinated [Aberg, et al. 2014] and counseled to avoid exposure to HAV because they remain susceptible to infection, although a small study reported that 31% of primary nonresponders (n = 16)

subsequently seroconverted after completing the 2-dose vaccination series [Cheng, et al. 2017]. If patients are susceptible to both HAV and HBV, the combined HAV/HBV vaccine (3 doses at 0, 1, and 6 months) can be used regardless of the patient’s immune status [Aberg, et al. 2014].

## Hepatitis B Virus (HBV)

Table 9: HBV Vaccine	
<b>Trade Names</b>	<ul style="list-style-type: none"> <li>• HBV 2-dose series: HEPLISAV-B (see note in comments)</li> <li>• HBV 3-dose series: Engerix-B; Recombivax HB</li> <li>• Hepatitis A virus (HAV) inactivated + HBV: Twinrix</li> </ul>
<b>Indications</b>	<p>Patients who are negative for hepatitis B surface antibody (anti-HBs) and do not have chronic HBV infection (see <i>CDC: Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States 2018</i> and the New York State Department of Health AIDS Institute (NYSDOH AI) guideline <i>HBV-HIV Coinfection &gt; Figure 3</i>).</p>
<b>Administration</b>	<ul style="list-style-type: none"> <li>• Administer according to the <i>CDC Immunization Schedule</i> for all adults [Schillie, et al. 2018]</li> <li>• Alternative administration strategies, such as a 3- or 4-injection double-dose vaccination series or an accelerated schedule of 0, 1, and 3 weeks, may be considered [AIDSinfo 2019]</li> <li>• Test for anti-HBs 1 to 2 months after administration of the last dose of the vaccination series [Rubin, et al. 2014]</li> </ul>
<b>Revaccination</b>	<p>Nonresponders to the primary HBV vaccination series (anti-HBs &lt;10 IU/L) should receive a double-dose revaccination series; a 4-dose schedule should be considered</p>
<b>Comments</b>	<ul style="list-style-type: none"> <li>• In patients at risk for HBV infection, initial vaccination should not be deferred if CD4 count is &lt;200 cells/mm<sup>3</sup> [AIDSinfo 2019]</li> <li>• If an accelerated schedule is used, a fourth dose booster should be administered at least 6 months after initiation of the series; the accelerated schedule is not recommended for patients with CD4 counts &lt;500 cells/mm<sup>3</sup></li> <li>• The HAV/HBV combined vaccine is not recommended for the double-dose or 4-injection HBV vaccination strategy</li> <li>• HEPLISAV-B, a 2-dose (1 month apart) recombinant HBV surface antigen vaccine with a novel adjuvant is now available [Dynavax 2017]. There are no data available on use among people with HIV. There were no autoimmune adverse events among people with HIV exposed to the adjuvant [FDA 2017]</li> <li>• See the NYSDOH AI guideline <i>HBV-HIV Coinfection</i></li> <li>• Covered by the <i>Vaccine Injury Compensation Program</i></li> </ul>

**Discussion:** The HBV vaccine is recommended for all adults with HIV who do not have immunity to HBV and who do not have chronic HBV infection [CDC 2019c]. The antibody response to the HBV vaccine is reduced in persons with HIV compared with those who do not have HIV; the reported immune response to the standard dose (20 µg) ranges from 34% to 89% [Mast, et al. 2006; Mena, et al. 2015], with diminishing response with lower CD4 cell counts [Overton, et al. 2005; Kim, et al. 2008; Pettit, et al. 2010; Pollack, et al. 2016]. Undetectable or very low viral load is associated with increased response to HBV vaccination [Overton, et al. 2005; Kim, et al. 2008; Mena, et al. 2012]. Initial vaccination should not be deferred in patients with low CD4 cell counts; some patients with HIV and CD4 counts ≤200 cells/mm<sup>3</sup> may have an immune response [Whitaker, et al. 2012; AIDSinfo 2019].

Improved immune response has been reported using a 4-injection double-dose (40 µg) regimen [Launay, et al. 2011; Chaiklang, et al. 2013]. Studies of a 3-injection double-dose regimen reported increased seroconversion rates compared to standard dose only among adults with HIV with CD4 counts >350 cells/mm<sup>3</sup> and low or undetectable HIV viral load [Fonseca, et al. 2005; Potsch, et al. 2012]. Accelerated schedules (0, 1, and 3 weeks) may increase adherence to the full vaccination series but are not recommended for patients with CD4 counts ≤500 cells/mm<sup>3</sup> due to the increased likelihood of nonresponse [de Vries-Sluijs, et al. 2011]. Patients with HIV should be tested for anti-HBs 1 to 2 months after completing the vaccination series [Aberg, et al. 2014; AIDSinfo 2019]. Other strategies to improve immune response have demonstrated some success, including intradermal administration [Launay, et al. 2011] and addition of adjuvants [Sasaki, et al. 2003; Cooper CL, et al. 2005; Overton, et al. 2010], but the evidence is not sufficient to make a recommendation.

Nonresponders to primary vaccination should be revaccinated using a double-dose regimen with consideration of a 4-dose schedule. Several studies have reported increased response rates from double-dose revaccination among nonresponders [Cardell, et al. 2008; de Vries-Sluijs, et al. 2008; Pseudos, et al. 2010], although the only randomized controlled trial comparing a 3-injection standard dose (20 µg) to a 3-injection, double-dose (40 µg) regimen for revaccination found no difference in response rates. However, the double-dose regimen resulted in a greater and more durable immune response [Rey, et al. 2015]. HBV revaccination can be deferred among nonresponders who are initiating antiretroviral therapy until CD4 counts increase to ≥200 cells/mm<sup>3</sup> [AIDSinfo 2019]. Revaccination should not be delayed in patients who are unlikely to achieve an increased CD4 cell count. For more detailed information, see NYSDOH AI guideline [HBV-HIV Coinfection](#).

Three HBV vaccination formulations are available in the United States. The efficacy of these vaccines has been reported to be equivalent when used in patients who do not have HIV; however, the 3 formulations have not yet been established to be equally effective in patients with HIV. For persons who are susceptible to both HAV and HBV, the combined HAV/HBV vaccine can be used regardless of immune status, with 3 doses, administered at 0, 1, and 6 months. Because no data are available regarding double-dose or 4-injection HBV vaccination with the combined HAV/HBV vaccine in the presence of HIV, the combined vaccine is not recommended for the double-dose or 4-injection HBV vaccination strategy. A 2-dose (1 month apart) recombinant hepatitis B surface antigen vaccine with a novel adjuvant is available. There are no data available on use in people with HIV, but seroprotective rates were superior to comparator 3-dose series among older adults and adults with diabetes [Schillie, et al. 2018]. No autoimmune adverse events were reported among people with HIV exposed to the adjuvant [FDA 2017]. The 2-dose option may facilitate completion rates for the vaccination series. For more information, see NYSDOH AI guideline [HBV-HIV Coinfection > Prevention](#).

## Human Papillomavirus (HPV)

Table 10: HPV Vaccine	
Trade Names	Gardasil 9
Indications	All patients aged 9 to 26 years who were not previously vaccinated or did not receive a complete 3-dose series (see <a href="#">CDC: Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States 2018</a> ).
Administration	Administer through age 26 years as a 3-dose series according to the <a href="#">CDC Immunization Schedule</a> for adults with immunocompromising conditions.
Revaccination	None
Comments	<ul style="list-style-type: none"> <li>• A 2-dose schedule is not recommended [CDC 2019b]</li> <li>• Because of the broader coverage offered by the 9-valent HPV vaccine, it is the only HPV vaccine currently available in the United States (see <a href="#">CDC HPV Home &gt; Information for Healthcare Professionals</a> for more information)</li> <li>• Although the 9-valent vaccine has not been specifically studied in people with HIV, it is expected that the response will be the same in this population as with the 4-valent vaccine</li> <li>• Follow recommendations for cervical and anal cancer screening in women with HIV and men who have received the HPV vaccine [AIDSinfo 2019]</li> <li>• Covered by the <a href="#">Vaccine Injury Compensation Program</a></li> </ul>

**Discussion:** The HPV vaccine is safe and immunogenic among individuals with HIV [Giacomet, et al. 2014; Kojic, et al. 2014; Markowitz, et al. 2014; Toft, et al. 2014; Faust, et al. 2016] and is recommended for women and men aged 9 to 26 years who did not already receive a complete 3-dose series [CDC 2019c]. Routine HPV vaccination is recommended for all adolescents at age 11 to 12 years [CDC 2018]. Available data do not support HPV vaccination in all adults older than 26 years, including those with HIV [Wilkin, et al. 2016]. Mathematical modeling based on the quadrivalent vaccine has demonstrated that offering HPV vaccination up to age 40 years to MSM with HIV likely would be cost-effective [Lin, et al. 2017]; however, this study did not account for lower vaccine response rates with increased age. Other analyses demonstrate 1) efficacy in adults older than 26 years, although at rates lower than in adolescents; 2) a comparable immune response for HPV type 16; and 3) a slightly lower immune response for HPV types 6, 11, and 18 among women aged 25 to 45 years [Munoz, et al. 2009; Westra, et al. 2011].

The HPV vaccine is U.S. Food and Drug Administration-approved for preventive but not therapeutic use; there are no data to support the use of the HPV vaccine to ameliorate existing disease. In individuals who have had an abnormal Pap test result before being vaccinated, the HPV vaccine may protect against infection from HPV types other than those that caused earlier

or existing cervical abnormalities. HPV vaccination should be offered regardless of CD4 cell count [AIDSinfo 2019]. Lower seroconversion rates after HPV vaccination have been reported among women with HIV who are not taking antiretroviral therapy [Kahn, et al. 2013] or who have CD4 counts <200 cells/mm<sup>3</sup> and/or HIV viral load >10,000 copies/mL than among women who do not have HIV [Kojic, et al. 2014]. In another study, women with HIV and a suppressed viral load had a 1.74 to 3.03 times higher peak antibody response than those who did not have viral suppression at the time of first injection; the clinical significance of this finding is not known [Money, et al. 2016].

In individuals who have had an abnormal Pap test before being vaccinated, the HPV vaccine may protect against infection from HPV subtypes other than those that caused earlier or existing cervical abnormalities. However, the vaccine does not cover all HPV serotypes that increase risk of cancer, and the vaccine may be less effective in individuals with HIV. In women and men with HIV who have received the HPV vaccine, clinicians should continue to follow recommendations for cervical and anal cytologic screening, including visual inspection of the anogenital area during annual examinations [AIDSinfo 2019]. (See the New York State Department of Health AIDS Institute guidelines on *Cervical Screening for Dysplasia and Cancer* and *Anal Dysplasia and Cancer*).

