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Screening for HIV: U.S. Preventive Services Task Force Recommendation Statement

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Description: Update of the 2005 U.S. Preventive Services Task Force (USPSTF) recommendation statement on screening for HIV.

Methods: The USPSTF reviewed new evidence on the effectiveness of treatments in HIV-infected persons with CD4 counts greater than 0.200×10^9 cells/L; effects of screening, counseling, and antiretroviral therapy (ART) use on risky behaviors and HIV transmission risk; and long-term cardiovascular harms of ART.

Population: These recommendations apply to adolescents, adults, and pregnant women.

Recommendation: The USPSTF recommends that clinicians screen adolescents and adults aged 15 to 65 years for HIV infection. Younger adolescents and older adults who are at increased risk should also be screened. (Grade A recommendation)

The USPSTF recommends that clinicians screen all pregnant women for HIV, including those who present in labor who are untested and whose HIV status is unknown. (Grade A recommendation)

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The U.S. Preventive Services Task Force (USPSTF) makes recommendations about preventive care services for patients without recognized signs or symptoms of the target condition.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

Summary of Recommendations and Evidence

The USPSTF recommends that clinicians screen for HIV infection in adolescents and adults aged 15 to 65 years. Younger adolescents and older adults who are at increased risk should also be screened. (A recommendation)

See the Clinical Considerations for more information about screening intervals.

The USPSTF recommends that clinicians screen all pregnant women for HIV, including those who present in labor who are untested and whose HIV status is unknown. (A recommendation)

See the **Figure** for a summary of the recommendations and suggestions for clinical practice.

Appendix Table 1 describes the USPSTF grades, and **Appendix Table 2** describes the USPSTF classification of levels of certainty about net benefit (both tables are available at www.annals.org).

Rationale

Importance

An estimated 1.2 million persons in the United States are currently living with HIV infection, and the annual incidence of the disease is approximately 50 000 cases. Since the first cases of AIDS were reported in 1981, more than 1.1 million persons have been diagnosed and nearly 595 000 have died from the condition. Approximately 20% to 25% of individuals living with HIV infection are unaware of their positive status.

Detection

The USPSTF found convincing evidence that conventional and rapid HIV antibody tests are highly accurate in diagnosing HIV infection.

See also:

Print
Editorial comment
Summary for Patients

Web-Only

Figure. **Screening for HIV: clinical summary of U.S. Preventive Services Task Force recommendation.**

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U.S. Preventive Services TASK FORCE
www.USPreventiveServicesTaskForce.org

SCREENING FOR HIV
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Adolescents and adults aged 15 to 65 years, younger adolescents and older adults at increased risk for infection, and pregnant women
Recommendation	Screen for HIV infection. Grade: A

Risk Assessment	Men who have sex with men and active injection drug users are at high risk for new HIV infection. Other persons at high risk include those who have acquired or request testing for other sexually transmitted infections. Behavioral risk factors for HIV infection include: Having unprotected vaginal or anal intercourse Having sexual partners who are HIV-infected, bisexual, or injection drug users Exchanging sex for drugs or money The USPSTF recognizes that the above categories are not mutually exclusive, the degree of sexual risk is on a continuum, and individuals may not be aware of their sexual partners' risk factors for HIV infection.
Screening Tests	The conventional serum test for diagnosing HIV infection is repeatedly reactive immunoassay, followed by confirmatory Western blot or immunofluorescent assay. Conventional HIV test results are available within 1 to 2 days from most commercial laboratories. Rapid HIV testing may use either blood or oral fluid specimens and can provide results in 5 to 40 minutes; however, initial positive results require confirmation with conventional methods. Other U.S. Food and Drug Administration–approved tests for detection and confirmation of HIV infection include combination tests (for p24 antigen and HIV antibodies) and qualitative HIV-1 RNA.
Interventions	At present, there is no cure for chronic HIV infection. However, appropriately timed interventions in HIV-positive persons can reduce risks for clinical progression, complications or death from the disease, and disease transmission. Effective interventions include antiretroviral therapy (ART) (specifically, the use of combined ART), immunizations, and prophylaxis for opportunistic infections.
Balance of Benefits and Harms	The net benefit of screening for HIV infection in adolescents, adults, and pregnant women is substantial.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on behavioral counseling to prevent sexually transmitted infections. This recommendation is available at www.uspreventiveservicestaskforce.org.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.uspreventiveservicestaskforce.org.

