Screening for Human Immunodeficiency Virus Infection

Clinical Recommendations
The Women’s Preventive Services Initiative recommends prevention education and risk assessment for human immunodeficiency virus (HIV) infection in adolescents and women at least annually throughout the lifespan. All women should be tested for HIV at least once during their lifetime. Additional screening should be based on risk, and screening annually or more often may be appropriate for adolescents and women with an increased risk of HIV infection.

Screening for HIV is recommended for all pregnant women upon initiation of prenatal care with retesting during pregnancy based on risk factors. Rapid HIV testing is recommended for pregnant women who present in active labor with an undocumented HIV status. Screening during pregnancy enables prevention of vertical transmission.

Implementation Considerations
The Women’s Preventive Services Initiative recommends as a preventive service for women, prevention education and risk assessment for HIV infection in adolescents and women at least annually throughout the lifespan. More frequent screening for high-risk women, as determined by clinical judgment, is also recommended as a preventive service. Annual or more frequent HIV testing may be needed and is recommended as a preventive service for women who are identified or self-identify as high risk.

This recommendation refers to routine HIV screening, which is different from incident-based or exposure-based HIV testing. Risk factors for HIV infection in women include, but are not limited to, being an active injection drug user; having unprotected vaginal or anal intercourse; having multiple sexual partners; initiating a new sexual relationship; having sexual partners who are HIV-infected, bisexual, or injection drug users; exchanging sex for drugs or money; being a victim of sex trafficking; being incarcerated (currently or previously); and having other sexually transmitted infections.

Approximately 20–26% of infected patients are not identified by risk-based screening. Early detection and treatment improves outcomes for patients and reduces transmission; therefore, based on clinical best practice, screening annually or more frequently may be reasonable.
Evidence Summary: Screening for Human Immunodeficiency Virus Infection

**EVIDENCE MAP**

Prevention education and risk assessment for human immunodeficiency virus (HIV) infection in adolescents and women at least annually throughout the lifespan.

<table>
<thead>
<tr>
<th>Systematic Reviews</th>
<th>Additional Studies</th>
<th>USPSTF; Bright Futures</th>
</tr>
</thead>
</table>
| • 2013 USPSTF review on HIV: no studies evaluated the effect of counseling interventions on transmission risk for HIV. | No studies specific to HIV:  
• Reduced sexual risk taking behaviors after various behavioral interventions in adolescents was reported in 2 RCTs.  
• A brief sexuality intervention had no effect on safer sexual practices and reducing STIs versus a brief general health intervention in one RCT.  
No studies on optimal intervals for prevention education and risk assessment for HIV infection. | • USPSTF: The USPSTF recommends high-intensity behavioral counseling to prevent STIs for all sexually active adolescents and for adults at increased risk for infection. HIV counseling is included in this general recommendation. (Level B; 2013)  
• Bright Futures: Risk reduction for STIs should be discussed in adolescent visits as part of routine health supervision. Anticipatory guidance should include discussions about sexuality and healthy sexual development and provide an opportunity for risk screening, health promotion, counseling, and sex education. |
| • 2014 USPSTF review of 31 trials: counseling was effective for promoting safer sexual practices and reducing STIs in general. |  |  |
| • Systematic review of 13 meta-analyses and systematic reviews: behavioral counseling was effective for promoting safer sexual practices and reducing STIs in general. |  |  |
| • Systematic review of 31 trials: brief sexuality communication showed some effect for promoting safer sexual practices and reducing STIs in general. |  |  |

All women should be tested for HIV at least once during their lifetime.

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| 2013 USPSTF review:  
• No studies comparing screening versus no screening reported clinical outcomes.  
• No studies compared different screening strategies (e.g. risk-based screening versus routine screening). | One RCT found initiation of treatment for HIV infection at CD4 counts of >0.500 x 10^9 cells/L reduced risk of a composite endpoint that included death and serious AIDS-related and serious non-AIDS-related events (HR 0.43, 95% CI 0.30 to 0.62) compared with initiation of treatment at CD4 counts of 0.350 x 10^9 cells/L. | • USPSTF: Screen for HIV infection in adolescents and adults aged 15-65 years. Younger adolescents and older adults who are at increased risk should also be screened. (Level A; 2013)  
• Bright Futures: Screen all sexually active high-risk teens for HIV at least once a year. High-risk teens include, but are not limited to, STI clinic patients, youth in detention centers, and injection drug users. |

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Evidence map continued on page 109.
### Systematic Reviews

- 1 RCT and 6 observational studies found a significant reduction in risk of HIV transmission with early treatment compared with delayed treatment.
- 2 RCTs and 5 observational studies consistently found early treatment of HIV infection significantly reduced risk of death/AIDS-related morbidity compared with delayed treatment.