HPV testing is not required before administration of the vaccine [Markowitz, et al. 2014]. The 2-dose schedule is not recommended for immunocompromised adults, including those with HIV [Meites, et al. 2016]. There is no recommendation for obtaining follow-up antibody titers because the minimum protective titers have not been established and the immune response rate is high [Markowitz, et al. 2014]. Although the 9-valent vaccine has not been specifically studied in people with HIV, it is the preferred vaccine because of the broader range of HPV subtypes seen in this population [AIDSinfo 2019].

## Influenza

Table 11: Influenza Vaccine	
Trade Names	See Centers for Disease Control and Prevention (CDC) flu vaccines table
Indications	For all patients, as determined by CDC guidelines for all adults
Administration	Administer annually during flu season (October through May) according to CDC guidelines for all adults
Revaccination	None
Comments	Covered by the Vaccine Injury Compensation Program

**Discussion:** People with HIV are at greater risk of severe morbidity from an influenza infection [Kunisaki and Janoff 2009; Grohskopf, et al. 2019] than people who do not have HIV and should be vaccinated annually during flu season (October through May) according to standard (CDC) guidelines for all adults [Aberg, et al. 2014; Grohskopf, et al. 2019]. Inactivated influenza vaccine offers protective immunity in adults with HIV [Beck, et al. 2012; Remschmidt, et al. 2014; Grohskopf, et al. 2019]. Live, attenuated influenza vaccine should not be used for individuals with HIV. Antibody titers lower than those observed in the general population have been reported among adults with HIV, especially among those with advanced HIV disease who are older than 35 years, have low CD4 cell counts, and have detectable viremia [Kroon, et al. 2000; Yamanaka, et al. 2005; Evison, et al. 2009; Crum-Cianflone, et al. 2011a; Garg, et al. 2016]. Studies comparing intradermal and intramuscular vaccines report no difference in immunogenicity, but intradermal vaccination is associated with increased likelihood of redness, swelling, and tenderness at the injection site [Garg, et al. 2016; Seo, et al. 2016].

The CDC does not recommend a second vaccination in individuals with HIV [Grohskopf, et al. 2019], although one study reported that a second dose of an adjuvanted vaccine significantly increased the rate of seroprotective responses [Bickel, et al. 2011]. There is some evidence that influenza seroprotection is higher for people aged 18 years or older who are given a double-dose vaccine than for those given the standard dose vaccine, but the clinical significance of this remains unknown [Cooper C, et al. 2011; McKittrick, et al. 2013]. Another study among children and young adults (aged 3 to 21 years) found no increased immunity among participants with HIV who received the double-dose vaccine [Hakim, et al. 2016]. The high-dose vaccine is not licensed for people older than 65 years.

Results of 2 studies suggest a possible benefit to delaying influenza vaccination to after mid-November; patients vaccinated later in the flu season had lower rates of laboratory-confirmed influenza and influenza-like illnesses than those vaccinated earlier in the season [Werker, et al. 2014; Glinka, et al. 2016]. Monitoring regional influenza activity will help ensure appropriate timing of influenza vaccination. There is no recommendation for post-vaccination serologic testing to determine immune response [Grohskopf, et al. 2019].

## Measles, Mumps, Rubella (MMR)

Table 12: MMR Vaccine	
Trade Names	<ul style="list-style-type: none"> <li>• M-M-R II</li> <li>• MMR + varicella: ProQuad</li> </ul>
Indications	For patients with CD4 counts $\geq 200$ cells/mm <sup>3</sup> who do not have evidence of MMR immunity, as determined by the CDC’s <i>Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States 2018</i>
Administration	Two doses at least 28 days apart (see the <i>CDC Immunization Schedule</i> )
Revaccination	Recommended only in the setting of an outbreak (see the <i>CDC Immunization Schedule</i> )
Comments	<ul style="list-style-type: none"> <li>• <b>Contraindicated</b> for patients with CD4 counts <math>&lt; 200</math> cells/mm<sup>3</sup> (see the <i>CDC Immunization Schedule</i>)</li> <li>• MMR + varicella (MMRV) should not be substituted for MMR [McLean, et al. 2013; Rubin, et al. 2014]</li> <li>• Those who previously received 2 doses of a mumps-containing vaccine and are at increased risk for mumps in the setting of an outbreak should receive a third dose to improve protection against mumps disease and related complications [Marin, et al. 2018]</li> <li>• Covered by the <i>Vaccine Injury Compensation Program</i></li> </ul>

**Discussion:** Immunocompromised persons are at increased risk of serious and life-threatening complications if infected with measles [McLean, et al. 2013]. Patients with HIV who have CD4 counts  $\geq 200$  cells/mm<sup>3</sup> and who do not have evidence of immunity to MMR should be vaccinated with 2 doses of MMR vaccine at least 28 days apart. Documentation of previous age-appropriate vaccination or laboratory confirmation of prior disease is acceptable evidence of immunity. Serologic screening is required if other acceptable evidence of immunity is not available and to determine rubella immunity among individuals of childbearing potential. In the absence of other evidence of immunity, persons with perinatally acquired HIV who received childhood vaccination with MMR before establishment of effective ART should be revaccinated (2 doses) after effective antiretroviral therapy (ART) is established [McLean, et al. 2013]. There is no recommendation for post-vaccination serologic testing to determine immune response [McLean, et al. 2013].

Two studies that examined the antibody response after MMR vaccination in adults with HIV taking ART reported high levels of protective antibodies post-vaccination, although the levels were lower than in adults without HIV. A study conducted in Mexico among adults with HIV who were seronegative for measles reported no significant difference in initial antibody response to measles vaccination between adults with and without HIV (81% vs 85%). However, at 1 year, the observed decline in antibody response was faster in adults with HIV than in those without HIV [Belaunzaran-Zamudio, et al. 2009]. A study in Thailand reported protective antibodies to measles (74.1%), mumps (65.7%), and rubella (93.3%) among adults with HIV 8 to 12 weeks after vaccination with MMR. Compared with adults without HIV, the seroconversion rates were lower but reached statistical significance only for mumps [Chaiwarith, et al. 2016].

No data are available on revaccination in adults with HIV. Revaccination has improved measles antibody response in children with HIV on ART who had an inadequate initial response to vaccination [Aurpibul, et al. 2007; Abzug, et al. 2012]. If persons previously vaccinated with 2 doses of a mumps-containing vaccine are identified as at increased risk for mumps by public health authorities because of an outbreak, these at-risk individuals should receive a third dose of a mumps-containing vaccine to improve protection against mumps disease and related complications [Marin, et al. 2018].

MMR vaccination contains live virus and is contraindicated for patients with CD4 counts  $< 200$  cells/mm<sup>3</sup> due to reports of adverse events, such as measles pneumonitis, in severely compromised patients [CDC 1996; Angel, et al. 1998]. Serious adverse effects have not been reported in adults who were not severely immunocompromised [Belaunzaran-Zamudio, et al. 2009; McLean, et al. 2013; Chaiwarith, et al. 2016]. MMRV has not been adequately studied in individuals with HIV and is not recommended as a substitute for MMR in this population [McLean, et al. 2013; Rubin, et al. 2014].

## Meningococcal Serotype Non-B (MenACWY)

Table 13: MenACWY Vaccine	
Trade Names	<ul style="list-style-type: none"> <li>MenACWY: Menactra</li> <li>MCV4: Menveo</li> </ul>
Indications	<ul style="list-style-type: none"> <li>All patients with HIV (see the CDC’s <i>Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States 2018</i>)</li> <li>See <i>NYSDOH Meningococcal Disease Health Advisories</i></li> </ul>
Administration	<ul style="list-style-type: none"> <li>Administer 2 doses of MenACWY at least 8 weeks apart in those not previously vaccinated (see the <i>CDC Immunization Schedule</i>)</li> <li>For those previously vaccinated with 1 dose of MenACWY, administer the second dose at the earliest opportunity at least 8 weeks after the previous dose (see the <i>CDC Immunization Schedule</i>)</li> </ul>
Revaccination	Administer 1 booster dose of MenACWY every 5 years (see the <i>CDC Immunization Schedule</i> )
Comments	<ul style="list-style-type: none"> <li>MenACWY is preferred over MPSV4 in adults with HIV &gt;55 years of age</li> <li>Covered by the <i>Vaccine Injury Compensation Program</i></li> </ul>

**Discussion:** Adults with HIV are at increased risk of invasive meningococcal disease due to serogroups C, W, and Y. [MacNeil, et al. 2016; Folaranmi, et al. 2017]. A recent study in New York City reported a 10-fold increased risk of invasive meningococcal disease in patients with HIV, with the highest risk among those with CD4 counts  $\leq 200$  cells/mm<sup>3</sup> [Miller, et al. 2014]. As of 2017, the CDC recommends vaccinating all previously unvaccinated adults with HIV with a 2-dose primary series of MenACWY (MenACWY-CRM or MenACWY-D) administered at least 8 weeks apart [MacNeil, et al. 2016].

Data on meningococcal vaccine efficacy among adults with HIV are not currently available [MacNeil, et al. 2016]. Among adolescents with HIV, available evidence indicates that the vaccine is immunogenic and serious adverse events are rare, but adolescents with HIV (and especially those with lower CD4 cell counts and higher viral loads) had reduced antibody levels compared with adolescents without HIV [Siberry, et al. 2010; Lujan-Zilbermann, et al. 2012]. Adding a second vaccine dose significantly improved antibody levels 28 and 72 weeks after immunization, particularly among adolescents with CD4%  $\geq 15$  [Lujan-Zilbermann, et al. 2012].

Booster doses every 5 years are needed to maintain immunity. Although MPSV4 is the only meningococcal vaccine licensed for persons aged 56 years or older, MenACWY is preferred among older adults because of the need for revaccination. Limited data among adults without HIV suggest a greater immune response after a booster dose of MenACWY than with MPSV4; however, no data are available for adults with HIV. There is no recommendation for post-vaccination serologic testing to determine immune response [MacNeil, et al. 2016].

## Meningococcal Serotype B (MenB)

Table 14: MenB Vaccine	
Trade Names	Bexsero; Trumenba
Indications	Patients at risk of MenB infection, as determined by the CDC’s <i>Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States 2018</i>
Administration	Administer according to the <i>CDC Immunization Schedule</i> for patients at risk
Revaccination	None
Comments	<ul style="list-style-type: none"> <li>Not routinely recommended for people with HIV in the absence of other risk factors (see the <i>CDC Immunizations Schedule</i>)</li> <li>Covered by the <i>Vaccine Injury Compensation Program</i></li> </ul>

**Discussion:** MenB vaccine is not routinely recommended for adults with HIV unless they have another indication for immunization. No increased risk of serogroup B meningococcal disease among individuals with HIV has been reported [CDC 2019c].