Benefits of Detection and Early Intervention

The USPSTF found convincing evidence that identification and treatment of HIV infection is associated with a markedly reduced risk for progression to AIDS, AIDS-related events, and death in individuals with immunologically advanced disease (defined as a CD4 count $<0.200 \times 10^9$ cells/L). Adequate evidence shows that initiating combined antiretroviral therapy (ART) earlier (that is, at CD4 counts between 0.200 and 0.500×10^9 cells/L)—when individuals are more likely to be asymptomatic and detected by screening rather than clinical presentation—is also associated with reduced risk for AIDS-related events or death. The USPSTF found convincing evidence that the use of ART is associated with a substantially decreased risk for transmission from HIV-positive persons to uninfected heterosexual partners. Convincing evidence also shows that identification and treatment of HIV-positive pregnant women dramatically reduces rates of mother-to-child transmission. The overall benefits of screening for HIV infection in adolescents, adults, and pregnant women are substantial.

Harms of Detection and Early Intervention

The USPSTF found convincing evidence that individual antiretroviral drugs, drug classes, and combinations are all associated with short-term adverse events; however, many of these events are transient or self-limited, and effective alternatives can often be found. Although the long-term use of certain antiretroviral drugs may be associated with increased risk for cardiovascular and other adverse events, the magnitude of risk seems to be small. The overall harms of screening for and treatment of HIV infection in adolescents, adults, and pregnant women are small.

USPSTF Assessment

The USPSTF concludes with high certainty that the net benefit of screening for HIV infection in adolescents, adults, and pregnant women is substantial.

Clinical Considerations

Patient Population Under Consideration

These recommendations apply to adolescents, adults, and pregnant women.

Screening for HIV infection could begin at age 15 years unless an individual is identified at an earlier age with risk factors for HIV infection. Screening after age 65 years is indicated if there is ongoing risk for HIV infection, as indicated by risk assessment (for example, new sexual partners).

Assessment of Risk

According to estimates from the Centers for Disease Control and Prevention (CDC), men who have sex with men account for about 60% of HIV-positive persons in the United States (1). Among men living with HIV infection who were diagnosed at age 13 years or older, 68% of infections are attributed to male-to-male sexual contact, 8% are attributed to male-to-male sexual contact and injection drug use, and 11% are attributed to heterosexual contact. Among women living with HIV infection, 74% of infections are attributed to heterosexual contact and the remainder to injection drug use (1, 2). According to the CDC, heterosexual contact accounted for an estimated 25% of new HIV infections in 2010 and 27% of existing infections in 2009 (3, 4). Data from the CDC on HIV prevalence in different subpopulations are available at www.cdc.gov/hiv/topics/surveillance.

On the basis of HIV prevalence data, the USPSTF considers men who have sex with men and active injection drug users to be at very high risk for new HIV infection. Behavioral risk factors for HIV infection include having unprotected vaginal or anal intercourse; having sexual partners who are HIV-infected, bisexual, or injection drug users; or exchanging sex for drugs or money. Other persons at high risk include those who have acquired or request testing for other sexually transmitted infections (STIs). Patients may request HIV testing in the absence of reported risk factors. Individuals not at increased risk for HIV infection include persons who are not sexually active, those who are sexually active in exclusive monogamous relationships with uninfected partners, and those who do not fall into any of the aforementioned categories. The USPSTF recognizes that these categories are not mutually exclusive, the degree of sexual risk is on a continuum, and individuals may not be aware of their sexual partners' risk factors for HIV infection. For patients younger than 15 years and older than 65 years, it would be reasonable for clinicians to consider HIV risk factors among individual patients, especially those with new sexual partners. However, clinicians should bear in mind that adolescent and adult patients may be reluctant to disclose having HIV risk factors, even when asked.

Screening Intervals

The evidence is insufficient to determine optimum time intervals for HIV screening. One reasonable approach would be 1-time screening of adolescent and adult patients to identify persons who are already HIV-positive, with repeated screening of those who are known to be at risk for HIV infection, those who are actively engaged in risky behaviors, and those who live or receive medical care in a high-prevalence setting. According to the CDC, a high-prevalence setting is a geographic location or community with an HIV seroprevalence of at least 1%. These settings include sexually transmitted disease (STD) clinics, correctional facilities, homeless shelters, tuberculosis clinics, clinics serving men who have sex with men, and adolescent health clinics with a high prevalence of STDs. Patient populations that would more likely benefit from more frequent testing include those who are known to be at higher risk for HIV infection, those who are actively engaged in risky behaviors, and those who live in a high-prevalence setting. Given the paucity of available evidence for specific screening intervals, a reasonable approach may be to rescreen groups at very high risk (see Assessment of Risk) for new HIV infection at least annually and individuals at increased risk at somewhat longer intervals (for example, 3 to 5 years). Routine rescreening may not be necessary for individuals who have not been at increased risk since they were found to be HIV-negative. Women screened during a previous pregnancy should be rescreened in subsequent pregnancies.

