JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for HIV Infection
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE Approximately 1.1 million persons in the United States are currently living with HIV, and more than 700 000 persons have died of AIDS since the first cases were reported in 1981. There were approximately 38 300 new diagnoses of HIV infection in 2017. The estimated prevalence of HIV infection among persons 13 years and older in the United States is 0.4%, and data from the Centers for Disease Control and Prevention show a significant increase in HIV diagnoses starting at age 15 years. An estimated 8700 women living with HIV give birth each year in the United States. HIV can be transmitted from mother to child during pregnancy, labor, delivery, and breastfeeding. The incidence of perinatal HIV infection in the United States peaked in 1992 and has declined significantly following the implementation of routine prenatal HIV screening and the use of effective therapies and precautions to prevent mother-to-child transmission.

OBJECTIVE To update the 2013 US Preventive Services Task Force (USPSTF) recommendation on screening for HIV infection in adolescents, adults, and pregnant women.

EVIDENCE REVIEW The USPSTF reviewed the evidence on the benefits and harms of screening for HIV infection in nonpregnant adolescents and adults, the yield of screening for HIV infection at different intervals, the effects of initiating antiretroviral therapy (ART) at a higher vs lower CD4 cell count, and the longer-term harms associated with currently recommended ART regimens. The USPSTF also reviewed the evidence on the benefits (specifically, reduced risk of mother-to-child transmission of HIV infection) and harms of screening for HIV infection in pregnant persons, the yield of repeat screening for HIV at different intervals during pregnancy, the effectiveness of currently recommended ART regimens for reducing mother-to-child transmission of HIV infection, and the harms of ART during pregnancy to the mother and infant.

FINDINGS The USPSTF found convincing evidence that currently recommended HIV tests are highly accurate in diagnosing HIV infection. The USPSTF found convincing evidence that identification and early treatment of HIV infection is of substantial benefit in reducing the risk of AIDS-related events or death. The USPSTF found convincing evidence that the use of ART is of substantial benefit in decreasing the risk of HIV transmission to uninfected sex partners. The USPSTF also found convincing evidence that identification and treatment of pregnant women living with HIV infection is of substantial benefit in reducing the rate of mother-to-child transmission. The USPSTF found adequate evidence that ART is associated with some harms, including neuropsychiatric, renal, and hepatic harms, and an increased risk of preterm birth in pregnant women. The USPSTF concludes with high certainty that the net benefit of screening for HIV infection in adolescents, adults, and pregnant women is substantial.

CONCLUSIONS AND RECOMMENDATION The USPSTF recommends screening for HIV infection in adolescents and adults aged 15 to 65 years. Younger adolescents and older adults who are at increased risk of infection should also be screened. (A recommendation) The USPSTF recommends screening for HIV infection in all pregnant persons, including those who present in labor or at delivery whose HIV status is unknown. (A recommendation)

JAMA. doi:10.1001/jama.2019.6587
Published online June 11, 2019.

Editorial
Author Audio Interview
Related articles and JAMA Patient Page
Related articles at jamainternalmedicine.com jamanetworkopen.com

Group Information: The US Preventive Services Task Force (USPSTF) members are listed at the end of this article.

Corresponding Author: Douglas K. Owens, MD, MS, Stanford University, 616 Serra St, Encina Hall, Room C336, Stanford, CA 94305-6019 (chair@uspstf.net).

The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms.

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 of infection should also be screened (A recommendation) (**Figure 1**).

The USPSTF recommends that clinicians screen for HIV infection in all pregnant persons, including those who present in labor or at delivery whose HIV status is unknown. (A recommendation)

See the Clinical Considerations section for more information about assessment of risk, screening intervals, and rescreening in pregnancy.

Rationale

Importance

Approximately 1.1 million persons in the United States are currently living with HIV,[1] and more than 700 000 persons have died of AIDS since the first cases were reported in 1981.[2] The estimated prevalence of HIV infection among persons 13 years and older in the United States is 0.4% (0.7% in males and 0.2% in females),[3] and data from the Centers for Disease Control and Prevention (CDC) 2017 HIV Surveillance Report show a significant increase in HIV diagnoses starting at age 15 years (compared with ages 13-14 years).[2] The annual number of new cases of HIV infection diagnosed in the United States has decreased slightly in recent years, from about 41 200 new cases in 2012 to 38 300 in 2017.[2] Approximately 15% of persons living with HIV are unaware of their infection.[1,3,4] It is estimated that persons unaware of their HIV status are responsible for 40% of transmission of HIV in the United States.[4]

An estimated 8700 women living with HIV give birth each year in the United States.[5] HIV can be transmitted from mother to child during pregnancy, labor, delivery, and breastfeeding. The incidence of perinatal HIV infection in the United States peaked in 1992[6] and has declined significantly following the implementation of routine prenatal HIV screening and the use of effective therapies and precautions to prevent mother-to-child transmission. Nearly 22 000 perinatal infections were prevented between 1994 and 2010 because of screening and preventive measures.[7]

Detection

The USPSTF found convincing evidence that currently recommended HIV tests are highly accurate in diagnosing HIV infection.

Benefits of Detection and Early Treatment

The USPSTF found convincing evidence that identification and early treatment of HIV infection is of substantial benefit in reducing the risk of AIDS-related events or death. The USPSTF found convincing evidence that the use of antiretroviral therapy (ART) is of substantial benefit in decreasing the risk of HIV transmission to uninfected sex partners. The USPSTF also found convincing evidence that identification and treatment of pregnant women living with HIV infection is of substantial benefit in reducing the rate of mother-to-child transmission. The overall magnitude of the benefit of screening for HIV infection in adolescents, adults, and pregnant women is substantial.

Harms of Detection and Early Treatment

The USPSTF found adequate evidence that individual antiretroviral drugs, ART drug classes, and ART combinations are associated with some harms, including neuropsychiatric, renal, and hepatic harms and an increased risk of preterm birth in pregnant women. The overall magnitude of the harms of screening for and treatment of screen-detected HIV infection in adolescents, adults, and pregnant women is 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

This recommendation applies to adolescents, adults, and all pregnant persons regardless of age (**Figure 2**). Based on the age-stratified incidence of HIV infection and data on sexual activity in youth, the USPSTF recommends screening for HIV infection beginning at age 15 years. Adolescents younger than 15 years and adults older than 65 years should be screened if they have risk factors for HIV infection.

Assessment of Risk

Although all adolescents and adults aged 15 to 65 years should be screened, there are a number of risk factors that increase risk. Among adolescents younger than 15 years and adults older than 65 years, clinicians should consider the risk factors of their patients, especially those with new sex partners, and offer testing to patients at increased risk.

Most (67%) new diagnoses of HIV infection are attributed to male-to-male sexual contact,[2] and the estimated prevalence of HIV infection among men who have sex with men is 12%.[3] Injection drug use is another important risk factor for HIV infection; the estimated prevalence of HIV infection among persons who inject drugs is 1.9%.[3] In 2017, male individuals 13 years and older accounted for 81% of new diagnoses of HIV infection.[2] Most (83%) of these new diagnoses of HIV infection were attributed to male-to-male sexual

Figure 1. USPSTF Grades and Levels of Evidence

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 or 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 or 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 or 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.

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. 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 not generalizable to routine primary care practice. lack of information on important health outcomes. More information may allow 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 based on the nature of the overall evidence available to assess the net benefit of a preventive service.	