## Pneumococcal

<b>Table 15: Pneumococcal Vaccine: 13-Valent and 23-Valent (PCV13, PPSV23)</b>	
<b>Trade Names</b>	Prevnar 13 (PCV130); Pneumovax 23 (PPSV23)
<b>Indications</b>	All patients with HIV (see the CDC’s <i>Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States 2018</i> )
<b>Administration</b>	<ul style="list-style-type: none"> <li>The complete series of vaccinations is 1 dose of PCV13 and 2 doses of PPSV23 before age 65 years, followed by 1 additional dose of PPSV23 after age 65 years (see the <i>CDC Immunization Schedule</i>)</li> <li>See Table 16, below, for detailed administration guidelines based on age and previous vaccination history</li> </ul>
<b>Revaccination</b>	See Table 16, below
<b>Comments</b>	The PCV13 vaccine should be not be deferred for patients with CD4 count <200 cells mm <sup>3</sup> and/or detectable viral load; however, the follow-up secondary administration of PPSV23 vaccine may be deferred until the patient’s CD4 count is >200 cells mm <sup>3</sup> and/or viral load is undetectable

**Discussion:** Individuals with HIV are at increased risk of serious disease due to *Streptococcus pneumoniae*, including bacteremia, meningitis, and pneumonia. Pneumococcal vaccination is recommended for all adults with HIV as soon as possible after HIV diagnosis [CDC 2019c; Matanock, et al. 2019]. The complete series is 1 dose of PCV13 as a priming vaccine, followed by 2 doses of PPSV23 before age 65 years and 1 additional dose of PPSV23 after age 65 years. Because only 1 dose of PPSV23 is recommended after a patient reaches age 65 years, those who begin vaccination at age 65 years or older should receive 1 dose of PCV13 and 1 dose of PPSV23 [Tomczyk, et al. 2014]. There is no recommendation for post-vaccination serologic testing to determine immune response [CDC 2019c; Matanock, et al. 2019]. See Table 16 for vaccination recommendations by previous pneumococcal immunization history and age at time of initial evaluation.

Pneumococcal vaccination has been demonstrated to reduce pneumococcal bacteremia and mortality among adults with HIV [Hung, et al. 2004; Grau, et al. 2005; Rodriguez-Barradas, et al. 2008; Chowers, et al. 2017]. Both polysaccharide and conjugate pneumococcal vaccines appear to be safe and immunogenic among adults with HIV who have CD4 counts ≥200 cells/mm<sup>3</sup> [Ho, et al. 2013; Bhorat, et al. 2015; Rodriguez-Barradas, et al. 2015; Lombardi, et al. 2016]. In a randomized controlled trial, the prime-boost regimen of PCV13 followed by PPSV23 significantly increased antibody response compared with PPSV23 alone in adults with HIV [Sadlier, et al. 2016].

Patients with CD4 counts <200 cells/mm<sup>3</sup> are at the highest risk of pneumococcal disease. Because immunogenicity has been demonstrated for individuals with HIV with CD4 counts <200 cells/mm<sup>3</sup> who received PCV7 [French, et al. 2010], use of PCV13 may be considered in severely immunocompromised patients. Patients with HIV who have not previously received any pneumococcal vaccine should receive a dose of PCV13, regardless of CD4 cell count. Although there is evidence of the effectiveness of PPSV23 among patients with CD4 counts <200 cells/mm<sup>3</sup>, the benefit appears to be greatest among patients with viral loads <100,000 copies/mL and among those who are on antiretroviral therapy.

If zoster vaccine is also being administered, it should be separated from the pneumococcal vaccine by at least 4 weeks [Merck 2017].

<b>Table 16: Pneumococcal Vaccination Recommendations for Adults with HIV, by Previous Pneumococcal Immunization History and Age at Time of Initial Evaluation (see <i>CDC Immunization Schedule</i>)</b>		
<b>Previous Immunization History</b>	<b>Aged 18-64 Years</b>	<b>Aged 65 Years or Older</b>
No previous PCV13/PPSV23* or unknown status *by clinical documentation or patient self-report	<ul style="list-style-type: none"> <li>1 dose of PCV13, then</li> <li>1st dose of PPSV23 ≥8 weeks later, then</li> <li>2nd dose of PPSV23 ≥5 years after 1st dose of PPSV23, then</li> <li>3rd dose of PPSV23 if 65 years or older <i>and</i> ≥5 years since 2nd dose of PPSV23 <i>and</i> 2nd dose of PPSV23 given before age 65 years</li> </ul>	<ul style="list-style-type: none"> <li>1 dose of PCV13, then</li> <li>1 dose of PPSV23 ≥8 weeks later</li> </ul>

<b>Table 16: Pneumococcal Vaccination Recommendations for Adults with HIV, by Previous Pneumococcal Immunization History and Age at Time of Initial Evaluation (see <i>CDC Immunization Schedule</i>)</b>		
<b>Previous Immunization History</b>	<b>Aged 18-64 Years</b>	<b>Aged 65 Years or Older</b>
No PCV13 + 1 dose of PPSV23	<ul style="list-style-type: none"> <li>• 1 dose of PCV13 <math>\geq 1</math> year after 1st dose of PPSV23, then</li> <li>• 2nd dose of PPSV23 if both <math>\geq 8</math> weeks after PCV13 dose <i>and</i> <math>\geq 5</math> years after 1st dose of PPSV23, then</li> <li>• 3rd dose of PPSV23 if 65 years or older <i>and</i> <math>\geq 5</math> years since 2nd dose of PPSV23 <i>and</i> 2nd dose of PPSV23 given before age 65 years</li> </ul>	<ul style="list-style-type: none"> <li>• 1 dose of PCV13 <math>\geq 1</math> year after 1st dose of PPSV23, then</li> <li>• 2nd dose of PPSV23 if both <math>\geq 8</math> weeks after PCV13 dose <i>and</i> <math>\geq 5</math> years after 1st dose of PPSV23 <i>and</i> 1st dose of PPSV23 was given before age 65 years</li> </ul>
No PCV13 + 2 doses of PPSV23	<ul style="list-style-type: none"> <li>• 1 dose of PCV13 <math>\geq 1</math> year after most recent dose of PPSV23 <i>and</i></li> <li>• 3rd dose of PPSV23 if 65 years or older <i>and</i> <math>\geq 5</math> years after 2nd dose of PPSV23 <i>and</i> 2nd dose of PPSV23 given before age 65 years <i>and</i> <math>\geq 8</math> weeks after PCV13 dose</li> </ul>	<ul style="list-style-type: none"> <li>• 1 dose of PCV13 <math>\geq 1</math> year after most recent dose of PPSV23, then</li> <li>• 3rd dose of PPSV23 if <math>\geq 5</math> years after 2nd dose of PPSV23 <i>and</i> 2nd dose of PPSV23 given before age 65 years <i>and</i> <math>\geq 8</math> weeks after PCV13 dose</li> </ul>
1 dose of PCV13 + No PPSV23	<ul style="list-style-type: none"> <li>• 1st dose of PPSV23 <math>\geq 8</math> weeks after PCV13 dose, then</li> <li>• 2nd dose of PPSV23 <math>\geq 5</math> years later, then</li> <li>• 3rd dose of PPSV23 if 65 years or older <i>and</i> <math>\geq 5</math> years since 2nd dose of PPSV23 <i>and</i> 2nd dose of PPSV23 given before age 65 years</li> </ul>	<ul style="list-style-type: none"> <li>• 1 dose of PPSV23 <math>\geq 8</math> weeks after PCV13 dose</li> </ul>
1 dose of PCV13 + 1 dose of PPSV23	<ul style="list-style-type: none"> <li>• 2nd dose of PPSV23 if <math>\geq 8</math> weeks after PCV13 dose <i>and</i> <math>\geq 5</math> years since 1st dose of PPSV23, then</li> <li>• 3rd dose of PPSV23 if both 65 years or older <i>and</i> <math>\geq 5</math> years since 2nd dose of PPSV23 <i>and</i> 2nd dose of PPSV23 given before age 65 years</li> </ul>	<ul style="list-style-type: none"> <li>• If 1st dose of PPSV23 given before age 65 years: 2nd dose of PPSV23 <math>\geq 8</math> weeks after PCV13 dose <i>and</i> <math>\geq 5</math> years after 1st dose of PPSV23</li> <li>• If 1st dose of PPSV23 given at 65 years or older: No further doses of PPSV23 required</li> </ul>
1 dose of PCV13 + 2 doses of PPSV23	<ul style="list-style-type: none"> <li>• If 2nd dose of PPSV23 given before age 65 years: 3rd dose of PPSV23 if 65 years or older <i>and</i> <math>\geq 5</math> years since 2nd dose of PPSV23</li> </ul>	<ul style="list-style-type: none"> <li>• If 2nd dose of PPSV23 given before age 65 years: 3rd dose of PPSV23 <math>\geq 8</math> weeks after PCV13 dose <i>and</i> <math>\geq 5</math> years since 2nd dose of PPSV23</li> <li>• If 2nd dose of PPSV23 given at 65 years or older: No 3rd dose of PPSV23 required</li> </ul>

## Tetanus, Diphtheria, and Pertussis (Tdap) and Tetanus-Diphtheria (Td)

<b>Table 17: Tdap and Td Vaccines</b>	
<b>Trade Names</b>	<ul style="list-style-type: none"> <li>• Tdap: Adacel; Boostrix</li> <li>• Td: Tenivac; Decavac (generic 9Td)</li> </ul>
<b>Indications</b>	For all patients, as determined by the CDC's <i>Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States 2018</i> for all adults
<b>Administration</b>	Administer according to the <i>CDC Immunization Schedule</i> for all adults
<b>Revaccination</b>	Td is usually given as a booster dose every 10 years, but it can also be given earlier after a severe and dirty wound or burn
<b>Comments</b>	Covered by the <i>Vaccine Injury Compensation Program</i>

**Discussion:** The recommendations for Tdap and Td vaccination of adults with HIV are the same as for all adults [CDC 2019c]. The safety and efficacy of vaccination with Tdap has not been studied in this population [Rubin, et al. 2014].