Screening Tests

The conventional serum test for diagnosing HIV infection is the repeatedly reactive immunoassay followed by confirmatory Western blot or immunofluorescent assay. The test is highly accurate (sensitivity and specificity, >99.5%), and results are available within 1 to 2 days from most commercial laboratories.

Rapid HIV testing may use either blood or oral fluid specimens and can provide results in 5 to 40 minutes. The sensitivity and specificity of the rapid test are also both greater than 99.5%; however, initial positive results require confirmation with conventional methods.

Other U.S. Food and Drug Administration–approved tests for detection and confirmation of HIV infection include combination tests (for p24 antigen and HIV antibodies) and qualitative HIV-1 RNA.

Treatment

No cure for chronic HIV infection currently exists. However, appropriately timed interventions in HIV-positive persons can reduce risks for clinical progression, complications or death from the disease, and disease transmission. Effective interventions include ART (specifically, the use of combined ART, defined as ≥3 antiretroviral

agents used together, usually from ≥2 classes), immunizations, and prophylaxis for opportunistic infections.

Other Approaches to Prevention

The USPSTF recognizes that the most effective strategy for reducing HIV-related morbidity and mortality in the United States is primary prevention or avoidance of exposure to HIV infection. Condom use can also substantially decrease the risk for transmission of HIV and other STIs.

The USPSTF recommends high-intensity behavioral counseling to prevent STIs for all sexually active adolescents and for adults at increased risk for infection. More information can be found at www.uspreventiveservicestaskforce.org/uspstf/uspsstds.htm.

The Community Preventive Services Task Force has made several recommendations related to the prevention of HIV, AIDS, and other STIs, including person-to-person behavioral interventions (information and skill building to change knowledge, attitudes, beliefs, and self-efficacy) for men who have sex with men that can be implemented at the individual, group, or community level. It also recommends health provider notification and encouragement for HIV testing for sexual or needle-sharing partners of individuals diagnosed with HIV, as well as comprehensive risk reduction interventions in adolescents. More information can be found at www.thecommunityguide.org/hiv/index.html.

Other Resources

More information about HIV and AIDS is available at www.aids.gov and www.cdc.gov/hiv/default.htm.

The CDC's recommendations on HIV testing in adults, adolescents, and pregnant women in health care settings are available at www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm.

More information on HIV testing is available at www.cdc.gov/hiv/topics/testing/index.htm and www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm117922.htm.

Antiretroviral treatment guidelines are regularly updated and available at http://aidsinfo.nih.gov/guidelines.

Information about state-based HIV and AIDS hotlines is available at http://hab.hrsa.gov/gethelp/statehotlines.html.

Other Considerations

Implementation

For populations in which the prevalence of undiagnosed HIV infection is known to be 0.1% or less (that is, ≤1 person in 1000 is HIV-positive), where the potential benefit per person screened is low, it is reasonable to forgo routine HIV screening and instead screen on the basis of risk assessment. The CDC suggests that for populations in which the prevalence of HIV infection has not been documented, clinicians should initiate voluntary routine screening. If no HIV-infected patients are found after screening of approximately 4000 patients, the upper limit of the 95% CI for prevalence is less than 0.1% (5) and routine screening may be discontinued and replaced with risk-based screening.

The USPSTF concurs with the CDC's recommendation that HIV screening should be voluntary and done only with the patient's knowledge and understanding. Patients should be informed orally or in writing that HIV testing will be performed unless they decline (opt-out screening). The USPSTF further concurs with the CDC's recommendation that before HIV testing, patients should receive an explanation of HIV infection and the meaning of positive and negative test results. Patients should also be offered the opportunity to ask questions and to decline testing. The CDC's recommendations on HIV testing in adults, adolescents, and pregnant women in health care settings are available at www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm.

Cost-Effectiveness Analysis

The USPSTF's deliberations on grade recommendations for the effectiveness of clinical preventive services do not include cost or cost-effectiveness considerations. For policy context, however, the USPSTF reviewed some cost-effectiveness analyses published since its previous review (6–9). These analyses, which include downstream costs, support the cost-effectiveness of HIV screening in settings with low or average HIV prevalence. No studies directly compared universal versus targeted screening in low-prevalence populations or explicitly considered the potential long-term cardiovascular harms of ART.

Research Needs and Gaps

Individuals who begin ART tend to continue receiving it for an extended length of time. Better evidence is needed about the long-term harms of ART, including risks for cardiovascular and kidney disease. Further follow-up is necessary to better delineate potential long-term harms of ART initiation at higher CD4 cell counts. It would also be helpful to better elucidate the potential risks and long-term outcomes associated with in utero or perinatal exposure to ART. Antiretroviral treatment guidelines are regularly updated and available at http://aidsinfo.nih.gov/guidelines.