USPSTF indicates US Preventive Services Task Force.

contact, while 9% were attributed to heterosexual contact, 4% to injection drug use, and 4% to both male-to-male sexual contact and injection drug use.[2] Among female individuals 13 years and older, 87% of all new diagnoses were attributed to heterosexual contact and 12% to injection drug use.[2]

Additional risk factors for HIV infection include having anal intercourse without a condom, having vaginal intercourse without a condom and with more than 1 partner whose HIV status is unknown, exchanging sex for drugs or money (transactional sex), having other sexually transmitted infections (STIs) or a sex partner with an STI, and having a sex partner who is living with HIV or is in a high-risk category. Persons who request testing for STIs, including HIV, are also considered at increased risk.

The USPSTF recognizes that these risk categories are not mutually exclusive, that the degree of risk exists on a continuum, and that persons may not be aware of the HIV or risk status of their sex partner or the person with whom they share injection drug equipment. Patients may also be reluctant to disclose risk factors to clinicians.

Screening Tests

Current CDC guidelines recommend testing for HIV infection with an antigen/antibody immunoassay approved by the US Food

Figure 2. Clinical Summary: Screening for HIV Infection

Population	Adolescents and adults aged 15 to 65 years	Pregnant persons
Recommendation	Screen for HIV infection. Grade: A	Screen for HIV infection. Grade: A

Risk Assessment	Although all adolescents and adults aged 15 to 65 years should be screened, there are a number of risk factors that increase risk. Among adolescents younger than 15 years and adults older than 65 years, clinicians should offer testing to patients at increased risk. Most new diagnoses of HIV infection are attributed to male-to-male sexual contact; injection drug use is another important risk factor. Additional risk factors include having anal intercourse without a condom, having vaginal intercourse without a condom and with more than 1 partner whose HIV status is unknown, exchanging sex for drugs or money (transactional sex), having other STIs or a sex partner with an STI, and having a sex partner who is living with HIV or is in a high-risk category. Persons who request testing for STIs, including HIV, are also considered to be at increased risk.
Screening Tests	Current CDC guidelines recommend testing for HIV infection with an antigen/antibody immunoassay approved by the US Food and Drug Administration that detects HIV-1 and HIV-2 antibodies and the HIV-1 p24 antigen, with supplemental testing following a reactive assay to differentiate between HIV-1 and HIV-2 antibodies. If supplemental testing for HIV-1/HIV-2 antibodies is nonreactive or indeterminate (or if acute HIV infection or recent exposure is suspected or reported), an HIV-1 nucleic acid test is recommended to differentiate acute HIV-1 infection from a false-positive test result.
Screening Intervals	The USPSTF found insufficient evidence to determine appropriate or optimal time intervals or strategies for repeat HIV screening. However, repeat screening is reasonable for persons known to be at increased risk of HIV infection, such as sexually active men who have sex with men; persons with a sex partner who is living with HIV; or persons who engage in behaviors that may convey an increased risk of HIV infection, such as injection drug use, transactional sex or commercial sex work, having 1 or more new sex partners whose HIV status is unknown, or having other factors that can place a person at increased risk of HIV infection (see "Risk Assessment"). Repeat screening is also reasonable for persons who live or receive medical care in a high-prevalence setting, such as a sexually transmitted disease clinic, tuberculosis clinic, correctional facility, or homeless shelter. The CDC and ACOG recommend repeat prenatal screening for HIV during the third trimester of pregnancy in women with risk factors for HIV acquisition and in women living or receiving care in high-incidence settings, and the CDC notes that repeat screening for HIV during the third trimester may be considered in all women.
Treatment and Interventions	No cure or vaccine for HIV infection currently exists. However, early initiation of ART and other interventions effectively reduce the risk of clinical progression to AIDS, AIDS-defining clinical events, and mortality. Also, studies to date have shown that when ART leads to viral suppression, no cases of virologically linked HIV transmission have been observed. Interventions other than ART include prophylaxis for opportunistic infections when clinically indicated, immunizations, and cancer screening. In addition, ART treatment in pregnant persons living with HIV and use of other precautions substantially decrease the risk of transmission to the fetus, newborn, or infant.

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

U.S. Preventive Services TASK FORCE

JAMA

ACOG indicates American College of Obstetricians and Gynecologists; ART, antiretroviral therapy; CDC, Centers for Disease Control and Prevention; STI, sexually transmitted infection; USPSTF, US Preventive Services Task Force.

and Drug Administration that detects HIV-1 and HIV-2 antibodies and the HIV-1 p24 antigen, with supplemental testing after a reactive assay to differentiate between HIV-1 and HIV-2 antibodies.[8,9] If supplemental testing for HIV-1/HIV-2 antibodies is nonreactive or indeterminate (or if acute HIV infection or recent exposure is suspected or reported), an HIV-1 nucleic acid test is recommended to differentiate acute HIV-1 infection from a false-positive test result.[8,9]

Antigen/antibody tests for HIV are highly accurate, with reported sensitivity ranging from 99.76% to 100% and specificity ranging from 99.50% to 100%, and results can be available in 2 days or less.[8] Rapid antigen/antibody tests are also available.[9]

When using a rapid HIV test for screening, positive results should be confirmed. Pregnant women presenting in labor with unknown HIV status should be screened with a rapid HIV test to get results as soon as possible.

Screening Intervals

The USPSTF found insufficient evidence to determine appropriate or optimal time intervals or strategies for repeat HIV screening. Repeat screening is reasonable for persons known to be at increased risk of HIV infection, such as sexually active men who have sex with men; persons with a sex partner who is living with HIV; or persons who engage in behaviors that may convey an increased risk of HIV infection, such as injection drug use, transactional sex or commercial sex work, having 1 or more new (ie, since a prior HIV test) sex partners whose HIV status is unknown, or having other factors that can place a person at increased risk

of HIV infection (see the Assessment of Risk section). Repeat screening is also reasonable for persons who live or receive medical care in a high-prevalence setting, such as a sexually transmitted disease clinic, tuberculosis clinic, correctional facility, or homeless shelter. The CDC recommends annual screening in persons at increased risk[10] but recognizes that clinicians may wish to screen high-risk men who have sex with men more frequently (eg, every 3 or 6 months) depending on the patient's risk factors, local HIV prevalence, and local policies.[11] Routine rescreening may not be necessary for persons who have not been at increased risk since they last tested negative for HIV.

The USPSTF found no evidence on the yield of repeat prenatal screening for HIV compared with 1-time screening during a single pregnancy. The CDC[10] and the American College of Obstetricians and Gynecologists (ACOG)[12] recommend repeat prenatal screening for HIV during the third trimester of pregnancy in women with risk factors for HIV acquisition and in women living or receiving care in high-incidence settings, and the CDC notes that repeat screening for HIV during the third trimester in all women who test negative early in pregnancy may be considered. Women screened during a previous pregnancy should be rescreened in subsequent pregnancies.

Treatment

No cure or vaccine for HIV infection currently exists. However, early initiation of ART and other interventions effectively reduce the risk of clinical progression to AIDS, AIDS-defining clinical events, and mortality. Also, studies to date have shown that when ART leads to viral suppression, no cases of virologically linked HIV transmission have been observed. Interventions other than ART include prophylaxis for opportunistic infections when clinically indicated, immunizations, and cancer screening. In addition, ART treatment in pregnant women living with HIV and use of other precautions substantially decrease the risk of transmission to the fetus, newborn, or infant.