## Varicella

Table 18: Varicella Vaccine	
Trade Names	<ul style="list-style-type: none"> <li>Varicella: Varivax</li> <li>Measles, mumps, and rubella (MMR) + varicella (MMRV): ProQuad</li> </ul>
Indications	<ul style="list-style-type: none"> <li>For patients with CD4 counts <math>\geq 200</math> cells/mm<sup>3</sup> who do not have evidence of immunity to varicella, as determined by the CDC’s <i>Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States 2018</i></li> <li>HIV-infected children <math>\geq 12</math> months old with CD4+ T-lymphocyte percentages <math>\geq 15\%</math></li> </ul>
Administration	Administer according to the <i>CDC Immunization Schedule</i> for all adults
Revaccination	None
Comments	<ul style="list-style-type: none"> <li><b>Contraindicated</b> for patients with CD4 counts <math>&lt; 200</math> cells/mm<sup>3</sup> (see the <i>CDC Immunization Schedule</i>)</li> <li>Anti-varicella IgG screening should be performed in patients with no known history of chickenpox or shingles [Marin, et al. 2007]</li> <li>MMRV should not be used [Rubin, et al. 2014]</li> <li>Antiherpetic agents should be avoided at least 24 hours before and 14 days after administration [Ezeanolue, et al. 2019]</li> <li>An interval of at least 3 months is recommended between administration of post-exposure varicella IgG (VariZIG) and varicella vaccination [Cohn, et al. 2013]</li> <li>Clinical disease due to varicella after vaccination, a very rare event, should be treated with acyclovir [AIDSinfo 2019]</li> <li>Covered by the <i>Vaccine Injury Compensation Program</i></li> </ul>

**Discussion:** Patients with HIV who have CD4 counts  $\geq 200$  cells/mm<sup>3</sup> and do not have immunity to varicella should be vaccinated according to [CDC guidelines](#) for all adults, with 2 doses of single-antigen varicella vaccine 4 to 8 weeks apart or a second dose if they have received only 1 dose. Varicella vaccination contains live virus and is contraindicated for patients with CD4 counts  $< 200$  cells/mm<sup>3</sup> because of the risk of disseminated disease [Kramer, et al. 2001; Marin, et al. 2007; CDC 2019c]. Data on the effectiveness of varicella vaccination among adults with HIV are lacking, but vaccination has been shown to be effective among children with HIV [Marin, et al. 2007; CDC 2012; Crum-Cianflone and Wallace 2014].

Clinicians should verify varicella immunity due to the possibility of severe disease in individuals with HIV. Birth before 1980 is not accepted as evidence of immunity in immunocompromised persons; anti-varicella IgG screening should be performed in patients with HIV who have no known history of chickenpox or shingles [Marin, et al. 2007]. Post-vaccination serologic testing to determine immune response is not recommended because commercially available assays lack sensitivity and may give false-negative results [Marin, et al. 2007]. Clinical disease due to varicella after vaccination, a very rare event, should be treated with acyclovir [Marin, et al. 2007; AIDSinfo 2019]. If household members or close contacts develop a rash after vaccination, individuals with HIV should avoid contact with the affected person until after the rash resolves [Marin, et al. 2007; Rubin, et al. 2014; Ezeanolue, et al. 2019]. Because they can interfere with vaccine virus replication and decrease vaccine effectiveness, all antiherpetic agents should be avoided for at least 72 hours before varicella vaccination through 14 days after [CDC 2016]. If post-exposure varicella immune globulin is given, clinicians should wait at least 5 months before vaccination [Ezeanolue, et al. 2019].

## Zoster

Table 19: Zoster Vaccine	
Trade Names	Shingrix: Recombinant zoster vaccine (RZV), adjuvanted— <b>PREFERRED</b>
Indications	<i>Medical Care Criteria Committee</i> recommendation: Patients with HIV $\geq 50$ years of age (A2)

Table 19: Zoster Vaccine	
<b>Administration</b>	<ul style="list-style-type: none"> <li>• Two IM doses, spaced 2 to 6 months apart, regardless of past receipt of zoster live vaccine (ZVL)</li> <li>• RZV is preferred over ZVL [Dooling, et al. 2018] (A2)</li> <li>• Perform anti-varicella immunoglobulin G (IgG) screening in patients with no known history of chickenpox or shingles</li> </ul>
<b>Comments</b>	<ul style="list-style-type: none"> <li>• RZV provides strong protection against shingles and post-herpetic neuralgia. Currently, there are no data on immunogenicity specific to people with HIV; however, superior efficacy and longer duration of protection have been demonstrated among the elderly, and a recombinant vaccine is preferred people with HIV</li> <li>• ZVL (brand name Zostavax) is also available but is not recommended for people with HIV and is <i>contraindicated</i> in patients with CD4 count &lt;200 cells/mm<sup>3</sup> (see <a href="#">Centers for Disease Control and Prevention [CDC] guidelines</a>). If RZV is not available and ZVL must be administered:               <ul style="list-style-type: none"> <li>– Perform anti-varicella IgG screening in patients with no known history of chickenpox or shingles</li> <li>– Instruct patients to avoid antiherpetic agents for 1 to 2 days before vaccination through 14 days after [Marin, et al. 2007]</li> <li>– Separate administration of ZVL from administration of pneumococcal vaccine by at least 4 weeks [Merck 2017]</li> </ul> </li> </ul>

**Discussion:** Patients with HIV are at increased risk of zoster (initial episodes and recurrences) at all stages of HIV disease; the risk is greater among those with severe immunodeficiency and lower CD4 cell counts [Harpaz, et al. 2008; Blank, et al. 2012]. Zoster vaccination may reduce disease burden in individuals with HIV; however, data on the use of zoster vaccine among adults with HIV are limited.

The Advisory Committee on Immunization Practices recommends RZV for use in immunocompetent adults aged ≥50 years [Dooling, et al. 2018]. As noted above, the [Medical Care Criteria Committee](#) recommends 2 doses of RZV, administered 2 to 6 months apart, for adults with HIV ≥50 years of age. RZV provides strong protection against shingles and post-herpetic neuralgia. There is no specific data on immunogenicity in people with HIV; however, superior efficacy and longer duration of seroprotection have been demonstrated in the elderly, and a recombinant vaccine is preferred over a live, attenuated vaccine in this population [Dooling, et al. 2018].

Limited data are available on the immunogenicity of live, attenuated zoster vaccine in people with HIV (ZVL). The Committee does not recommend use of ZVL in people with HIV because of the potential for adverse effects and for interference by co-administered antiviral and immunoglobulin therapy [Benson, et al. 2012; Shafran 2016]. If ZVL is used due to lack of access to RZV, [CDC guidelines](#) recommend that, if possible, antiherpetic agents should be avoided 1 to 2 days before through 14 days after administration of the zoster vaccine [Harpaz, et al. 2008]. In addition, zoster vaccine should be separated from pneumococcal vaccine by at least 4 weeks [Merck 2017]. Anti-varicella IgG screening should be performed in patients with no known history of chickenpox or shingles. Zoster vaccination is contraindicated for patients with CD4 counts <200 cells/mm<sup>3</sup> [Harpaz, et al. 2008]. There is no recommendation for post-vaccination serologic testing to determine immune response [Harpaz, et al. 2008].

## Summary of Recommended Vaccines for Adults With HIV

Table 20: Summary of Recommended Vaccines for Adults With HIV			
Vaccine Trade Name	Indications	Administration and Revaccination	Comments
<b>Haemophilus Influenzae Type B Conjugate (Hib)</b> <ul style="list-style-type: none"> <li>Hiberix; ActHIB</li> </ul>	Patients at risk of Hib infection; see CDC guidelines for all adults	<ul style="list-style-type: none"> <li>Administer according to CDC guidelines for all adults at risk</li> <li><b>Revaccination:</b> None</li> </ul>	Not routinely recommended for people with HIV in the absence of other risk factors
<b>Hepatitis A (HAV)</b> <ul style="list-style-type: none"> <li>HAV: Havrix; Vaqta</li> <li>HAV inactivated + HBV: Twinrix</li> </ul>	All patients aged ≥1 year with HIV	<ul style="list-style-type: none"> <li>Administer according to CDC guidelines</li> <li>Obtain HAV IgG at least 1 month after final dose of vaccination series to identify nonresponders</li> <li>If immune reconstitution appears likely, then consider deferring until patient’s CD4 count &gt;200 cells/mm<sup>3</sup></li> <li><b>Revaccination:</b> Nonresponders to primary HAV vaccination series should be revaccinated and counseled to avoid exposure</li> </ul>	<ul style="list-style-type: none"> <li>Covered by the Vaccine Injury Compensation Program*</li> <li>See NYSDOH AI guideline HAV-HIV Coinfection</li> </ul>
<b>Hepatitis B (HBV)</b> <ul style="list-style-type: none"> <li>HBV 2-dose series: HEPLISAV-B</li> <li>HBV 3-dose series: Engerix-B, Recombivax HB</li> <li>HAV inactivated + HBV: Twinrix</li> </ul>	Patients who are negative for anti-HBs and do not have chronic HBV infection; see NYSDOH AI guideline <i>HBV-HIV Coinfection</i> , Figure 3	<ul style="list-style-type: none"> <li>Administer according to CDC guidelines for all adults</li> <li>Alternative administration strategies, such as a 3- or 4-injection double-dose vaccination series or an accelerated schedule of 0, 1, and 3 weeks, may be considered</li> <li>Test for anti-HBs 1 to 2 months after administration of the last dose of the vaccination series</li> <li><b>Revaccination:</b> Nonresponders to the primary HBV vaccination series (anti-HBs)</li> </ul>	<ul style="list-style-type: none"> <li>In patients at risk for HBV infection, initial vaccination should not be deferred if CD4 cell count is &lt;200 cells/mm<sup>3</sup></li> <li>If an accelerated schedule is used, a 4th dose booster should be administered at least 6 months after initiation of the series; the accelerated schedule is not recommended for patients with CD4 counts &lt;500 cells/mm<sup>3</sup></li> <li>The HAV/HBV combined vaccine is not recommended for the double-dose or 4-injection HBV vaccination strategy</li> <li>A 2-dose (1 month apart) recombinant HBV surface antigen vaccine with a novel adjuvant (HEPLISAV-B) is available. There are no data available on use among people with HIV. There were no autoimmune adverse events among people with HIV exposed to the adjuvant</li> <li>See NYSDOH AI guideline <i>HBV-HIV Coinfection</i></li> <li>Covered by the Vaccine Injury Compensation Program*</li> </ul>