Direct evidence of the effectiveness of ART and behavioral counseling in reducing HIV transmission among men who have sex with men and other high-risk groups could also guide prevention and treatment strategies. Similarly, additional studies are needed to better define the optimum timing for treatment initiation. More research is needed about the differential effects of various HIV screening strategies on testing acceptability and uptake, linkage to and receipt of care, and harms. Information that could quantify any incremental benefits and harms of repeated HIV screening and identify ideal time intervals for re-screening in different populations would be useful.

Discussion

Burden of Disease

Since the first cases of AIDS were reported in 1981, nearly 600 000 persons in the United States have died from the condition (10). Despite the decrease in AIDS cases and deaths after the introduction of ART, the CDC estimates that more than 1.1 million persons in the United States were living with HIV infection at the end of 2008, including 236 400 (20%) who did not know they were infected (10). Risk factors for HIV infection include having unprotected vaginal or anal intercourse with more than 1 partner; having sexual partners who are HIV-infected, bisexual, or injection drug users; exchanging sex for drugs or money; or engaging in injection drug use. According to the CDC, late diagnosis of HIV infection is common. Among persons with newly diagnosed HIV in 2008, 33% developed AIDS within 1 year of initial HIV diagnosis (1).

Scope of Review

In 2005, the USPSTF strongly recommended that clinicians screen for HIV in all adolescents and adults at increased risk for HIV infection, as well as all pregnant women (11). The USPSTF found good evidence that standard and rapid HIV screening tests are highly accurate and that most ART-associated adverse events, including metabolic disturbances associated with an increased risk for cardiovascular events, could be alleviated by changes in regimen or appropriate treatment. The USPSTF found good evidence that treatment of HIV-positive patients at immunologically advanced stages of disease (defined as a CD4 count $<0.200 \times 10^9$ cells/L) results in markedly decreased risk for AIDS-related clinical events and death.

At that time, the USPSTF made no recommendation for or against routine HIV screening in adolescents and adults not at increased risk for HIV infection. This was based largely on several considerations. First, the USPSTF determined that HIV screening in patients without known risk factors would yield less than targeted screening. It estimated that the benefits of HIV screening would be substantial in high-risk patients and settings but small for populations not at increased risk for infection. Second, the USPSTF found insufficient evidence that initiation of ART in patients with CD4 counts greater than 0.200×10^9 cells/L would result in improved clinical outcomes. Third, the USPSTF found insufficient evidence that knowledge of HIV-positive status would actually result in decreased HIV transmission, either through initiation of highly active ART or reductions in risky behaviors.

For this update, the USPSTF reviewed new evidence on the effectiveness of treatments in HIV-infected persons with CD4 counts greater than 0.200×10^9 cells/L; effects of screening, counseling, and ART use on risky behaviors and HIV transmission risk; and long-term cardiovascular harms of ART.

Accuracy of Screening Tests

The 2005 USPSTF review found that standard and rapid HIV tests are highly accurate, with greater than 99.5% sensitivity and specificity (11). However, studies indicate that in lower-prevalence settings, rapid testing is associated with a lower positive predictive value (that is, a decreased proportion of positive results that are "true" positives), although results are generally confirmed before treatment.

Effectiveness of Early Detection or Treatment

The 2005 USPSTF review found convincing evidence that initiation of ART in HIV-positive patients with CD4 counts less than 0.200×10^9 cells/L markedly reduces AIDS-related morbidity and mortality. At that time, however, the USPSTF found inadequate evidence to conclude that initiation of ART in patients with higher CD4 cell counts would result in improved clinical outcomes.

To date, no randomized trials or observational studies have evaluated clinical outcomes among patients who are screened versus those not screened for HIV infection, the yield of repeated versus 1-time HIV screening, or the yield of different screening strategies (for example, risk-based vs. routine repeated screening). However, new evidence shows treatment benefits for HIV-positive patients with CD4 counts between 0.200 and 0.500×10^9 cells/L, which dramatically increases the pool of patients that could benefit from early detection.

Several studies show that initiation of ART at CD4 counts between 0.200 and 0.500×10^9 cells/L is associated with reduced risk for AIDS-related events or death. At this stage of HIV infection, patients are likely to be asymptomatic and detected via screening rather than clinical presentation.

The updated USPSTF review found 2 good-quality randomized trials (12, 13), 1 retrospective subgroup analysis from 1 randomized trial (14), and 5 observational studies (15–20) that evaluated clinical outcomes after initiation of ART at different CD4 cell count thresholds.