### Additional Studies

Additional screening should be based on risk, and screening annually or more often may be appropriate for adolescents and women with an increased risk of HIV infection.

### USPSTF; Bright Futures

USPSTF9: Evidence is insufficient to determine optimum time intervals for HIV screening. A reasonable approach may be to rescreen groups at very high risk (e.g., injection drug users) for new HIV infection at least annually and individuals at increased risk at somewhat longer intervals (for example, 3-5 years). Routine rescreening may not be necessary for individuals not at increased risk since they were found to be HIV-negative.

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Evidence map continued on page 110.
Risk factors for HIV infection in women include, but are not limited to, being an active injection drug user; having unprotected vaginal or anal intercourse; having multiple sexual partners; initiating a new sexual relationship; having sexual partners who are HIV-infected, bisexual, or injection drug users; exchanging sex for drugs or money; being a victim of sex trafficking; being incarcerated (currently or previously); and having other sexually transmitted infections.

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| None               | Risk factors based on CDC surveillance reports. | • USPSTF: High risk includes active injection drug use; having unprotected vaginal or anal intercourse; having sexual partners who are HIV-infected, bisexual, or injection drug users; exchanging sex for drugs or money; acquiring or requesting testing for other sexually transmitted infections (STIs).  
• Bright Futures: High-risk teens include, but are not limited to, STI clinic patients, youth in detention centers, and injection drug users. |

Abbreviations: ACA=Affordable Care Act, AIDS=acquired immunodeficiency syndrome, CD4=cluster of differentiation 4 glycoprotein, CDC=Centers for Disease Control and Prevention, CI=confidence interval, HIV=human immunodeficiency virus, HR=hazard ratio, IOM=Institute of Medicine, L=liter, RCT=randomized controlled trial, STI=sexually transmitted infection, USPSTF=U.S. Preventive Services Task Force

**SUMMARY OF EVIDENCE**

This summary of evidence does not include screening for pregnant women, which is covered under previous recommendations of the U.S. Preventive Services Task Force (USPSTF).

**Introduction**

Human immunodeficiency virus (HIV) causes infection leading to acquired immunodeficiency syndrome (AIDS) if untreated. AIDS is characterized by progressive failure of the immune system resulting in life-threatening infections and cancer. HIV cannot be cured, but can be controlled with antiretroviral therapy which can prolong life and reduce transmission to others, particularly when used during early stages of infection. Screening for HIV infection detects individuals who are unaware of their infection and would otherwise miss the opportunity to benefit from early therapy.

**Current Recommendations and Coverage of Services**

The gap in services provided under the provisions of the Patient Protection and Affordable Health Care Act of 2010 (ACA) previously identified by the Institute of Medicine (IOM) Committee was that screening was limited
to pregnant women and high-risk adolescents and adults. The IOM Committee recommended expanding this scope to annual counseling and screening for HIV infection for all sexually active women (Table 1). In 2013, the USPSTF updated its recommendation for HIV screening to include all adolescents and adults aged 15 to 65 years; and younger adolescents and older adults who are at increased risk. Individuals at increased risk include men who have sex with men; active injection drug users; those with sexually transmitted infections; having unprotected vaginal or anal intercourse; having sexual partners who are HIV-infected, bisexual, or injection drug users; and exchanging sex for drugs or money. Screening for pregnant women is also included under this USPSTF recommendation. An update began in late 2016.