Table 20: Summary of Recommended Vaccines for Adults With HIV			
Vaccine Trade Name	Indications	Administration and Revaccination	Comments
<b>Human Papillomavirus (HPV)</b> <ul style="list-style-type: none"> <li>Gardasil 9</li> </ul>	All patients aged 9 to 26 years who were not previously vaccinated or did not receive a complete 3-dose series	<ul style="list-style-type: none"> <li>Administer through age 26 years as a 3-dose series according to CDC guidelines for adults with immuno-compromising conditions</li> <li><b>Revaccination:</b> None</li> </ul>	<ul style="list-style-type: none"> <li>A 2-dose schedule is not recommended</li> <li>Because of the broader coverage offered by the 9-valent HPV vaccine, it is the only HPV vaccine currently available in the United States (see CDC <i>HPV Home &gt; Information for Healthcare Professionals</i> for more information)</li> <li>Although the 9-valent vaccine has not been specifically studied in people with HIV, it is expected that the response will be the same in this population as with the 4-valent vaccine</li> <li>Follow recommendations for cervical and anal cancer screening in women with HIV and men who have received the HPV vaccine</li> <li>Covered by the Vaccine Injury Compensation Program*</li> </ul>
<b>Influenza</b> <ul style="list-style-type: none"> <li>For brand names, see CDC flu vaccines table</li> </ul>	For all patients, as determined by CDC guidelines for all adults	<ul style="list-style-type: none"> <li>Administer annually during flu season (October through May) according to CDC guidelines for all adults</li> <li><b>Revaccination:</b> None</li> </ul>	Covered by the Vaccine Injury Compensation Program*
<b>Measles, Mumps, and Rubella (MMR)</b> <ul style="list-style-type: none"> <li>M-M-R II</li> <li>MMR + varicella: ProQuad</li> </ul>	For patients with CD4 cell counts $\geq 200$ cells/mm <sup>3</sup> who do not have evidence of MMR immunity, as determined by CDC guidelines for all adults	<ul style="list-style-type: none"> <li>Two doses at least 28 days apart</li> <li><b>Revaccination:</b> Recommended only in the setting of an outbreak</li> </ul>	<ul style="list-style-type: none"> <li>Contraindicated for patients with CD4 counts <math>&lt; 200</math> cells/mm<sup>3</sup></li> <li>MMRV should not be substituted for MMR</li> <li>Those who previously received 2 doses of a mumps-containing vaccine and are at increased risk for mumps in the setting of an outbreak should receive a third dose to improve protection against mumps disease and related complications</li> <li>Covered by the Vaccine Injury Compensation Program*</li> </ul>
<b>Meningococcal Serotype Non-B (MenACWY)</b> <ul style="list-style-type: none"> <li>MenACWY: Menactra</li> <li>MCV4: Menveo</li> </ul>	<ul style="list-style-type: none"> <li>All patients with HIV</li> <li>See NYSDOH Health Advisories on Meningococcal Disease</li> </ul>	<ul style="list-style-type: none"> <li>Administer 2 doses of MenACWY at least 8 weeks apart in those not previously vaccinated</li> <li>For those previously vaccinated with 1 dose of MenACWY, administer the 2nd dose at the earliest opportunity at least 8 weeks after the previous dose</li> <li><b>Revaccination:</b> Administer 1 booster dose of MenACWY every 5 years</li> </ul>	<ul style="list-style-type: none"> <li>MenACWY is preferred over MPSV4 in adults with HIV <math>&gt; 55</math> years of age</li> <li>Covered by the Vaccine Injury Compensation Program*</li> </ul>

<b>Table 20: Summary of Recommended Vaccines for Adults With HIV</b>			
<b>Vaccine Trade Name</b>	<b>Indications</b>	<b>Administration and Revaccination</b>	<b>Comments</b>
<b>Meningococcal Serotype B (MenB)</b> <ul style="list-style-type: none"> <li>• Bexsero;</li> <li>• Trumenba</li> </ul>	Patients at risk of MenB infection, as determined by CDC guidelines	<ul style="list-style-type: none"> <li>• Administer according to CDC guidelines for patients at risk</li> <li>• <b>Revaccination:</b> None</li> </ul>	<ul style="list-style-type: none"> <li>• Not routinely recommended for people with HIV in the absence of other risk factors</li> <li>• Covered by the Vaccine Injury Compensation Program*</li> </ul>
<b>Pneumococcal</b> <ul style="list-style-type: none"> <li>• 13-valent: Prevnar 13 (PCV130)</li> <li>• 23-valent: Pneumovax 23 (PPSV23)</li> </ul>	All patients with HIV	<ul style="list-style-type: none"> <li>• The complete series of vaccinations is 1 dose of PCV13 and 2 doses of PPSV23 before age 65 years, followed by 1 additional dose of PPSV23 after age 65 years</li> <li>• See Table 16 for detailed administration guidelines based on age and previous vaccination history</li> </ul>	The PCV13 vaccine should be not be deferred for patients with CD4 count <200 cells mm <sup>3</sup> and/or detectable viral load; however, the follow-up secondary administration of PPSV23 vaccine may be deferred until the patient’s CD4 count is >200 cells/mm <sup>3</sup> and/or viral load is undetectable
<b>Tetanus, Diphtheria, and Pertussis (Tdap) and Tetanus-Diphtheria (Td)</b> <ul style="list-style-type: none"> <li>• Tdap: Adacel; Boostrix</li> <li>• Td: Tenivac; Decavac (generic 9Td)</li> </ul>	For all patients, as determined by CDC guidelines for all adults	<ul style="list-style-type: none"> <li>• Administer according to CDC guidelines for all adults</li> <li>• <b>Revaccination:</b> Td is usually given as a booster dose every 10 years, but it can also be given earlier after a severe and dirty wound or burn</li> </ul>	Covered by the Vaccine Injury Compensation Program*
<b>Varicella</b> <ul style="list-style-type: none"> <li>• Varicella: Varivax</li> <li>• MMR + varicella: ProQuad</li> </ul>	<ul style="list-style-type: none"> <li>• For patients with CD4 cell counts ≥200 cells/mm<sup>3</sup> who do not have evidence of immunity to varicella, as determined by CDC guidelines for all adults</li> <li>• HIV-infected children ≥12 months old with CD4+ T-lymphocyte percentages ≥15%</li> </ul>	<ul style="list-style-type: none"> <li>• Administer according to CDC guidelines for all adults</li> <li>• <b>Revaccination:</b> None</li> </ul>	<ul style="list-style-type: none"> <li>• Contraindicated for patients with CD4 counts &lt;200 cells/mm<sup>3</sup></li> <li>• Anti-varicella IgG screening should be performed in patients with no known history of chickenpox or shingles</li> <li>• MMRV should not be used</li> <li>• Antiherpetic agents should be avoided at least 24 hours before and 14 days after administration</li> <li>• An interval of at least 3 months is recommended between administration of post-exposure varicella IgG (VariZIG) and varicella vaccination</li> <li>• Clinical disease due to varicella after vaccination, a very rare event, should be treated with acyclovir</li> <li>• Covered by the Vaccine Injury Compensation Program*</li> </ul>

Table 20: Summary of Recommended Vaccines for Adults With HIV			
Vaccine Trade Name	Indications	Administration and Revaccination	Comments
<b>Zoster</b> <ul style="list-style-type: none"> <li>RZV: Shingrix— PREFERRED</li> <li>For information on ZVL (brand name Zostavax), see Table 19</li> </ul>	MCCC recommendation: Patients aged ≥50 years with HIV (A2)	<ul style="list-style-type: none"> <li>Two IM doses, spaced 2 to 6 months apart, regardless of past receipt of ZVL</li> <li>See CDC information on administering Shingrix</li> <li>Perform anti-varicella IgG screening in patients with no known history of chickenpox or shingles</li> <li><b>Revaccination:</b> None</li> </ul>	<ul style="list-style-type: none"> <li>RZV is preferred over ZVL (A2)</li> <li>RZV provides strong protection against shingles and post-herpetic neuralgia. Currently, there are no data on efficacy specific to people with HIV; however, superior efficacy and longer duration of protection have been demonstrated among the elderly, and a recombinant vaccine is preferred people with HIV</li> <li>In addition, immunogenicity and safety following a 3-dose schedule has been demonstrated among people with HIV infection.</li> </ul> <p><i>Note: RZV is administered IM in distinction to ZVL which is delivered by SQ injection.</i></p>
<p><b>Abbreviations:</b> CDC: Centers for Disease Control and Prevention; MMR: measles, mumps, and rubella; NYSDOH AI: New York State Department of Health AIDS Institute; RZV: recombinant zoster vaccine; ZVL: zoster vaccine live.</p> <p>*Vaccine injury compensation program: Tel: 1-800-338-2382; U.S. Court of Federal Claims, 717 Madison Place, NW, Washington DC 20005</p>			

## References

Aberg JA, Gallant JE, Ghanem KG, et al. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis* 2014;58(1):1-10. [PMID: 24343580] <https://pubmed.ncbi.nlm.nih.gov/24343580>

Abzug MJ, Qin M, Levin MJ, et al. Immunogenicity, immunologic memory, and safety following measles revaccination in HIV-infected children receiving highly active antiretroviral therapy. *J Infect Dis* 2012;206(4):512-522. [PMID: 22693229] <https://pubmed.ncbi.nlm.nih.gov/22693229>

AIDSinfo. Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. 2019 <https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection/whats-new-guidelines> [accessed 2019 Nov 26]

Angel JB, Walpita P, Lerch RA, et al. Vaccine-associated measles pneumonitis in an adult with AIDS. *Ann Intern Med* 1998;129(2):104-106. [PMID: 9669968] <https://pubmed.ncbi.nlm.nih.gov/9669968>

Aurpibul L, Puthanakit T, Sirisanthana T, et al. Response to measles, mumps, and rubella revaccination in HIV-infected children with immune recovery after highly active antiretroviral therapy. *Clin Infect Dis* 2007;45(5):637-642. [PMID: 17683001] <https://pubmed.ncbi.nlm.nih.gov/17683001>

Beck CR, McKenzie BC, Hashim AB, et al. Influenza vaccination for immunocompromised patients: systematic review and meta-analysis by etiology. *J Infect Dis* 2012;206(8):1250-1259. [PMID: 22904335] <https://pubmed.ncbi.nlm.nih.gov/22904335>

Belaunzaran-Zamudio PF, Garcia-Leon ML, Wong-Chew RM, et al. Early loss of measles antibodies after MMR vaccine among HIV-infected adults receiving HAART. *Vaccine* 2009;27(50):7059-7064. [PMID: 19799846] <https://pubmed.ncbi.nlm.nih.gov/19799846>

Benson CA, Hua L, W. AJ, et al. Zostavax is generally safe and immunogenic in HIV-infected adults with CD4 counts ≥200 cells/μL virologically suppressed on ART: Results of a Phase 2, randomized, placebo-controlled trial. Oral abstract 96. CROI; 2012 Mar 5-8; Seattle, WA. [http://www.viraled.com/modules/info/files/files\\_4f68abf5b1ba1.pdf](http://www.viraled.com/modules/info/files/files_4f68abf5b1ba1.pdf)