The randomized, controlled trial with the largest population was the HPTN 052 (HIV Prevention Trials Network 052) study (13), which compared mortality and clinical outcomes among 886 HIV-positive patients who received "early" ART (when CD4 counts were between 0.350 and 0.550×10^9 cells/L) with 877 HIV-positive patients who received "delayed" ART (after a decrease in CD4 count to $\leq 0.200 \times 10^9$ cells/L or symptom onset). This study was conducted in 9 countries, with 54% of participants from Africa. It did not detect a significant difference in mortality between treatment groups. However, serious HIV-related clinical events, including death, were less likely among patients who received early treatment than among those who received delayed treatment (2.4 vs. 4.0 events/person-y; hazard ratio [HR], 0.59 [95% CI, 0.40 to 0.88]). According to the investigators, differences in the rates of serious HIV clinical events were driven

largely by intergroup differences in the incidence of extrapulmonary tuberculosis, most of which were observed in India.

Another randomized, open-label, controlled trial conducted in Haiti compared 408 HIV-positive patients who received "early" ART (when CD4 counts were between 0.201 and 0.350×10^9 cells/L) with 408 HIV-positive patients who received "standard" treatment (when CD4 counts were $\leq 0.200 \times 10^9$ cells/L) (12). Deaths occurred more frequently in the standard treatment group than in the early treatment group (6% vs. 2%; HR, 4.0 [CI, 1.6 to 9.8]; $P = 0.001$), as did incident cases of tuberculosis (9% vs. 4%; HR, 2.0 [CI, 1.2 to 3.6]; $P = 0.001$). Because the study was not blinded, there may have been differential reporting and detection of nonfatal outcomes, which could affect progression to mortality. In addition, the study was conducted in a resource-poor setting with high rates of tuberculosis, malnutrition, and co-infection with tropical diseases, which limits the generalizability of the findings to the U.S. primary care population and may partially account for the large effect size. Accordingly, clinical benefits observed in the United States might not be as dramatic as those seen in these 2 trials.

Data from a third large randomized trial conducted primarily in Europe and North America (the SMART [Strategies for Management of Antiretroviral Therapy] study) (14) were reexamined in a post hoc exploratory analysis. In a retrospective subgroup analysis of 477 patients, initiation of ART at CD4 counts less than 0.250×10^9 cells/L was associated with increased risk for death or opportunistic disease compared with initiation at CD4 counts greater than 0.350×10^9 cells/L (2.7% vs. 0.5%; HR, 3.5 [CI, 1.3 to 9.6]; $P = 0.02$) (14). Because this question was not part of the original study plan, the investigators acknowledged that their findings could be less reliable and warranted further confirmation.

Fair-quality observational studies consistently found that initiation of ART at CD4 counts between 0.350 and 0.500×10^9 cells/L was associated with decreased risk for death (or a trend toward decreased risk) compared with deferred or no ART. Studies on initiation of ART at CD4 counts greater than 0.500×10^9 cells/L yielded less consistent results, as did studies of the combined outcome of death and AIDS-defining events. Limitations of these studies include insufficient information about baseline differences in patients who initiated ART at different CD4 cell count thresholds, suboptimum reporting of attrition, unblinded assessment of outcomes and analysis of data, and possible residual confounding.

Recent studies have also shown that early initiation of ART can reduce risk for HIV transmission to uninfected sexual partners. The HPTN 052 study enrolled 1763 serodiscordant couples (that is, one partner was HIV-positive and the other was HIV-negative), most of which were heterosexual. Patients with HIV who had CD4 counts between 0.350 and 0.550×10^9 cells/L were randomly assigned to receive early (immediate) or delayed ART (after a decrease in CD4 count to $\leq 0.200 \times 10^9$ cells/L or symptom onset). At a median follow-up of 1.7 years, with most couples reporting 100% condom use, the incidence of seroconversion in HIV-negative partners was significantly lower among those whose HIV-positive partners had received early rather than delayed ART (0.3 vs. 2.2 events/100 person-y; HR, 0.11 [CI, 0.04 to 0.32]; $P < 0.001$). Seven observational studies of heterosexual transmission included in the USPSTF review were consistent with the results of this randomized trial. The potential effects of ART on HIV transmission have not been well-studied and could be attenuated in men who have sex with men or other high-risk populations, which account for most HIV-infected individuals in the United States.