The clinical treatment of HIV infection is a dynamic scientific field. The Panel on Antiretroviral Guidelines for Adults and Adolescents of the US Department of Health and Human Services regularly updates guidelines for HIV treatment regimens.[13]

Additional 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. Avoiding behaviors that may convey an increased risk of HIV infection and consistent use of condoms can decrease the risk of transmission of HIV and other STIs. The USPSTF recommends providing intensive behavioral counseling for all sexually active adolescents and for adults at increased risk of STIs.[14]

The Community Preventive Services Task Force has made several recommendations related to the prevention of HIV/AIDS and other STIs.[15]

Prophylactic intervention with antiretroviral medications, both preexposure and postexposure, can prevent HIV infection. Postexposure prophylaxis is used in persons who do not have HIV and may have been exposed to it via sexual contact, occupational or nonoccupational needle stick or other injury, or sharing injection drug equipment. When initiated soon after possible exposure, postexposure prophylaxis can prevent HIV infection. Preexposure prophylaxis is used in persons who do not have HIV and are at high risk of acquiring HIV infection. It consists of antiretroviral medication taken every day, before potential exposure. The USPSTF recommends offering preexposure prophylaxis to persons at high risk of HIV acquisition.[16]

Useful Resources

More information about HIV and AIDS is available at HIV.gov[17] and from the CDC.[18] The CDC has made recommendations on screening for HIV in adolescents, adults, and pregnant women in health care settings[10] and the prevention of HIV transmission in adolescents and adults living with HIV[19]; guidelines on the use of ART and the potential adverse effects of ART are regularly updated at https://www.aidsinfo.nih.gov.[13]

Other Considerations

Implementation

As recommended by the CDC, HIV screening should be voluntary and performed only with the patient's knowledge and understanding.[10] Patients should be informed orally or in writing that HIV testing will be performed unless they decline (known as "opt-out screening"). 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 substantial benefit of screening is realized only if detection of HIV is followed by initiation of appropriate ART and provision of other services for persons found to have HIV. Thus, entry into care for persons identified as having HIV is essential. The CDC provides guidance on counseling, referral to care, treatment, and prevention of HIV transmission.[19,20] Clinicians should be aware that some persons with HIV may face substantial barriers to receiving appropriate services.

Research Needs and Gaps

Research is needed on the yield of repeat vs 1-time screening for HIV and different repeat screening intervals to inform recommendations on optimal screening intervals. Data on optimal rescreening strategies in pregnant women are needed.

Persons who initiate ART tend to continue receiving it for an extended length of time. Thus, continued research on the potential harms of long-term use of ART is an important research need. Further research is also needed to understand the effects of in utero exposure to ART on pregnancy outcomes and long-term effects in exposed children, to optimize the selection of ART regimens during pregnancy.

Discussion

Burden of Disease

Since the first cases of AIDS were reported in 1981, more than 700 000 persons in the United States have died of AIDS.[2] The CDC estimates that 1.1 million persons in the United States are currently living with HIV infection, including an estimated 15% who

are unaware of their infection.[1,3,4] The annual number of new HIV diagnoses in the United States has decreased slightly in recent years, from about 41 200 new diagnoses in 2012 to 38 300 in 2017.[2] Of new diagnoses of HIV infection in 2017, 81% were among males and 19% were among females.[2] Groups disproportionately affected by HIV infection in the United States include men who have sex with men, black/African American populations, and Hispanic/Latino populations. For example, the estimated overall prevalence of HIV infection in the United States is 0.4%, while the estimated prevalence among men who have sex with men is 12%.[3] From 2012 to 2017, HIV diagnosis rates increased in adults aged 25 to 29 years, as well as in the American Indian/Alaska Native population.[2]

Perinatal HIV transmission has decreased substantially since its peak in 1992.[6] There were 99 diagnoses of perinatally acquired HIV infection in 2016,[2] and approximately 8700 women living with HIV give birth each year.[5] There are racial/ethnic disparities in rates of perinatally acquired HIV infection; rates are 5 times greater in black/African American women than in white or Hispanic/Latino women.[21] Of the 99 diagnoses of perinatally acquired HIV infection reported in 2016, 65% occurred in black/African American mothers.[21]

Scope of Review

To update its 2013 recommendation, the USPSTF commissioned a systematic evidence review[22,23] on the benefits and harms of screening for HIV infection in nonpregnant adolescents and adults, the yield of screening for HIV infection at different intervals, the effects of initiating ART at a higher (ie, >500 cells/mL^3) vs lower CD4 (a type of white blood cell in the immune system) count, and the longer-term harms associated with currently recommended ART regimens. The USPSTF also commissioned a systematic evidence review[24,25] on the benefits (specifically, reduced risk of mother-to-child transmission of HIV infection) and harms of screening for HIV infection in pregnant persons, the yield of repeat screening for HIV at different intervals during pregnancy, the effectiveness of currently recommended ART regimens for reducing mother-to-child transmission of HIV infection, and the harms of ART during pregnancy to the mother and infant.

Accuracy of Screening Tests

Currently recommended antigen/antibody tests for HIV are highly accurate, with reported sensitivity ranging from 99.76% to 100% and specificity ranging from 99.50% to 100%.[8] Recommended rapid HIV tests have similar sensitivity and somewhat lower reported specificity ranging from 98.6% to 100%.[26]

Effectiveness of Early Detection and Treatment

The USPSTF found no randomized clinical trials (RCTs) or observational studies that compared clinical outcomes between adolescents and adults screened and not screened for HIV infection. The USPSTF found no studies that evaluated the yield of repeated screening for HIV compared with 1-time screening or that compared the yield of different strategies for repeat screening (eg, risk-based screening vs routine repeat testing or repeat screening at different intervals) in adolescents and adults. The USPSTF also found no studies comparing the yield of 1-time vs repeat screening or of different frequencies of screening for HIV infection in pregnancy.

The USPSTF reviewed 3 RCTs—the HIV Prevention Trials Network (HPTN 052) trial (n = 1763),[27,28] the International Network for Strategic Initiatives in Global HIV Trials Strategic Timing of Antiretroviral Treatment (INSIGHT START or START) trial (n = 4685),[29] and the Early Antiretroviral Treatment and/or Early Isoniazid Prophylaxis Against Tuberculosis in HIV-Infected Adults (TEMPRANO ANRS) trial (n = 2056)[30]—and 3 large fair-quality cohort studies, ranging in sample size from 3532 to 55 826 (total n = 63 478),[31-33] that provided evidence on the benefits of early initiation of ART.

The HPTN 052 trial randomly assigned participants to initiation of ART at CD4 cell counts of 350/mL^3 to 550/mL^3 or delayed initiation at CD4 cell counts of 250/mL^3 or less.[27] At a mean follow-up of 2.1 years, initiation of ART at higher CD4 counts was associated with decreased risk of AIDS-related events (4.5% vs 7.0%; relative risk [RR], 0.65 [95% CI, 0.44-0.95]). Effects on other outcomes (including all-cause mortality; AIDS-related mortality; and a composite outcome including death, serious AIDS-related events, and serious non–AIDS-related events, such as bacterial infection or cancer) favored early initiation of ART but were not statistically significant.[28] The START trial found decreased risk of a composite end point of all-cause mortality, serious AIDS-related events, and serious non–AIDS-related events,[29] and the TEMPRANO ANRS trial found decreased risk of a composite end point of all-cause mortality, progression to AIDS, AIDS-defining cancer, and non–AIDS-defining invasive bacterial disease[30] in participants treated with immediate ART at CD4 cell counts greater than 500/mL^3, compared with delayed treatment at lower CD4 counts.