Table 1. Summary of Recommendations Currently Covered by the Affordable Care Act

<table>
<thead>
<tr>
<th>IOM Committee</th>
<th>Annual counseling and screening for HIV infection for sexually active women. HIV counseling is also included under a separate recommendation for STI counseling.</th>
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</table>
| USPSTF⁹⁹       | • HIV screening for adolescents and adults aged 15 to 65 years and younger adolescents and older adults who are at increased risk (Level A; 2013).  
• HIV screening for all pregnant women, including those who present in labor who are untested and whose HIV status is unknown (Level A; 2013). |
| Bright Futures¹⁰ | Screening all sexually active high-risk teens for HIV at least once a year. High-risk teens include, but are not limited to, STI clinic patients, youth in detention centers, men who have sex with men, and injection drug users. |

Abbreviations: HIV=human immunodeficiency virus; IOM=Institute of Medicine; STI=sexually transmitted infection; USPSTF=U.S. Preventive Services Task Force

Background

An estimated 1.2 million individuals age 13 years and older were living with HIV infection in the United States in 2012, including 156,300 (12.8%) whose infections had not been diagnosed. In 2014, the estimated number of new HIV diagnoses in the United States was 44,073. These included an estimated 35,571 diagnoses among adult and adolescent males (13 years or older), 8,328 among adult and adolescent females, and 174 among children younger than 13 years. Among women with HIV infection, 74% of infections are attributed to heterosexual contact and the reminder to injection drug use. Adults age 20 to 29 years accounted for the most new cases of infection (15,738) among different age groups. Blacks accounted for the most (44%) new cases among racial/ethnic groups, with whites accounting for 27% and Hispanics 23%. HIV infection among men who have sex with men accounted for 63% of new HIV diagnoses.

Risk factors for HIV infection in women include active injection drug use; unprotected vaginal or anal intercourse; sexual partners who are HIV-infected, bisexual, or injection drug users; exchanging sex for drugs or money; and having other sexually transmitted infections. However, women may not be aware of their sexual partner’s HIV risk. Primary prevention involves behavioral counseling to prevent STIs and condom use.
Several tests are approved for screening including the conventional serum test (reactive immunoassay followed by confirmatory Western blot or immunofluorescent assay); rapid HIV test using blood or oral fluid specimens; combination tests (p24 antigen and HIV antibodies); and qualitative HIV-1 RNA. Tests are highly sensitive and specific. Clinical progression and disease transmission can be reduced with effective combined antiretroviral therapy using three or more antiretroviral agents, immunizations, and prophylaxis for opportunistic infections.

Several professional organizations have issued recommendations for screening (Table 2).

### Table 2. Recommendations of Professional Organizations

<table>
<thead>
<tr>
<th>Organization</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td>American College of Obstetricians and Gynecologists (ACOG)</td>
<td>Females age 13 to 64 years be tested at least once in their lifetime and annually thereafter based on factors related to risk. Obstetrician–gynecologists should annually review patients’ risk factors for HIV and assess the need for retesting. Repeat HIV testing should be offered at least annually to women who are injection drug users or sex partners of injection-drug users; exchange sex for money or drugs; are sex partners of HIV-infected persons; have had sex with men who have sex with men since the most recent HIV test; have had more than one sex partner since their most recent HIV test.</td>
</tr>
<tr>
<td>American Academy of Family Physicians (AAFP)</td>
<td>Screen adolescents and adults ages 18 to 65 years for HIV infection. Younger adolescents and older adults who are at increased risk should also be screened. Screen all pregnant women for HIV, including those who present in labor whose HIV status is unknown.</td>
</tr>
<tr>
<td>American College of Physicians (ACP)</td>
<td>Clinicians adopt routine screening for HIV and encourage patients to be tested; clinicians determine the need for repeat screening on an individual basis.</td>
</tr>
<tr>
<td>Centers for Disease Control and Prevention (CDC)</td>
<td>Diagnostic HIV testing and opt-out HIV screening as a part of routine clinical care in all health-care settings for women age 13 to 64 years, while also preserving the patient’s option to decline HIV testing and ensuring a provider-patient relationship conducive to optimal clinical and preventive care. The guidelines address HIV testing in health-care settings only; they do not modify existing guidelines concerning HIV counseling, testing, and referral for persons at high risk for HIV who seek or receive HIV testing in nonclinical settings.</td>
</tr>
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**Evidence Summary: Screening for Human Immunodeficiency Virus Infection**