Despite the potential effectiveness of ART as an HIV prevention strategy, it does not prevent the transmission of other STIs. Early diagnosis of HIV infection allows for risk reduction counseling and behavior change to reduce transmission of HIV and other STIs. In 2008, the USPSTF recommended high-intensity behavioral counseling to prevent STIs for all sexually active adolescents and for adults at increased risk for infection. The 2005 USPSTF review on screening for HIV included 2 systematic reviews that found consistent condom use to be associated with substantially reduced risk for sexual transmission of HIV infection; these findings have been confirmed in more recent observational studies. Self-reported condom use was associated with a 93% reduction in risk for heterosexual HIV transmission in a prospective cohort study ($n = 476$) (21). Inconsistent condom use was associated with an 8-fold increase in risk for seroconversion in another study of 1927 serodiscordant heterosexual couples (adjusted relative risk, 8.4 [CI, 4.8 to 15]) (22). In 1 modeling analysis, earlier initiation of ART combined with modifications in risky sexual behavior reduced new infections by up to 65% (9).

Observational studies included in the current USPSTF review found that knowledge of HIV-positive status was associated with reductions in several high-risk behaviors, including having unprotected intercourse, having sex in exchange for money or drugs, having sex with commercial sex workers, using intravenous drugs, and needle sharing among injection drug users. Reductions in high-risk behaviors occurred in all populations studied, including men who have sex with men, injection drug users, and heterosexual persons. Similarly, observational studies also reported no clear association between initiation of ART and high-risk sexual behaviors.

In its deliberations about the age at which to begin screening, the USPSTF considered the prevalence of sexual activity and STDs among different age groups. According to CDC Youth Risk Behavior Surveillance data from 2011, nearly half of U.S. high school students had engaged in sexual intercourse and one third were currently sexually active (23). Of students who had been sexually active, one third had engaged in sexual intercourse before age 16 years

(24). Although adolescents and young adults comprise one quarter of the sexually experienced population in the United States, they account for nearly one half of all cases of newly acquired STDs (25). As such, routine HIV screening starting at age 15 years would be reasonable. Because HIV prevalence markedly decreases after age 65 years, routine screening may not be necessary in older patients.

In its 2005 review, the USPSTF found convincing evidence that recommended regimens of ART resulted in significantly reduced rates of mother-to-child transmission. For its updated review, the USPSTF identified no new randomized trials of full-course combination ART during pregnancy in settings comparable to the United States. Three U.S. and European cohort studies published since 2005 found perinatal full-course triple ART to be associated with decreased risk for mother-to-child transmission (<1% to 2.4% among treated women vs. 9% to 22% among untreated women) (26–28).

Potential Harms of Screening and Treatment

The USPSTF's previous systematic review found that true-positive HIV test results may result in anxiety, depression, social stigma, changes in relationships with sexual partners, and discrimination (29). The USPSTF believes that patients who are diagnosed with HIV infection could benefit from counseling and ART. Because of the high specificity of conventional and rapid HIV testing strategies, false-positive test results are rare; reported rates of such results with conventional testing are 1 in 250 000 tests in low-prevalence populations (30). Evidence about potential consequences of receiving a false-positive HIV test result (for example, anxiety, psychological distress, or labeling) is limited and largely anecdotal (31). The actual consequences of initial false-positive rapid test results depend on whether patients are notified of these results before confirmatory testing. Most patients with initial positive results would not receive ART before confirmatory testing; one possible exception would be pregnant women in labor whose HIV status is unknown (described later). No studies directly evaluated psychological or other adverse effects associated with rapid versus conventional testing.

In the randomized trials comparing clinical outcomes among patients who received early versus standard ART, severe or life-threatening drug reactions did not occur more frequently in the early treatment group after exclusion of primary clinical end points (12, 13, 32). However, the early treatment group in the HPTN 052 study had ART-related adverse events more frequently (27% vs. 18%; $P < 0.001$), particularly grade 3 or 4 laboratory abnormalities, which the study investigators described as having unclear clinical significance (13).

Individual antiretroviral drugs, drug classes, and combinations are all associated with short-term adverse events; many of these events are transient or self-limited, and effective alternatives are often available. Longer-term use of ART regimens may increase the risk for cardiovascular and bone disease, as well as liver, renal, lipid, and glucose abnormalities (33). Aside from being potentially fatal, untreated HIV infection can contribute to these and other long-term complications (34).

A small increase in cardiovascular risk has been associated with specific protease inhibitors and nucleoside reverse transcriptase inhibitors in observational studies. The estimates of risk and the drugs implicated vary among studies. The 2005 USPSTF review included results from the large, ongoing DAD (Data Collection on Adverse Events of Anti-HIV Drugs) study, which found a 26% adjusted relative increase in the annual incidence of myocardial infarction during the first 4 to 6 years of exposure to ART (relative risk, 1.26 [CI, 1.12 to 1.41]; $P < 0.001$). In patients with more prolonged exposure to ART, the absolute risk for myocardial infarction was less than 0.6% and absolute event rates were low (3.5/1000 person-y) (35). Subsequent analyses from the DAD study (36–38) and other cohort studies (39, 40) also report cardiovascular harms associated with ART.