The 3 cohort studies[31-33] also provide evidence of benefit to early initiation of ART. Seven-year follow-up from the HIV Cohorts Analyzed Using Structural Approaches to Longitudinal (HIV CAUSAL) Collaboration showed that ART initiation at CD4 cell counts greater than 500/mL^3 was associated with decreased risk of all-cause mortality and a composite end point of progression to AIDS or death compared with initiation at CD4 cell counts less than 350/mL^3.[31] A second cohort study from Canada found that initiation of ART at CD4 cell counts greater than 500/mL^3 was associated with lower probability of mortality and AIDS-related morbidity than initiation at CD4 cell counts less than 500/mL^3 or less than 350/mL^3.[32] Last, a US-based cohort study found that compared with initiation of ART within 6 months of CD4 cell counts decreasing to less than 500/mL^3, there were greater risks of 10-year all-cause mortality associated with ART initiation within 6 months of CD4 cell counts decreasing to less than 350/mL^3 (RR, 1.08 [95% CI, 1.00-1.16]) or 200/mL^3 (RR, 1.25 [95% CI, 1.08-1.44]).[33]

Early initiation of ART and viral suppression has also been shown to decrease risk of HIV transmission.[27] Longer-term follow-up from the HPTN 052 trial showed that early ART initiation is associated with a reduction in risk of HIV transmission to uninfected partners (RR for virologically linked transmission, 0.07 [95% CI, 0.02-0.22]),[34] and 3 observational studies (Partners of People on ART—A New Evaluation of the Risks [PARTNER],[35] PARTNER2,[36] and Opposites Attract[37]) found no cases of HIV transmission among serodiscordant couples when the partner living with HIV was treated with ART and had viral suppression, during 1238, 1593, and 232.2 couple-years of follow-up, respectively.

In its discussions about the age range for routine screening, the USPSTF considered the evidence on the age-stratified incidence of HIV infection and data on the prevalence of sexual activity in youth. Data from the CDC 2017 HIV Surveillance Report show a significant increase in HIV diagnoses in the United States starting at age 15 years (compared with ages 13-14 years).[2] In addition, 52% of youth in grades 9 through 12 reported engaging in sexual contact in the most recent Youth Risk Behavior Surveillance survey,[38] and in earlier survey data, approximately one-third of youth reported engaging in sexual intercourse before age 16 years.[39] CDC surveillance data also show a significant decrease in HIV diagnoses among adults 65 years and older.[2]

The USPSTF found no studies that compared rates of mother-to-child transmission of HIV infection between pregnant women screened and not screened for HIV infection. The USPSTF found several cohort studies and RCTs that provided evidence on the effectiveness of ART in decreasing rates of mother-to child transmission of HIV infection in pregnant women living with HIV.[24,25] The cohort studies, all conducted in North America, Europe, or Israel, reported rates of mother-to-child transmission of less than 1.0% to 2.8% among women treated with 3 antiretroviral drugs, compared with 9.1% to as much as 67% in 1 small cohort study among untreated women.[24,25] The RCTs were conducted in Africa or India (ie, settings with a lower United Nations Human Development Index than the United States) and compared the effects of a heterogeneous group of prenatal, peripartum, and postpartum ART interventions of varying durations on rates of mother-to-child transmission of HIV infection. Across all studies (both the cohort studies and RCTs), later initiation of ART during pregnancy or treatment with fewer than 3 antiretroviral drugs was associated with greater risk of mother-to-child transmission of HIV infection.[24,25]

Potential Harms of Screening and Treatment

Longer-term use of individual antiretroviral drugs and different ART regimens may be associated with several harms. The USPSTF reviewed several studies that reported on the long-term cardiovascular, neuropsychiatric, hepatic, renal, or bone (fracture) harms associated with the use of various antiretroviral drugs and ART regimens.[22,23]

Two good-quality RCTs (duration, 2.8-5 years) found no differences in risk of serious cardiovascular or cerebrovascular events between different ART regimens.[40,41] Findings on the cardiovascular harms of the drug abacavir are mixed. A meta-analysis of 26 trials found no association between abacavir use and risk of myocardial infarction,[42] but 2 cohort studies found that abacavir was associated with increased risk (RR, 1.98 [95% CI, 1.72-2.29] and odds ratio, 1.50 [95% CI, 1.26-1.79]).[43,44]

The drug efavirenz has been linked to neuropsychiatric adverse events, including depression and suicidal ideation.[45] A systematic review (n = 8466; mean duration, 78 weeks) reported rates of neuropsychiatric adverse events among participants taking efavirenz; 29.6% (95% CI, 21.9%-37.3%) experienced events of any grade, 6.1% (95% CI, 4.3%-7.9%) experienced severe neuropsychiatric adverse events, 3.3% (95% CI, 2.2%-4.3%) had depression, and 0.6% (95% CI, 0.2%-1.1%) had suicidal ideation.[46] However, an analysis of the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study, a large (n >49 000) international study of 11 prospective cohorts from Europe, Australia, and the United States, found no association between use of efavirenz and death from suicide,[47] and an analysis of a large (n = 19 983) US administrative cohort found no association between initiation of efavirenz and increased risk of suicidal ideation.[48]

An analysis of the D:A:D cohorts found that tenofovir disoproxil fumarate (relative rate, 1.46 [95% CI, 1.11-1.93]) and fosamprenavir (relative rate, 1.47 [95% CI, 1.01-2.15]) were associated with increased risk of end-stage liver disease or hepatocellular carcinoma, independent of viral hepatitis status, and that emtricitabine was associated with decreased risk of these outcomes (relative rate, 0.51 [95% CI, 0.32-0.83]).[49] However, the absolute risk of ART-related liver deaths in the D:A:D cohorts was low (0.04 deaths per 1000 person-years).[50] Another D:A:D analysis found an association between use of tenofovir disoproxil fumarate (rate ratio, 1.14 cases per year of exposure [95% CI, 1.10-1.19]) or ritonavir-boosted atazanavir (rate ratio, 1.20 cases per year of exposure [95% CI, 1.13 to 1.26]) and increased risk of chronic kidney disease.[51] A second observational study also found that tenofovir disoproxil fumarate was associated with an increased risk of renal adverse events,[52] and a third observational study found that tenofovir disoproxil fumarate was associated with kidney dysfunction, which was relatively mild and tended to be stable over several years.[53]

A cohort study found that ever use of tenofovir disoproxil fumarate was associated with increased risk of fracture compared with nonuse (adjusted incidence rate ratio, 1.40 [95% CI, 1.05-1.70]) after follow-up of more than 86 000 person-years. However, there was no difference in risk of fracture based on cumulative duration of use (adjusted incidence rate ratio per 5 years of exposure, 1.08 [95% CI, 0.94-1.25]).[54]

The USPSTF reviewed several studies that assessed the harms of ART during pregnancy.[24,25] One fair-quality RCT and 7 cohort studies found that antenatal ART was associated with increased risk of preterm birth (before 37 weeks of gestation) compared with no treatment or zidovudine monotherapy.[55-62] No clear associations were found between ART and overall birth defects, low birth weight, small size for gestational age, stillbirth, or neonatal death.[24,25] There were mixed findings on cardiovascular congenital anomalies.[24,25] Two studies of HIV-exposed, uninfected infants and children found that in utero exposure to ART was not associated with lower scores on Wechsler intelligence and achievement tests in children aged 7 to 13 years[63] and may be associated with less neurodevelopmental impairment[64] compared with no in utero exposure to ART.