- Bhorat AE, Madhi SA, Laudat F, et al. Immunogenicity and safety of the 13-valent pneumococcal conjugate vaccine in HIV-infected individuals naive to pneumococcal vaccination. *AIDS* 2015;29(11):1345-1354. [PMID: 25888646] <https://pubmed.ncbi.nlm.nih.gov/25888646>
- Bickel M, von Hentig N, Wieters I, et al. Immune response after two doses of the novel split virion, adjuvanted pandemic H1N1 influenza A vaccine in HIV-1-infected patients. *Clin Infect Dis* 2011;52(1):122-127. [PMID: 21148530] <https://pubmed.ncbi.nlm.nih.gov/21148530>
- Blank LJ, Polydefkis MJ, Moore RD, et al. Herpes zoster among persons living with HIV in the current antiretroviral therapy era. *J Acquir Immune Defic Syndr* 2012;61(2):203-207. [PMID: 22766968] <https://pubmed.ncbi.nlm.nih.gov/22766968>
- Briere EC, Rubin L, Moro PL, et al. Prevention and control of haemophilus influenzae type b disease: recommendations of the advisory committee on immunization practices (ACIP). *MMWR Recomm Rep* 2014;63(Rr-01):1-14. [PMID: 24572654] <https://pubmed.ncbi.nlm.nih.gov/24572654>
- Cardell K, Akerlind B, Sallberg M, et al. Excellent response rate to a double dose of the combined hepatitis A and B vaccine in previous nonresponders to hepatitis B vaccine. *J Infect Dis* 2008;198(3):299-304. [PMID: 18544037] <https://pubmed.ncbi.nlm.nih.gov/18544037>
- CDC. Disseminated mycobacterium bovis infection from BCG vaccination of a patient with acquired immunodeficiency syndrome. *MMWR Morb Mortal Wkly Rep* 1985;34(16):227-228. [PMID: 3920493] <https://pubmed.ncbi.nlm.nih.gov/3920493>
- CDC. Measles pneumonitis following measles-mumps-rubella vaccination of a patient with HIV infection, 1993. *MMWR Morb Mortal Wkly Rep* 1996;45(28):603-606. [PMID: 8676852] <https://pubmed.ncbi.nlm.nih.gov/8676852>
- CDC. FDA approval of an extended period for administering VariZIG for postexposure prophylaxis of varicella. *MMWR Morb Mortal Wkly Rep* 2012;61(12):212. [PMID: 22456121] <https://pubmed.ncbi.nlm.nih.gov/22456121>
- CDC. Varicella. Epidemiology and prevention of vaccine-preventable diseases. 2016 Dec 30. <https://www.cdc.gov/vaccines/pubs/pinkbook/index.html> [accessed 2018 Mar 27]
- CDC. Recommended immunization schedule for children and adolescents aged 18 years or younger, United States, 2018. 2018 Mar 2. <https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf> [accessed 2018 Mar 27]
- CDC. ACIP recommendations. 2019a <https://www.cdc.gov/vaccines/acip/recommendations.html> [accessed 2019 Dec 6]
- CDC. HPV vaccine schedule and dosing. 2019b <https://www.cdc.gov/hpv/hcp/schedules-recommendations.html> [accessed 2019 Dec 3]
- CDC. Immunization schedules. 2019c <https://www.cdc.gov/vaccines/schedules/hcp/adult.html> [accessed 2019 Dec 2]
- Chaiklang K, Wipasa J, Chaiwarith R, et al. Comparison of immunogenicity and safety of four doses and four double doses vs. standard doses of hepatitis B vaccination in HIV-infected adults: a randomized, controlled trial. *PLoS One* 2013;8(11):e80409. [PMID: 24265819] <https://pubmed.ncbi.nlm.nih.gov/24265819>
- Chaiwarith R, Praparattanapan J, Nuket K, et al. Seroprevalence of antibodies to measles, mumps, and rubella, and serologic responses after vaccination among human immunodeficiency virus (HIV)-1 infected adults in Northern Thailand. *BMC Infect Dis* 2016;16:190. [PMID: 27138005] <https://pubmed.ncbi.nlm.nih.gov/27138005>
- Cheng A, Chang SY, Sun HY, et al. Long-term durability of responses to 2 or 3 doses of hepatitis A vaccination in human immunodeficiency virus-positive adults on antiretroviral therapy. *J Infect Dis* 2017;215(4):606-613. [PMID: 28011921] <https://pubmed.ncbi.nlm.nih.gov/28011921>
- Chowers M, Regev-Yochay G, Mor O, et al. Invasive pneumococcal disease (IPD) in HIV infected patients in Israel since the introduction of pneumococcal conjugated vaccines (PCV): Analysis of a nationwide surveillance study, 2009-2014. *Hum Vaccin Immunother* 2017;13(1):216-219. [PMID: 27648488] <https://pubmed.ncbi.nlm.nih.gov/27648488>
- Cohn AC, MacNeil JR, Clark TA, et al. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2013;62(Rr-2):1-28. [PMID: 23515099] <https://pubmed.ncbi.nlm.nih.gov/23515099>
- Cooper C, Thorne A, Klein M, et al. Immunogenicity is not improved by increased antigen dose or booster dosing of seasonal influenza vaccine in a randomized trial of HIV infected adults. *PLoS One* 2011;6(3):e17758. [PMID: 21512577] <https://pubmed.ncbi.nlm.nih.gov/21512577>

- Cooper CL, Davis HL, Angel JB, et al. CPG 7909 adjuvant improves hepatitis B virus vaccine seroprotection in antiretroviral-treated HIV-infected adults. *AIDS* 2005;19(14):1473-1479. [PMID: 16135900] <https://pubmed.ncbi.nlm.nih.gov/16135900>
- Cortese MM, Parashar UD. Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2009;58(Rr-2):1-25. [PMID: 19194371] <https://pubmed.ncbi.nlm.nih.gov/19194371>
- Crum-Cianflone NF, Eberly LE, Duplessis C, et al. Immunogenicity of a monovalent 2009 influenza A (H1N1) vaccine in an immunocompromised population: a prospective study comparing HIV-infected adults with HIV-uninfected adults. *Clin Infect Dis* 2011a;52(1):138-146. [PMID: 21148532] <https://pubmed.ncbi.nlm.nih.gov/21148532>
- Crum-Cianflone NF, Wallace MR. Vaccination in HIV-infected adults. *AIDS Patient Care STDS* 2014;28(8):397-410. [PMID: 25029589] <https://pubmed.ncbi.nlm.nih.gov/25029589>
- Crum-Cianflone NF, Wilkins K, Lee AW, et al. Long-term durability of immune responses after hepatitis A vaccination among HIV-infected adults. *J Infect Dis* 2011b;203(12):1815-1823. [PMID: 21606540] <https://pubmed.ncbi.nlm.nih.gov/21606540>
- Davis LE, Bodian D, Price D, et al. Chronic progressive poliomyelitis secondary to vaccination of an immunodeficient child. *N Engl J Med* 1977;297(5):241-245. [PMID: 195206] <https://pubmed.ncbi.nlm.nih.gov/195206>
- de Vries-Sluijs TE, Hansen BE, van Doornum GJ, et al. A randomized controlled study of accelerated versus standard hepatitis B vaccination in HIV-positive patients. *J Infect Dis* 2011;203(7):984-991. [PMID: 21266513] <https://pubmed.ncbi.nlm.nih.gov/21266513>
- de Vries-Sluijs TE, Hansen BE, van Doornum GJ, et al. A prospective open study of the efficacy of high-dose recombinant hepatitis B rechallenge vaccination in HIV-infected patients. *J Infect Dis* 2008;197(2):292-294. [PMID: 18177248] <https://pubmed.ncbi.nlm.nih.gov/18177248>
- Dockrell DH, Poland GA, Steckelberg JM, et al. Immunogenicity of three Haemophilus influenzae type b protein conjugate vaccines in HIV seropositive adults and analysis of predictors of vaccine response. *Vaccine* 1999;17(22):2779-2785. [PMID: 10438047] <https://pubmed.ncbi.nlm.nih.gov/10438047>
- Dooling KL, Guo A, Patel M, et al. Recommendations of the Advisory Committee on Immunization Practices for use of herpes zoster vaccines. *MMWR Morb Mortal Wkly Rep* 2018;67(3):103-108. [PMID: 29370152] <https://pubmed.ncbi.nlm.nih.gov/29370152>
- Dynavax. HEPLISAV-B: Highlights of prescribing information. 2017 Nov. <https://www.heplisavb.com/assets/pdfs/HEPLISAV-B-Prescribing-Information.pdf> [accessed 2019 Dec 2]
- EACS. European AIDS Clinical Society guidelines version 10.0. 2019 [https://www.eacsociety.org/files/2019\\_guidelines-10.0\\_final.pdf](https://www.eacsociety.org/files/2019_guidelines-10.0_final.pdf) [accessed 2019 Nov 26]
- Evison J, Farese S, Seitz M, et al. Randomized, double-blind comparative trial of subunit and virosomal influenza vaccines for immunocompromised patients. *Clin Infect Dis* 2009;48(10):1402-1412. [PMID: 19361304] <https://pubmed.ncbi.nlm.nih.gov/19361304>
- Ezeanolue E, Harriman K, Hunter P, et al. General best practice guidelines for immunization. Best practices guidance of the Advisory Committee on Immunization Practices (ACIP). 2019 <https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/downloads/general-recs.pdf> [accessed 2019 Dec 2]
- Faust H, Toft L, Sehr P, et al. Human papillomavirus neutralizing and cross-reactive antibodies induced in HIV-positive subjects after vaccination with quadrivalent and bivalent HPV vaccines. *Vaccine* 2016;34(13):1559-1565. [PMID: 26896686] <https://pubmed.ncbi.nlm.nih.gov/26896686>
- FDA. Briefing document. Heplisav-B (Hepatitis B Vaccine Recombinant and 1018 ISS Adjuvant). 2017 Jul 28. <https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/VaccinesandRelatedBiologicalProductsAdvisoryCommittee/UCM568492.pdf> [accessed 2019 Dec 2]
- Fiore AE, Fry A, Shay D, et al. Antiviral agents for the treatment and chemoprophylaxis of influenza --- recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2011;60(1):1-24. [PMID: 21248682] <https://pubmed.ncbi.nlm.nih.gov/21248682>
- Fiore AE, Wasley A, Bell BP. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2006;55(Rr-7):1-23. [PMID: 16708058] <https://pubmed.ncbi.nlm.nih.gov/16708058>