In 1 study of rapid HIV testing of pregnant women in labor in a low-prevalence setting, infection was confirmed in 90% of women with positive test results. Because confirmatory testing is not available in time to inform emergent treatment decisions, a small percentage of HIV-negative mothers and their infants will potentially be exposed to the adverse effects of ART or surgical delivery.

Since the prior USPSTF review, several cohort studies of perinatal exposure to ART have reported increased risk for late preterm delivery, with no clear association between maternal use of ART and low birth weight, congenital anomalies, or differences in neurodevelopmental outcomes. Other studies reported echocardiographic abnormalities, mitochondrial dysfunction, anemia, and neutropenia among infants exposed to ART. However, the clinical significance of these findings remains unclear. The 11 studies included in this review were considered fair or poor quality.

Estimate of Magnitude of Net Benefit

The USPSTF recognizes that the most effective overall strategy for reduction of HIV-related morbidity and mortality in the United States is primary prevention or avoidance of exposure to HIV infection. The USPSTF concludes with high certainty that early detection and treatment of HIV transmission would result in substantial public health benefits in the United States. According to CDC estimates, more than 1.1 million persons were living with HIV infection in the United States at the end of 2008, including 236 400 (20%) who did not know they were infected. Screening for HIV infection in all adolescents and adults aged 15 to 65 years, persons at increased risk for infection, and pregnant women would allow for earlier and expanded detection of HIV infection, thus cre-

ating opportunities for earlier linkages to medical and behavioral interventions.

In the USPSTF's view, earlier initiation of ART in HIV-positive persons with CD4 counts less than 0.500×10^9 cells/L could substantially reduce disease burden in the United States. At an ART initiation threshold of a CD4 count of 0.500×10^9 cells/L or less, approximately 60 persons would need to be treated to prevent 1 death from HIV infection after 3 years. The USPSTF found good evidence that this intervention in this population could improve clinical outcomes and reduce sexual transmission. The USPSTF found adequate evidence that the harms of early detection and treatment of HIV infection are small and the clinical benefits of ART substantially outweigh potential risks of treatment in HIV-positive patients with CD4 counts less than 0.500×10^9 cells/L. The USPSTF also found convincing evidence that screening for HIV in pregnant women would confer substantial clinical benefits, with adequate evidence that the potential harms would be small.

The expected magnitude of benefit of HIV screening to an overall population is dependent, in part, on the frequency with which the disease occurs in that population. More individuals may benefit from routine HIV screening in a setting where HIV infection is more prevalent because the pool of affected individuals in which interventions could have a positive effect is larger. At the same time, an accurate assessment of the prevalence of HIV infection in a given geographic location may not be readily available, and in some cases, it can be difficult to reliably determine which individuals are actually at increased risk for HIV infection. Studies have shown that screening for HIV on the basis of risk factor assessment alone may miss 20% to 25% of HIV-positive individuals who report no risk factors.

On the basis of these findings, the USPSTF concludes with high certainty that early detection and treatment of HIV infection would result in substantial net benefit in the United States.

How Does Evidence Fit With Biological Understanding?

Late diagnosis of HIV infection is common. In 2008, one third of persons newly diagnosed with HIV developed AIDS within 1 year of diagnosis; according to the CDC, these persons had probably been infected for an average of 10 years before diagnosis. Moreover, 1 of 5 persons living with HIV infection did not know that they were infected (10). The long preclinical phase from HIV infection to symptom onset allows for the opportunity to screen, identify, and treat persons with HIV infection in order to reduce HIV-related morbidity and transmission. Reduction in viral load with ART can result in improved clinical outcomes for HIV-infected individuals and reduce transmission to uninfected persons.

Response to Public Comments

A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 19 November 2012 through 20 December 2012. In response to public comment, the USPSTF's final recommendation statement now includes a brief summary of its contextual review of cost-effectiveness analyses, clarifications of the potential harms that were examined in its systematic review, and an opt-out provision. The recommendation statement also includes more information about HIV prevalence and incidence in different population subgroups, HIV screening tests, and potential long-term harms of ART.

Update of Previous USPSTF Recommendation

This updated recommendation reaffirms and expands the USPSTF's previous recommendations on HIV screening (11). In 2005, the USPSTF strongly recommended that clinicians screen for HIV in all adolescents and adults at increased risk for HIV infection, as well as all pregnant women. At that time, the USPSTF made no recommendation for or against routine HIV screening in adolescents and adults not at increased risk for HIV infection.

In addition to reaffirming its recommendation for HIV screening in persons at increased risk and pregnant women, the USPSTF expands its prior recommendation to include adolescents and adults aged 15 to 65 years who are not known to be at increased risk for HIV infection.