Evidence on maternal harms associated with ART during pregnancy is limited. Three older studies suggest that ART (especially with a protease inhibitor) may be associated with an increased risk of gestational diabetes.[65-67] One RCT found no difference in risk of anemia between combination ART (zidovudine, lamivudine, and ritonavir-boosted lopinavir) starting at 28 to 36 weeks of gestation vs zidovudine monotherapy starting at 34 to 36 weeks of gestation until onset of labor, followed by zidovudine and a single dose of nevirapine at the onset of labor.[68] Another RCT found that treatment with zidovudine-based ART resulted in increased risk of maternal adverse events vs zidovudine monotherapy (21% vs 17%; $P = .008$) and increased risk of abnormalities in blood chemistry values (5.8% vs 1.3%; $P < .001$), primarily elevated alanine aminotransferase levels.[55]

Estimate of Magnitude of Net Benefit

The USPSTF concludes with high certainty that early detection and treatment of HIV infection would result in substantial benefits. Screening for HIV infection in all adolescents and adults aged 15 to 65 years, persons at increased risk of infection, and pregnant persons would allow for earlier and expanded detection of HIV infection, thus resulting in earlier medical and behavioral interventions and treatment.

The USPSTF found convincing evidence that early initiation of ART for HIV infection, regardless of CD4 cell count, improves clinical outcomes and reduces the risk of 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 the potential risks of treatment in persons living with HIV. The USPSTF also found convincing evidence that screening for HIV infection in pregnant women confers substantial clinical benefits for both the mother and infant, with adequate evidence that the potential harms are small.

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

How Does Evidence Fit With Biological Understanding?

Diagnosis and initiation of treatment of HIV infection at the earliest stage possible is associated with improved health outcomes. Screening with highly accurate tests allows for diagnosis in the relatively long preclinical phase of HIV infection. Early treatment with ART has been shown to effectively suppress viral load and decrease the risk of AIDS-related events, serious non–AIDS-related events, and death in persons living with HIV infection. Effective treatment also decreases risk of sexual transmission of HIV by suppressing viral load in infected persons. Diagnosis and effective treatment in pregnant persons living with HIV decreases the risk of mother-to-child transmission by suppressing viral load and allowing for implementation of other prevention strategies (ie, appropriate antiretroviral treatment of the newborn and counseling about avoidance of breastfeeding).

Response to Public Comment

A draft version of this recommendation was posted for public comment on the USPSTF website from November 20 through December 26, 2018. In response to public comment, the USPSTF added information and clarified language regarding assessment of risk, high-prevalence HIV settings, and persons who may be at increased risk and warrant rescreening, as well as the importance of linkage to care after an HIV diagnosis. The USPSTF also clarified that persons not at increased risk may not need rescreening. The USPSTF clarified language describing the epidemiology of HIV and provided additional details on the HPTN 052 study. The USPSTF also added information about the data it considered in its discussions about the age at which to start and end routine screening.

Update of Previous USPSTF Recommendation

In 2013, the USPSTF recommended screening for HIV infection in adolescents and adults aged 15 to 65 years, screening in younger adolescents and older adults at increased risk, and screening in all pregnant women.[69] The current updated recommendation continues to strongly recommend screening for HIV infection in adolescents and adults aged 15 to 65 years, younger adolescents and older adults at increased risk, and all pregnant persons.

Recommendations of Others

In 2006, the CDC recommended routine voluntary screening for HIV infection in all adolescents and adults aged 13 to 64 years, regardless of other recognized risk factors, unless HIV prevalence was documented to be less than 0.1% within a patient community.[10] The CDC recommends that all persons should be screened at least once in their lifetime and those with risk factors be screened more frequently (eg, annually); the CDC also recently recommended that clinicians consider testing sexually active men who have sex with men more frequently (eg, every 3 to 6 months) based on risk behaviors, community HIV prevalence, and other considerations.[11]

In 2009, the American College of Physicians recommended routine screening for HIV infection.[70] The Infectious Diseases Society of America recommends routine screening for HIV infection in all sexually active adults and pregnant women.[71] In 2017, ACOG reaffirmed a previous recommendation that all females aged 13 to 64 years be tested at least once in their lifetime and annually thereafter if they are assessed to have risk factors for HIV infection.[72] The American Academy of Pediatrics recommends universal screening for HIV infection once between the ages of 15 and 18 years, and annual reassessment and testing of persons at increased risk.[73] The American Academy of Family Physicians supports the 2013 USPSTF recommendations, except it recommends that routine screening begin at age 18 years and that only adolescents at increased risk be tested at younger ages.[74]

The CDC,[10] ACOG,[12] American Academy of Pediatrics,[75,76] American College of Physicians,[70] and American Academy of Family Physicians[74] recommend routine screening for HIV infection in all pregnant women using an opt-out approach, and rapid screening for women who present in labor whose HIV status is unknown. The CDC[10] and ACOG[12] recommend repeat testing during the third trimester in women with risk factors and in women living or receiving care in high-incidence settings who had a negative test result earlier in pregnancy; the CDC[10] notes that repeat testing in the third trimester may be considered for all women with a negative test result early in pregnancy.

ARTICLE INFORMATION

Published Online: June 11, 2019. doi:10.1001/jama.2019.6587

The US Preventive Services Task Force (USPSTF) members: Douglas K. Owens, MD, MS; Karina W. Davidson, PhD, MASc; Alex H. Krist, MD, MPH; Michael J. Barry, MD; Michael Cabana, MD, MA, MPH; Aaron B. Caughey, MD, PhD; Susan J. Curry, PhD; Chyke A. Doubeni, MD, MPH; John W. Epling Jr, MD, MSEd; Martha Kubik, PhD, RN; C. Seth Landefeld, MD; Carol M. Mangione, MD, MSPH; Lori Pbert, PhD; Michael Silverstein, MD, MPH; Melissa A. Simon, MD, MPH; Chien-Wen Tseng, MD, MPH, MSEE; John B. Wong, MD.

Affiliations of The US Preventive Services Task Force (USPSTF) members: Veterans Affairs Palo Alto Health Care System, Palo Alto, California (Owens); Stanford University, Stanford, California (Owens); Feinstein Institute for Medical Research at Northwell Health, Manhasset, New York (Davidson); Fairfax Family Practice Residency, Fairfax, Virginia (Krist); Virginia Commonwealth

University, Richmond (Krist); Harvard Medical School, Boston, Massachusetts (Barry); University of California, San Francisco (Cabana); Oregon Health & Science University, Portland (Caughey); University of Iowa, Iowa City (Curry); University of Pennsylvania, Philadelphia (Doubeni); Virginia Tech Carilion School of Medicine, Roanoke (Epling); Temple University, Philadelphia, Pennsylvania (Kubik); University of Alabama at Birmingham (Landefeld); University of California, Los Angeles (Mangione); University of Massachusetts Medical School, Worcester (Pbert); Boston University, Boston, Massachusetts (Silverstein); Northwestern University, Evanston, Illinois (Simon); University of Hawaii, Honolulu (Tseng); Pacific Health Research and Education Institute, Honolulu, Hawaii (Tseng); Tufts University, Medford, Massachusetts (Wong).