A systematic review of screening for HIV was used to update the USPSTF’s clinical recommendations in 2013. This review focused on the effectiveness universal versus targeted HIV screening; the yield of repeated versus one-time screening; the effectiveness of antiretroviral therapy (ART) on clinical outcomes for individuals with early infections and on sexual transmission of HIV; and harms of ART. Clinical outcomes of interest included HIV transmission, AIDS-related events, mortality; and risk of cardiovascular harms associated with long-term (≥2 years) ART use. The updated literature search for the WPSI identified one RCT published since the 2013
USPSTF review that is relevant to screening.\textsuperscript{11} Studies of behavioral counseling to prevent STIs in general (i.e., that are not specific to HIV) are described in the Counseling for Sexually Transmitted Infections Evidence Summary.

**Effectiveness of Screening**
The 2013 USPSTF review found no studies comparing clinical outcomes between adults and adolescents that were screened versus not screened for HIV infection or comparing the yield of repeated HIV screening with one-time screening.

**Effectiveness of Counseling on Transmission Risk**
The 2013 USPSTF review found no studies that evaluated the effects of counseling interventions on transmission risk.

**Effectiveness of ART in Reducing Sexual Transmission**
One RCT (n=1,763 primarily heterosexual, married couples) found that immediate ART in persons with a baseline CD4 count of 0.350 to 0.550 x 10^9 cells/L was associated with substantially lower risk for HIV transmission than delaying therapy until CD4 count was less than 0.250 x 10^9 cells/L (hazard ratio [HR] 0.04, 95% CI 0.01 to 0.27).\textsuperscript{21} Pooled results from six observational studies were consistent with the RCT (pooled HR 0.16, 95% CI 0.07 to 0.35.)

**Effectiveness of ART in Early Infections**
The 2013 USPSTF review included one randomized controlled trial (RCT) and a subgroup analysis from another RCT that found that initiating ART at CD4 counts less than 0.250 x 10^9 cells/L was associated with higher risk for death or AIDS events than initiation at CD4 counts greater than 0.350 x 10^9 cells/L (HR 1.7, 95% CI 1.1 to 2.5 and HR 5.3, 95% CI 1.3 to 9.6).\textsuperscript{16} Four large observational studies also found that initiating ART at CD4 counts between 0.350 and 0.500 x 10^9 cells/L was associated with significantly lower risk for death than deferred or no ART, and a fifth observational study reported similar results, although the reduction in risk was not statistically significant. Four studies on initiation of ART at CD4 counts greater than 0.500 x 10^9 cells/L did not consistently demonstrate clinical benefits.

One RCT published since the 2013 USPSTF review (n=4,685) compared initiation of ART at CD4 counts greater than 0.500 x 10^9 cells/L with delayed initiation at CD4 counts of 0.350 x 10^9 cells/L.\textsuperscript{11} The study found early initiation with ART significantly reduced risk of serious AIDS-related events (HR 0.28, 95% CI 0.15 to 0.50) and risk of a composite endpoint that included death, serious AIDS-related and serious non-AIDS-related events (HR 0.43, 95% CI 0.30 to 0.62.) All-cause mortality was also reduced, although the number of deaths in both groups was small (0.5% versus 0.9%) and the risk estimate was not statistically significant (HR 0.58, 95% CI 0.28 to 1.17.)
Harms of ART
Additional follow-up from a large cohort study found that some protease inhibitors were associated with increased risk for myocardial infarction (RR 1.1 to 1.2 per year of exposure). No clear association was shown between other antiretrovirals and increased risk for cardiovascular events, and the newer antiretrovirals are believed to not be associated with the cardiometabolic effects of the older regimens.

CONCLUSIONS
Screening for HIV infection detects individuals who are unaware of their infection and would otherwise miss the opportunity to benefit from early therapy. New studies of antiretroviral therapy indicate significantly reduced risks of serious AIDS-related events and death, as well as disease transmission, when treatment is initiated early in the infection. In addition, there are fewer adverse effects with the newer antiretroviral medications. This research strengthens the rationale for population screening.
REFERENCES


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