- Folaranmi TA, Kretz CB, Kamiya H, et al. Increased risk for meningococcal disease among men who have sex with men in the United States, 2012-2015. *Clin Infect Dis* 2017. [PMID: 28505234] <https://pubmed.ncbi.nlm.nih.gov/28505234>
- Fonseca MO, Pang LW, de Paula Cavalheiro N, et al. Randomized trial of recombinant hepatitis B vaccine in HIV-infected adult patients comparing a standard dose to a double dose. *Vaccine* 2005;23(22):2902-2908. [PMID: 15780739] <https://pubmed.ncbi.nlm.nih.gov/15780739>
- French N, Gordon SB, Mwalukomo T, et al. A trial of a 7-valent pneumococcal conjugate vaccine in HIV-infected adults. *N Engl J Med* 2010;362(9):812-822. [PMID: 20200385] <https://pubmed.ncbi.nlm.nih.gov/20200385>
- Garg S, Thongcharoen P, Praphasiri P, et al. Randomized controlled trial to compare immunogenicity of standard-dose intramuscular versus intradermal trivalent inactivated influenza vaccine in HIV-infected men who have sex with men in Bangkok, Thailand. *Clin Infect Dis* 2016;62(3):383-391. [PMID: 26486702] <https://pubmed.ncbi.nlm.nih.gov/26486702>
- Giacomet V, Penagini F, Trabattoni D, et al. Safety and immunogenicity of a quadrivalent human papillomavirus vaccine in HIV-infected and HIV-negative adolescents and young adults. *Vaccine* 2014;32(43):5657-5661. [PMID: 25149430] <https://pubmed.ncbi.nlm.nih.gov/25149430>
- Glinka ER, Smith DM, Johns ST. Timing matters - Influenza vaccination to HIV-infected patients. *HIV Med* 2016;17(8):601-604. [PMID: 26810556] <https://pubmed.ncbi.nlm.nih.gov/26810556>
- Grau I, Pallares R, Tubau F, et al. Epidemiologic changes in bacteremic pneumococcal disease in patients with human immunodeficiency virus in the era of highly active antiretroviral therapy. *Arch Intern Med* 2005;165(13):1533-1540. [PMID: 16009870] <https://pubmed.ncbi.nlm.nih.gov/16009870>
- Grohskopf LA, Alyanak E, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: Recommendations of the Advisory Committee on Immunization Practices - United States, 2019-20 influenza season. *MMWR Recomm Rep* 2019;68(3):1-21. [PMID: 31441906] <https://pubmed.ncbi.nlm.nih.gov/31441906>
- Hakim H, Allison KJ, Van de Velde LA, et al. Immunogenicity and safety of high-dose trivalent inactivated influenza vaccine compared to standard-dose vaccine in children and young adults with cancer or HIV infection. *Vaccine* 2016;34(27):3141-3148. [PMID: 27129426] <https://pubmed.ncbi.nlm.nih.gov/27129426>
- Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2008;57(Rr-5):1-30; quiz CE32-34. [PMID: 18528318] <https://pubmed.ncbi.nlm.nih.gov/18528318>
- Ho YL, Brandao AP, de Cunto Brandileone MC, et al. Immunogenicity and safety of pneumococcal conjugate polysaccharide and free polysaccharide vaccines alone or combined in HIV-infected adults in Brazil. *Vaccine* 2013;31(37):4047-4053. [PMID: 23684823] <https://pubmed.ncbi.nlm.nih.gov/23684823>
- Hung CC, Chen MY, Hsieh SM, et al. Clinical experience of the 23-valent capsular polysaccharide pneumococcal vaccination in HIV-1-infected patients receiving highly active antiretroviral therapy: a prospective observational study. *Vaccine* 2004;22(15-16):2006-2012. [PMID: 15121313] <https://pubmed.ncbi.nlm.nih.gov/15121313>
- Kahn JA, Xu J, Kapogiannis BG, et al. Immunogenicity and safety of the human papillomavirus 6, 11, 16, 18 vaccine in HIV-infected young women. *Clin Infect Dis* 2013;57(5):735-744. [PMID: 23667266] <https://pubmed.ncbi.nlm.nih.gov/23667266>
- Kim HN, Harrington RD, Van Rompaey SE, et al. Independent clinical predictors of impaired response to hepatitis B vaccination in HIV-infected persons. *Int J STD AIDS* 2008;19(9):600-604. [PMID: 18725550] <https://pubmed.ncbi.nlm.nih.gov/18725550>
- Kojic EM, Kang M, Cespedes MS, et al. Immunogenicity and safety of the quadrivalent human papillomavirus vaccine in HIV-1-infected women. *Clin Infect Dis* 2014;59(1):127-135. [PMID: 24723284] <https://pubmed.ncbi.nlm.nih.gov/24723284>
- Kolber MA, Gabr AH, De La Rosa A, et al. Genotypic analysis of plasma HIV-1 RNA after influenza vaccination of patients with previously undetectable viral loads. *AIDS* 2002;16(4):537-542. [PMID: 11872996] <https://pubmed.ncbi.nlm.nih.gov/11872996>
- Kramer JM, LaRussa P, Tsai WC, et al. Disseminated vaccine strain varicella as the acquired immunodeficiency syndrome-defining illness in a previously undiagnosed child. *Pediatrics* 2001;108(2):E39. [PMID: 11483849] <https://pubmed.ncbi.nlm.nih.gov/11483849>
- Kroon FP, van Dissel JT, de Jong JC, et al. Antibody response after influenza vaccination in HIV-infected individuals: a consecutive 3-year study. *Vaccine* 2000;18(26):3040-3049. [PMID: 10825608] <https://pubmed.ncbi.nlm.nih.gov/10825608>

- Kroon FP, van Dissel JT, Rijkers GT, et al. Antibody response to Haemophilus influenzae type b vaccine in relation to the number of CD4+ T lymphocytes in adults infected with human immunodeficiency virus. *Clin Infect Dis* 1997;25(3):600-606. [PMID: 9314445] <https://pubmed.ncbi.nlm.nih.gov/9314445>
- Kunisaki KM, Janoff EN. Influenza in immunosuppressed populations: a review of infection frequency, morbidity, mortality, and vaccine responses. *Lancet Infect Dis* 2009;9(8):493-504. [PMID: 19628174] <https://pubmed.ncbi.nlm.nih.gov/19628174>
- Launay O, van der Vliet D, Rosenberg AR, et al. Safety and immunogenicity of 4 intramuscular double doses and 4 intradermal low doses vs standard hepatitis B vaccine regimen in adults with HIV-1: a randomized controlled trial. *JAMA* 2011;305(14):1432-1440. [PMID: 21486976] <https://pubmed.ncbi.nlm.nih.gov/21486976>
- Lin A, Ong KJ, Hobbelen P, et al. Impact and cost-effectiveness of selective human papillomavirus vaccination of men who have sex with men. *Clin Infect Dis* 2017;64(5):580-588. [PMID: 28011615] <https://pubmed.ncbi.nlm.nih.gov/28011615>
- Lombardi F, Belmonti S, Fabbiani M, et al. Immunogenicity and safety of the 13-valent pneumococcal conjugate vaccine versus the 23-valent polysaccharide vaccine in unvaccinated HIV-infected adults: A pilot, prospective controlled study. *PLoS One* 2016;11(6):e0156523. [PMID: 27258647] <https://pubmed.ncbi.nlm.nih.gov/27258647>
- Lujan-Zilbermann J, Warshaw MG, Williams PL, et al. Immunogenicity and safety of 1 vs 2 doses of quadrivalent meningococcal conjugate vaccine in youth infected with human immunodeficiency virus. *J Pediatr* 2012;161(4):676-681.e672. [PMID: 22622049] <https://pubmed.ncbi.nlm.nih.gov/22622049>
- MacLennan CA, Richter A, Hodson J, et al. Brief report: Immunization of HIV-infected adults in the UK with haemophilus influenzae B/meningococcal C glycoconjugate and pneumococcal polysaccharide vaccines. *J Acquir Immune Defic Syndr* 2016;73(3):287-293. [PMID: 27163175] <https://pubmed.ncbi.nlm.nih.gov/27163175>
- MacNeil JR, Rubin LG, Patton M, et al. Recommendations for use of meningococcal conjugate vaccines in HIV-infected persons - Advisory Committee on Immunization Practices, 2016. *MMWR Morb Mortal Wkly Rep* 2016;65(43):1189-1194. [PMID: 27811836] <https://pubmed.ncbi.nlm.nih.gov/27811836>
- Marin M, Guris D, Chaves SS, et al. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2007;56(Rr-4):1-40. [PMID: 17585291] <https://pubmed.ncbi.nlm.nih.gov/17585291>
- Marin M, Marlow M, Moore KL, et al. Recommendation of the Advisory Committee on Immunization Practices for use of a third dose of mumps virus-containing vaccine in persons at increased risk for mumps during an outbreak. *MMWR Morb Mortal Wkly Rep* 2018;67(1):33-38. [PMID: 29324728] <https://pubmed.ncbi.nlm.nih.gov/29324728>
- Markowitz LE, Dunne EF, Saraiya M, et al. Human papillomavirus vaccination: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2014;63(Rr-05):1-30. [PMID: 25167164] <https://pubmed.ncbi.nlm.nih.gov/25167164>
- Mast EE, Weinbaum CM, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. *MMWR Recomm Rep* 2006;55(Rr-16):1-33; quiz CE31-34. [PMID: 17159833] <https://pubmed.ncbi.nlm.nih.gov/17159833>
- Matanock A, Lee G, Gierke R, et al. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged ≥65 years: Updated recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep* 2019;68(46):1069-1075. [PMID: 31751323] <https://pubmed.ncbi.nlm.nih.gov/31751323>
- McKittrick N, Frank I, Jacobson JM, et al. Improved immunogenicity with high-dose seasonal influenza vaccine in HIV-infected persons: a single-center, parallel, randomized trial. *Ann Intern Med* 2013;158(1):19-26. [PMID: 23277897] <https://pubmed.ncbi.nlm.nih.gov/23277897>
- McLean HQ, Fiebelkorn AP, Temte JL, et al. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2013;62(Rr-04):1-34. [PMID: 23760231] <https://pubmed.ncbi.nlm.nih.gov/23760231>
- Meites E, Kempe A, Markowitz LE. Use of a 2-dose schedule for human papillomavirus vaccination - Updated recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep* 2016;65(49):1405-1408. [PMID: 27977643] <https://pubmed.ncbi.nlm.nih.gov/27977643>