Author Contributions: Dr Owens had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The USPSTF members contributed equally to the recommendation statement.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Authors followed the policy regarding conflicts of interest described at https://www.uspreventiveservicestaskforce.org/Page/Name/conflict-of-interest-disclosures. All members of the USPSTF receive travel reimbursement and an honorarium for participating in USPSTF meetings.

Funding/Support: The USPSTF is an independent, voluntary body. The US Congress mandates that the Agency for Healthcare Research and Quality (AHRQ) support the operations of the USPSTF.

Role of the Funder/Sponsor: AHRQ staff assisted in the following: development and review of the research plan, commission of the systematic evidence review from an Evidence-based Practice Center, coordination of expert review and public comment of the draft evidence report and draft recommendation statement, and the writing and preparation of the final recommendation statement and its submission for publication. AHRQ staff had no role in the approval of the final recommendation statement or the decision to submit for publication.

Disclaimer: Recommendations made by the USPSTF are independent of the US government. They should not be construed as an official position of AHRQ or the US Department of Health and Human Services.

Additional Contributions: We thank Howard Tracer, MD (AHRQ), who contributed to the writing of the manuscript, and Lisa Nicolella, MA (AHRQ), who assisted with coordination and editing.

REFERENCES

1. Centers for Disease Control and Prevention (CDC). Estimated HIV Incidence and Prevalence in the United States, 2010–2016. CDC website. https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-supplemental-report-vol-24-1.pdf. Published February 2019. Accessed April 9, 2019.

2. Centers for Disease Control and Prevention (CDC). Diagnoses of HIV Infection in the United States and Dependent Areas, 2017. CDC website. https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2017-vol-29.pdf. Published November 2018. Accessed April 5, 2019.

3. Singh S, Song R, Johnson AS, McCray E, Hall HI. HIV incidence, prevalence, and undiagnosed infections in U.S. men who have sex with men. *Ann Intern Med*. 2018;168(10):685-694. doi:10.7326/M17-2082

4. Dailey AF, Hoots BE, Hall HI, et al. Vital signs: human immunodeficiency virus testing and diagnosis delays—United States. *MMWR Morb Mortal Wkly Rep*. 2017;66(47):1300-1306. doi:10.15585/mmwr.mm6647e1

5. Panel on Treatment of Pregnant Women With HIV Infection and Prevention of Perinatal Transmission, US Department of Health and Human Services. Recommendations for the Use of Antiretroviral Drugs in Pregnant Women With HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States. AIDSinfo website. https://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed April 5, 2019.

6. Nesheim SR, Wiener J, Fitz Harris LF, Lampe MA, Weidle PJ. Brief report: estimated incidence of perinatally acquired HIV infection in the United States, 1978-2013. *J Acquir Immune Defic Syndr*. 2017;76(5):461-464. doi:10.1097/QAI.0000000000001552

7. Little KM, Taylor AW, Borkowf CB, et al. Perinatal antiretroviral exposure and prevented mother-to-child HIV infections in the era of antiretroviral prophylaxis in the United States, 1994-2010. *Pediatr Infect Dis J*. 2017;36(1):66-71. doi:10.1097/INF.0000000000001355

8. Centers for Disease Control and Prevention (CDC). Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. CDC website. https://stacks.cdc.gov/view/cdc/23447. Published June 2014. Accessed April 5, 2019.

9. Centers for Disease Control and Prevention (CDC). 2018 Quick Reference Guide: Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens. CDC website. https://stacks.cdc.gov/view/cdc/50872. Updated January 2018. Accessed April 5, 2019.

10. Branson BM, Handsfield HH, Lampe MA, et al; Centers for Disease Control and Prevention (CDC). Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep*. 2006;55(RR-14):1-17.

11. DiNenno EA, Prejean J, Irwin K, et al. Recommendations for HIV screening of gay, bisexual, and other men who have sex with men—United States, 2017. *MMWR Morb Mortal Wkly Rep*. 2017;66(31):830-832. doi:10.15585/mmwr.mm6631a3

12. Committee on Obstetric Practice; HIV Expert Work Group. ACOG Committee Opinion No. 752: prenatal and perinatal human immunodeficiency virus testing. *Obstet Gynecol*. 2018;132(3):e138-e142. doi:10.1097/AOG.0000000000002825

13. US Department of Health and Human Services. Clinical guidelines. AIDSinfo website. https://aidsinfo.nih.gov/guidelines/. Updated 2019. Accessed April 5, 2019.

14. LeFevre ML; U.S. Preventive Services Task Force. Behavioral counseling interventions to prevent sexually transmitted infections: U.S. PreventiveServices Task Force recommendation statement. *Ann Intern Med*. 2014;161(12):894-901. doi:10.7326/M14-1965

15. HIV/AIDS, STIs and pregnancy. The Community Guide website. https://www.thecommunityguide.org/topic/hivaids-stis-and-pregnancy. Accessed April 5, 2019.

16. US Preventive Services Task Force. Preexposure prophylaxis for the prevention of HIV infection: US Preventive Services Task Force recommendation statement [published June 11, 2019]. *JAMA*. doi:10.1001/jama.2019.6390

17. HIV.gov website. https://www.hiv.gov/. Accessed April 5, 2019.

18. Centers for Disease Control and Prevention (CDC). HIV/AIDS. CDC website. https://www.cdc.gov/hiv/. Updated 2019. Accessed April 5, 2019.

19. Centers for Disease Control and Prevention (CDC). Recommendations for HIV Prevention With Adults and Adolescents With HIV in the United States, 2014: Summary for Clinical Providers. CDC website. https://stacks.cdc.gov/view/cdc/44065. Updated December 2016. Accessed April 5, 2019.

20. Centers for Disease Control and Prevention (CDC). 2015 Sexually Transmitted Diseases Treatment Guidelines: HIV infection: detection, counseling, and referral. CDC website. https://www.cdc.gov/std/tg2015/hiv.htm. June 2015. Accessed April 5, 2019.

21. Centers for Disease Control and Prevention (CDC). HIV and pregnant women, infants, and children. CDC website. https://www.cdc.gov/hiv/group/gender/pregnantwomen/index.html. Updated March 29, 2019. Accessed April 5, 2019.

22. Chou R, Dana T, Grusing S, Bougatsos C. *Screening for HIV Infection in Asymptomatic, Nonpregnant Adolescents and Adults: A Systematic Review for the US Preventive Services Task Force: Evidence Synthesis No. 176*. Rockville, MD: Agency for Healthcare Research and Quality; 2019. AHRQ publication 18-05246-EF-1.

23. Chou R, Dana T, Grusing S, Bougatsos C. Screening for HIV infection in asymptomatic, nonpregnant adolescents and adults: updated evidence report and systematic review for the US Preventive Services Task Force [published online June 11, 2019]. *JAMA*. doi:10.1001/jama.2019.2592

24. Selph S, Bougatsos C, Dana T, Grusing S, Chou R. *Screening for HIV Infection in Pregnant Women: A Systematic Review for the US Preventive Services Task Force: Evidence Synthesis No. 177*. Rockville, MD: Agency for Healthcare Research and Quality; 2019. AHRQ publication 18-05246-EF-2.