The USPSTF's expansion of its previous recommendation is based on studies published since 2005 that address previous evidence gaps. The USPSTF found that expanded HIV screening could identify a substantial number of persons with previously undiagnosed HIV infection, many of whom could benefit from initiation of ART, behavioral counseling, and other interventions. In particular, this recommendation includes new evidence that initiation of ART in HIV-infected persons with CD4 counts less than 0.500×10^9 cells/L could improve clinical outcomes and reduce sexual transmission.

Recommendations of Others

In 2006, the CDC recommended routine voluntary HIV screening in all adolescents and adults aged 13 to 64 years regardless of other recognized risk factors, unless the prevalence of undiagnosed HIV infection has been documented to be less than 0.1% (41). The CDC also recommended opt-out HIV testing, meaning that all patients should be informed about and undergo testing unless they specifically decline, without a requirement for prevention counseling before screening in order to reduce barriers to testing. In 2009, the American College of Physicians endorsed the CDC's approach (5). The Infectious Diseases Society of America recommends routine HIV screening for all sexually active adults (42). The American Congress of Obstetricians and Gynecologists recommends routine opt-

out screening in all women aged 19 to 64 years and targeted screening in women with risk factors outside of that age range (43). The American Academy of Pediatrics recommends offering routine HIV testing to all adolescents at least once by age 16 to 18 years when HIV prevalence is greater than 0.1% in the community, as well as testing of all sexually active adolescents and those with risk factors in low-prevalence settings (44). The American Academy of Family Physicians recommends that clinicians screen adolescents and adults aged 18 to 65 years for HIV infection, as well as younger adolescents and older adults who are at increased risk.

From the U.S. Preventive Services Task Force, Rockville, Maryland.

Disclaimer: Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

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Requests for Single Reprints: Reprints are available from the USPSTF Web site (www.uspreventiveservicestaskforce.org).

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Appendix: U.S. Preventive Services Task Force

Members of the U.S. Preventive Services Task Force at the time this recommendation was finalized† are Virginia A. Moyer, MD, MPH, *Chair* (Baylor College of Medicine, Houston, Texas); Michael L. LeFevre, MD, MSPH, *Co-Vice Chair* (University of Missouri School of Medicine, Columbia, Missouri); Albert L. Siu, MD, MSPH, *Co-Vice Chair* (Mount Sinai School of Medicine, New York, and James J. Peters Veterans Affairs Medical Center, Bronx, New York); Linda Ciofu Baumann, PhD, RN (University of Wisconsin, Madison, Wisconsin); Kirsten Bibbins-Domingo, PhD, MD (University of California, San Francisco, San Francisco, California); Susan J. Curry, PhD (University of Iowa College of Public Health, Iowa City, Iowa); Mark Ebell, MD, MS (University of Georgia, Athens, Georgia); Glenn Flores, MD (University of Texas Southwestern, Dallas, Texas); Francisco A.R. García, MD, MPH (Pima County Department of Health, Tucson, Arizona); Adelita Gonzales Cantu, RN, PhD (University of Texas Health Science Center, San Antonio, Texas); David C. Grossman, MD, MPH (Group Health Cooperative, Seattle, Washington); Jessica Herzstein, MD, MPH (Air Products, Allentown, Pennsylvania); Wanda K. Nicholson, MD, MPH, MBA (University of North Carolina School of Medicine, Chapel Hill, North Carolina); Douglas K. Owens, MD, MS (Veteran Affairs Palo Alto Health Care System, Palo Alto, and Stanford University, Stanford, California); William R. Phillips, MD, MPH (University of Washington, Seattle, Washington); Michael P. Pignone, MD, MPH (University of North Carolina, Chapel Hill, North Carolina); and Carolina Reyes, MD, MPH (Virginia Hospital Center, Arlington, Virginia). Former USPSTF members who contributed to the development of this recommendation include George Isham, MD, MS, and Timothy J. Wilt, MD, MPH.

† For a list of current Task Force members, go to www.uspreventiveservicestaskforce.org/members.htm.

Appendix Table 1. What the USPSTF Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer/provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Appendix Table 2. USPSTF Levels of Certainty Regarding Net Benefit

Level of Certainty*	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies; inconsistency of findings across individual studies; limited generalizability of findings to routine primary care practice; and lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: the limited number or size of studies; important flaws in study design or methods; inconsistency of findings across individual studies; gaps in the chain of evidence; findings that are not generalizable to routine primary care practice; and a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.

* The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general primary care population. The USPSTF assigns a certainty level on the basis of the nature of the overall evidence available to assess the net benefit of a preventive service.