- Mena G, Garcia-Basteiro AL, Bayas JM. Hepatitis B and A vaccination in HIV-infected adults: A review. *Hum Vaccin Immunother* 2015;11(11):2582-2598. [PMID: 26208678] <https://pubmed.ncbi.nlm.nih.gov/26208678>
- Mena G, Llopia A, Garcia-Basteiro AL, et al. Assessing the immunological response to hepatitis B vaccination in HIV-infected patients in clinical practice. *Vaccine* 2012;30(24):3703-3709. [PMID: 22446635] <https://pubmed.ncbi.nlm.nih.gov/22446635>
- Merck. Zostavax package insert. 2017 Aug. [https://www.merck.com/product/usa/pi\\_circulars/z/zostavax/zostavax\\_pi2.pdf](https://www.merck.com/product/usa/pi_circulars/z/zostavax/zostavax_pi2.pdf) [accessed 2019 Dec 2]
- Miller L, Arakaki L, Ramautar A, et al. Elevated risk for invasive meningococcal disease among persons with HIV. *Ann Intern Med* 2014;160(1):30-37. [PMID: 24166695] <https://pubmed.ncbi.nlm.nih.gov/24166695>
- Money DM, Moses E, Blitz S, et al. HIV viral suppression results in higher antibody responses in HIV-positive women vaccinated with the quadrivalent human papillomavirus vaccine. *Vaccine* 2016;34(40):4799-4806. [PMID: 27544584] <https://pubmed.ncbi.nlm.nih.gov/27544584>
- Munoz N, Manalastas R, Jr., Pitisuttithum P, et al. Safety, immunogenicity, and efficacy of quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine in women aged 24-45 years: a randomised, double-blind trial. *Lancet* 2009;373(9679):1949-1957. [PMID: 19493565] <https://pubmed.ncbi.nlm.nih.gov/19493565>
- Overton ET, Kang M, Peters MG, et al. Immune response to hepatitis B vaccine in HIV-infected subjects using granulocyte-macrophage colony-stimulating factor (GM-CSF) as a vaccine adjuvant: ACTG study 5220. *Vaccine* 2010;28(34):5597-5604. [PMID: 20600512] <https://pubmed.ncbi.nlm.nih.gov/20600512>
- Overton ET, Sungkanuparph S, Powderly WG, et al. Undetectable plasma HIV RNA load predicts success after hepatitis B vaccination in HIV-infected persons. *Clin Infect Dis* 2005;41(7):1045-1048. [PMID: 16142673] <https://pubmed.ncbi.nlm.nih.gov/16142673>
- Pettit NN, DePestel DD, Malani PN, et al. Factors associated with seroconversion after standard dose hepatitis B vaccination and high-dose revaccination among HIV-infected patients. *HIV Clin Trials* 2010;11(6):332-339. [PMID: 21239361] <https://pubmed.ncbi.nlm.nih.gov/21239361>
- Pollack TM, Trang le TT, Ngo L, et al. Response to hepatitis B vaccination among HIV-infected adults in Vietnam. *J Virus Erad* 2016;2(2):102-106. [PMID: 27482443] <https://pubmed.ncbi.nlm.nih.gov/27482443>
- Potsch DV, Camacho LA, Tuboi S, et al. Vaccination against hepatitis B with 4-double doses increases response rates and antibodies titers in HIV-infected adults. *Vaccine* 2012;30(41):5973-5977. [PMID: 22828589] <https://pubmed.ncbi.nlm.nih.gov/22828589>
- Pseudos G, Kim JH, Groce V, et al. Efficacy of double-dose hepatitis B rescue vaccination in HIV-infected patients. *AIDS Patient Care STDS* 2010;24(7):403-407. [PMID: 20586648] <https://pubmed.ncbi.nlm.nih.gov/20586648>
- Redfield RR, Wright DC, James WD, et al. Disseminated vaccinia in a military recruit with human immunodeficiency virus (HIV) disease. *N Engl J Med* 1987;316(11):673-676. [PMID: 3821799] <https://pubmed.ncbi.nlm.nih.gov/3821799>
- Remschmidt C, Wichmann O, Harder T. Influenza vaccination in HIV-infected individuals: systematic review and assessment of quality of evidence related to vaccine efficacy, effectiveness and safety. *Vaccine* 2014;32(43):5585-5592. [PMID: 25131742] <https://pubmed.ncbi.nlm.nih.gov/25131742>
- Rey D, Krantz V, Partisani M, et al. Increasing the number of hepatitis B vaccine injections augments anti-HBs response rate in HIV-infected patients. Effects on HIV-1 viral load. *Vaccine* 2000;18(13):1161-1165. [PMID: 10649616] <https://pubmed.ncbi.nlm.nih.gov/10649616>
- Rey D, Piroth L, Wendling MJ, et al. Safety and immunogenicity of double-dose versus standard-dose hepatitis B revaccination in non-responding adults with HIV-1 (ANRS HB04 B-BOOST): a multicentre, open-label, randomised controlled trial. *Lancet Infect Dis* 2015;15(11):1283-1291. [PMID: 26257021] <https://pubmed.ncbi.nlm.nih.gov/26257021>
- Rodriguez-Barradas MC, Goulet J, Brown S, et al. Impact of pneumococcal vaccination on the incidence of pneumonia by HIV infection status among patients enrolled in the Veterans Aging Cohort 5-Site Study. *Clin Infect Dis* 2008;46(7):1093-1100. [PMID: 18444830] <https://pubmed.ncbi.nlm.nih.gov/18444830>
- Rodriguez-Barradas MC, Serpa JA, Munjal I, et al. Quantitative and qualitative antibody responses to immunization with the pneumococcal polysaccharide vaccine in HIV-infected patients after initiation of antiretroviral treatment: Results from a randomized clinical trial. *J Infect Dis* 2015;211(11):1703-1711. [PMID: 25538270] <https://pubmed.ncbi.nlm.nih.gov/25538270>

- Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis* 2014;58(3):e44-100. [PMID: 24311479] <https://pubmed.ncbi.nlm.nih.gov/24311479>
- Sadlier C, O'Dea S, Bennett K, et al. Immunological efficacy of pneumococcal vaccine strategies in HIV-infected adults: a randomized clinical trial. *Sci Rep* 2016;6:32076. [PMID: 27580688] <https://pubmed.ncbi.nlm.nih.gov/27580688>
- Sasaki M, Focaccia R, de Messias-Reason JI. Efficacy of granulocyte-macrophage colony-stimulating factor (GM-CSF) as a vaccine adjuvant for hepatitis B virus in patients with HIV infection. *Vaccine* 2003;21(31):4545-4549. [PMID: 14575766] <https://pubmed.ncbi.nlm.nih.gov/14575766>
- Schillie S, Vellozzi C, Reingold A, et al. Prevention of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep* 2018;67(No. RR-1):1–31. [PMID: 29708811]
- Seo YB, Lee J, Song JY, et al. Safety and immunogenicity of influenza vaccine among HIV-infected adults: Conventional vaccine vs. intradermal vaccine. *Hum Vaccin Immunother* 2016;12(2):478-484. [PMID: 26431466] <https://pubmed.ncbi.nlm.nih.gov/26431466>
- Shafran SD. Live attenuated herpes zoster vaccine for HIV-infected adults. *HIV Med* 2016;17(4):305-310. [PMID: 26315285] <https://pubmed.ncbi.nlm.nih.gov/26315285>
- Siberry GK, Williams PL, Lujan-Zilbermann J, et al. Phase I/II, open-label trial of safety and immunogenicity of meningococcal (groups A, C, Y, and W-135) polysaccharide diphtheria toxoid conjugate vaccine in human immunodeficiency virus-infected adolescents. *Pediatr Infect Dis J* 2010;29(5):391-396. [PMID: 20431379] <https://pubmed.ncbi.nlm.nih.gov/20431379>
- Steinhoff MC, Auerbach BS, Nelson KE, et al. Antibody responses to Haemophilus influenzae type B vaccines in men with human immunodeficiency virus infection. *N Engl J Med* 1991;325(26):1837-1842. [PMID: 1683682] <https://pubmed.ncbi.nlm.nih.gov/1683682>
- Sullivan PS, Hanson DL, Dworkin MS, et al. Effect of influenza vaccination on disease progression among HIV-infected persons. *AIDS* 2000;14(17):2781-2785. [PMID: 11125897] <https://pubmed.ncbi.nlm.nih.gov/11125897>
- Toft L, Storgaard M, Muller M, et al. Comparison of the immunogenicity and reactogenicity of Cervarix and Gardasil human papillomavirus vaccines in HIV-infected adults: a randomized, double-blind clinical trial. *J Infect Dis* 2014;209(8):1165-1173. [PMID: 24273179] <https://pubmed.ncbi.nlm.nih.gov/24273179>
- Tomczyk S, Bennett NM, Stoecker C, et al. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged  $\geq 65$  years: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep* 2014;63(37):822-825. [PMID: 25233284] <https://pubmed.ncbi.nlm.nih.gov/25233284>
- Werker GR, Sharif B, Sun H, et al. Optimal timing of influenza vaccination in patients with human immunodeficiency virus: a Markov cohort model based on serial study participant hemoagglutination inhibition titers. *Vaccine* 2014;32(6):677-684. [PMID: 24355089] <https://pubmed.ncbi.nlm.nih.gov/24355089>
- Westra TA, Rozenbaum MH, Rogoza RM, et al. Until which age should women be vaccinated against HPV infection? Recommendation based on cost-effectiveness analyses. *J Infect Dis* 2011;204(3):377-384. [PMID: 21742836] <https://pubmed.ncbi.nlm.nih.gov/21742836>
- Whitaker JA, Roupael NG, Edupuganti S, et al. Strategies to increase responsiveness to hepatitis B vaccination in adults with HIV-1. *Lancet Infect Dis* 2012;12(12):966-976. [PMID: 23174382] <https://pubmed.ncbi.nlm.nih.gov/23174382>
- WHO. Hepatitis A outbreaks mostly affecting men who have sex with men—European Region and the Americas. 2017 Jun 7. <http://www.who.int/csr/don/07-june-2017-hepatitis-a/en/> [accessed 2019 Dec 2]
- Wilkin TJ, Chen H, Cespedes M, et al. ACTG A5298: A phase 3 trial of the quadrivalent HPV vaccine in older HIV+ adults. CROI; 2016 Feb 22-25; Boston, MA. <http://www.croiconference.org/sessions/actg-a5298-phase-3-trial-quadrivalent-hpv-vaccine-older-hiv-adults>
- Yamanaka H, Teruya K, Tanaka M, et al. Efficacy and immunologic responses to influenza vaccine in HIV-1-infected patients. *J Acquir Immune Defic Syndr* 2005;39(2):167-173. [PMID: 15905732] <https://pubmed.ncbi.nlm.nih.gov/15905732>