25. Selph SS, Bougatsos C, Dana T, Grusing S, Chou R. Screening for HIV infection in pregnant women: updated evidence report and systematic review for the US Preventive Services Task Force [published online June 11, 2019]. *JAMA*. doi:10.1001/jama.2019.2593

26. Centers for Disease Control and Prevention (CDC). Rapid HIV tests suitable for use in clinical settings (CLIA-moderate complexity). https://www.cdc.gov/hiv/pdf/testing/rapid-hiv-tests-clinical-moderate-complexity.pdf. Updated August 2016. Accessed April 5, 2019.

27. Cohen MS, Chen YQ, McCauley M, et al; HPTN 052 Study Team. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011;365(6):493-505. doi:10.1056/NEJMoa1105243

28. Grinsztejn B, Hosseinipour MC, Ribaudo HJ, et al; HPTN 052-ACTG Study Team. Effects of early versus delayed initiation of antiretroviral treatment

on clinical outcomes of HIV-1 infection: results from the phase 3 HPTN 052 randomised controlled trial. *Lancet Infect Dis*. 2014;14(4):281-290. doi:10.1016/S1473-3099(13)70692-3

29. Lundgren JD, Babiker AG, Gordin F, et al; INSIGHT START Study Group. Initiation of antiretroviral therapy in early asymptomatic HIV infection. *N Engl J Med*. 2015;373(9):795-807. doi:10.1056/NEJMoa1506816

30. Danel C, Moh R, Gabillard D, et al; TEMPRANO ANRS 12136 Study Group. A trial of early antiretrovirals and isoniazid preventive therapy in Africa. *N Engl J Med*. 2015;373(9):808-822. doi:10.1056/NEJMoa1507198

31. Lodi S, Phillips A, Logan R, et al; HIV-CAUSAL Collaboration. Comparative effectiveness of immediate antiretroviral therapy versus CD4-based initiation in HIV-positive individuals in high-income countries: observational cohort study. *Lancet HIV*. 2015;2(8):e335-e343. doi:10.1016/S2352-3018(15)00108-3

32. Lima VD, Reuter A, Harrigan PR, et al. Initiation of antiretroviral therapy at high CD4+ cell counts is associated with positive treatment outcomes [published correction appears in *AIDS*. 2016;30(4):677]. *AIDS*. 2015;29(14):1871-1882. doi:10.1097/QAD.0000000000000790

33. Edwards JK, Cole SR, Westreich D, et al; Centers for AIDS Research Network of Integrated Clinical Systems Investigators. Age at entry into care, timing of antiretroviral therapy initiation, and 10-year mortality among HIV-seropositive adults in the United States. *Clin Infect Dis*. 2015;61(7):1189-1195. doi:10.1093/cid/civ463

34. Cohen MS, Chen YQ, McCauley M, et al; HPTN 052 Study Team. Antiretroviral therapy for the prevention of HIV-1 transmission. *N Engl J Med*. 2016;375(9):830-839. doi:10.1056/NEJMoa1600693

35. Rodger AJ, Cambiano V, Bruun T, et al; PARTNER Study Group. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA*. 2016;316(2):171-181. doi:10.1001/jama.2016.5148

36. Rodger AJ, Cambiano V, Bruun T, et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study [published online May 2, 2019]. *Lancet*. doi:10.1016/S0140-6736(19)30418-0

37. Bavinton BR, Pinto AN, Phanuphak N, et al; Opposites Attract Study Group. Viral suppression and HIV transmission in serodiscordant male couples: an international, prospective, observational, cohort study. *Lancet HIV*. 2018;5(8):e438-e447. doi:10.1016/S2352-3018(18)30132-2

38. Kann L, McManus T, Harris WA, et al. Youth risk behavior surveillance—United States, 2017. *MMWR Surveill Summ*. 2018;67(8):1-114. doi:10.15585/mmwr.ss6708a1

39. Eaton DK, Kann L, Kinchen S, et al; Centers for Disease Control and Prevention (CDC). Youth risk behavior surveillance—United States, 2011. *MMWR Surveill Summ*. 2012;61(4):1-162.

40. Arribas JR, Thompson M, Sax PE, et al. Brief report: randomized, double-blind comparison of tenofovir alafenamide (TAF) vs tenofovir disoproxil fumarate (TDF), each coformulated with elvitegravir, cobicistat, and emtricitabine (E/C/F) for initial HIV-1 treatment: week 144 results. *J Acquir Immune Defic Syndr*. 2017;75(2):211-218. doi:10.1097/QAI.0000000000001350

41. Rockstroh JK, DeJesus E, Lennox JL, et al; STARTMRK Investigators. Durable efficacy and safety of raltegravir versus efavirenz when combined with tenofovir/emtricitabine in treatment-naive HIV-1-infected patients: final 5-year results from STARTMRK. *J Acquir Immune Defic Syndr*. 2013;63(1):77-85. doi:10.1097/QAI.0b013e31828ace69

42. Ding X, Andraca-Carrera E, Cooper C, et al. No association of abacavir use with myocardial infarction: findings of an FDA meta-analysis. *J Acquir Immune Defic Syndr*. 2012;61(4):441-447. doi:10.1097/QAI.0b013e31826f993c

43. Sabin CA, Reiss P, Ryom L, et al; D:A:D Study Group. Is there continued evidence for an association between abacavir usage and myocardial infarction risk in individuals with HIV? a cohort collaboration. *BMC Med*. 2016;14:61. doi:10.1186/s12916-016-0588-4

44. Desai M, Joyce V, Bendavid E, et al. Risk of cardiovascular events associated with current exposure to HIV antiretroviral therapies in a US veteran population. *Clin Infect Dis*. 2015;61(3):445-452. doi:10.1093/cid/civ316

45. Mollan KR, Smurzynski M, Eron JJ, et al. Association between efavirenz as initial therapy for HIV-1 infection and increased risk for suicidal ideation or attempted or completed suicide: an analysis of trial data. *Ann Intern Med*. 2014;161(1):1-10. doi:10.7326/M14-0293

46. Ford N, Shubber Z, Pozniak A, et al. Comparative safety and neuropsychiatric adverse events associated with efavirenz use in first-line antiretroviral therapy: a systematic review and meta-analysis of randomized trials. *J Acquir Immune Defic Syndr*. 2015;69(4):422-429. doi:10.1097/QAI.0000000000000606

47. Smith C, Ryom L, Monforte Ad, et al. Lack of association between use of efavirenz and death from suicide: evidence from the D:A:D study. *J Int AIDS Soc*. 2014;17(4)(suppl 3):19512. doi:10.7448/IAS.17.4.19512

48. Nkhoma ET, Coumbis J, Farr AM, et al. No evidence of an association between efavirenz exposure and suicidality among HIV patients initiating antiretroviral therapy in a retrospective cohort study of real world data. *Medicine (Baltimore)*. 2016;95(3):e2480. doi:10.1097/MD.0000000000002480

49. Ryom L, Lundgren JD, De Wit S, et al; D:A:D Study Group. Use of antiretroviral therapy and risk of end-stage liver disease and hepatocellular carcinoma in HIV-positive persons. *AIDS*. 2016;30(11):1731-1743. doi:10.1097/QAD.0000000000001018

50. Kovari H, Sabin CA, Ledergerber B, et al. Antiretroviral drug-related liver mortality among HIV-positive persons in the absence of hepatitis B or C virus coinfection: the Data Collection on Adverse Events of Anti-HIV Drugs study. *Clin Infect Dis*. 2013;56(6):870-879. doi:10.1093/cid/cis919

51. Ryom L, Mocroft A, Kirk O, et al; D:A:D Study Group. Association between antiretroviral exposure and renal impairment among HIV-positive persons with normal baseline renal function: the D:A:D study. *J Infect Dis*. 2013;207(9):1359-1369. doi:10.1093/infdis/jit043

52. Scherzer R, Estrella M, Li Y, et al. Association of tenofovir exposure with kidney disease risk in HIV infection. *AIDS*. 2012;26(7):867-875. doi:10.1097/QAD.0b013e328351f68f

53. Laprise C, Baril JG, Dufresne S, Trottier H. Association between tenofovir exposure and reduced kidney function in a cohort of HIV-positive patients: results from 10 years of follow-up. *Clin Infect Dis*. 2013;56(4):567-575. doi:10.1093/cid/cis937

54. Borges ÁH, Hoy J, Florence E, et al; EuroSIDA. Antiretrovirals, fractures, and osteonecrosis in a large international HIV cohort. *Clin Infect Dis*. 2017;64(10):1413-1421. doi:10.1093/cid/cix167

55. Fowler MG, Qin M, Fiscus SA, et al; IMPAACT 1077BF/1077FF PROMISE Study Team. Benefits and risks of antiretroviral therapy for perinatal HIV prevention. *N Engl J Med*. 2016;375(18):1726-1737. doi:10.1056/NEJMoa1511691

56. Chen JY, Ribaudo HJ, Souda S, et al. Highly active antiretroviral therapy and adverse birth outcomes among HIV-infected women in Botswana. *J Infect Dis*. 2012;206(11):1695-1705. doi:10.1093/infdis/jis553

57. Short CE, Douglas M, Smith JH, Taylor GP. Preterm delivery risk in women initiating antiretroviral therapy to prevent HIV mother-to-child transmission. *HIV Med*. 2014;15(4):233-238. doi:10.1111/hiv.12083

58. Zash R, Jacobson DL, Diseko M, et al. Comparative safety of antiretroviral treatment regimens in pregnancy. *JAMA Pediatr*. 2017;171(10):e172222. doi:10.1001/jamapediatrics.2017.2222

59. Kakkar F, Boucoiran I, Lamarre V, et al. Risk factors for pre-term birth in a Canadian cohort of HIV-positive women: role of ritonavir boosting? *J Int AIDS Soc*. 2015;18:19933. doi:10.7448/IAS.18.1.19933

60. Kreitchmann R, Li SX, Melo VH, et al. Predictors of adverse pregnancy outcomes in women infected with HIV in Latin America and the Caribbean: a cohort study. *BJOG*. 2014;121(12):1501-1508. doi:10.1111/1471-0528.12680

61. Sibiude J, Warszawski J, Tubiana R, et al. Premature delivery in HIV-infected women starting protease inhibitor therapy during pregnancy: role of the ritonavir boost? *Clin Infect Dis*. 2012;54(9):1348-1360. doi:10.1093/cid/cis198

62. Watts DH, Williams PL, Kacanek D, et al; Pediatric HIV/AIDS Cohort Study. Combination antiretroviral use and preterm birth. *J Infect Dis*. 2013;207(4):612-621. doi:10.1093/infdis/jis728

63. Nozyce ML, Huo Y, Williams PL, et al; Pediatric HIVAIDS Cohort Study. Safety of in utero and neonatal antiretroviral exposure: cognitive and academic outcomes in HIV-exposed, uninfected children 5-13 years of age. *Pediatr Infect Dis J*. 2014;33(11):1128-1133. doi:10.1097/INF.0000000000000410

64. Williams PL, Hazra R, Van Dyke RB, et al; Pediatric HIV/AIDS Cohort Study. Antiretroviral exposure during pregnancy and adverse outcomes in HIV-exposed uninfected infants and children using a trigger-based design. *AIDS*. 2016;30(1):133-144.

65. Watts DH, Balasubramanian R, Maupin RT Jr, et al; PACTG 316 Study Team. Maternal toxicity and pregnancy complications in human

immunodeficiency virus–infected women receiving antiretroviral therapy: PACTG 316. *Am J Obstet Gynecol*. 2004;190(2):506-516. doi:10.1016/j.ajog.2003.07.018

66. Tuomala RE, Watts DH, Li D, et al; Women and Infants Transmission Study. Improved obstetric outcomes and few maternal toxicities are associated with antiretroviral therapy, including highly active antiretroviral therapy during pregnancy. *J Acquir Immune Defic Syndr*. 2005;38(4):449-473. doi:10.1097/01.qai.0000139398.38236.4d

67. Martí C, Peña JM, Bates I, et al. Obstetric and perinatal complications in HIV-infected women: analysis of a cohort of 167 pregnancies between 1997 and 2003. *Acta Obstet Gynecol Scand*. 2007;86(4):409-415. doi:10.1080/00016340601148531

68. Sartorius BK, Chersich MF, Mwaura M, et al; Kesho Bora Study Group. Maternal anaemia and duration of zidovudine in antiretroviral regimens for preventing mother-to-child transmission: a randomized trial in three African countries. *BMC Infect Dis*. 2013;13:522. doi:10.1186/1471-2334-13-522

69. Moyer VA; US Preventive Services Task Force. Screening for HIV: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2013;159(1):51-60. doi:10.7326/0003-4819-159-1-201307020-00645

70. Qaseem A, Snow V, Shekelle P, Hopkins R Jr, Owens DK; Clinical Efficacy Assessment Subcommittee, American College of Physicians. Screening for HIV in health care settings: a guidance statement from the American College of Physicians and HIV Medicine Association. *Ann Intern Med*. 2009;150(2):125-131. doi:10.7326/0003-4819-150-2-200901200-00300

71. Lubinski C, Aberg J, Bardeguez AD, et al. HIV policy: the path forward—a joint position paper of the HIV Medicine Association of the Infectious Diseases Society of America and the American College of Physicians. *Clin Infect Dis*. 2009;48(10):1335-1344. doi:10.1086/598169

72. Committee on Gynecologic Practice. ACOG Committee Opinion No 596: routine human immunodeficiency virus screening. *Obstet Gynecol*. 2014;123(5):1137-1139. doi:10.1097/01.AOG.0000446828.64137.50

73. Committee on Practice and Ambulatory Medicine; Bright Futures Periodicity Schedule Workgroup. 2017 Recommendations for preventive pediatric health care. *Pediatrics*. 2017;139(4):e20170254. doi:10.1542/peds.2017-0254

74. American Academy of Family Physicians (AAFP). Clinical Preventive Service Recommendation: HIV Screening, Adolescents and Adults. AAFP website. https://www.aafp.org/patient-care/clinical-recommendations/all/hiv-screening.html. Published 2013. Accessed April 5, 2019.

75. American Academy of Pediatrics Committee on Pediatric AIDS. HIV testing and prophylaxis to prevent mother-to-child transmission in the United States. *Pediatrics*. 2008;122(5):1127-1134. doi:10.1542/peds.2008-2175

76. American Academy of Pediatrics. AAP publications reaffirmed and retired. *Pediatrics*. 2011;128:e748. doi:10.1542/peds.2011-1808