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Screening for Human Immunodeficiency Virus: Focused Update of a 2005 Systematic Evidence Review for the U. S. Preventive Services Task Force

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I. INTRODUCTION

This report updates an evidence synthesis commissioned by the U.S. Preventive Services Task Force (USPSTF) and completed in March 2005,[1] on screening for unsuspected human immunodeficiency virus (HIV) using HIV antibody (Ab) tests in non-pregnant adolescents (aged 13 to 18 years old) and adults. This brief update was requested by the USPSTF to determine whether there is sufficient new evidence to justify revision of recommendations based on the 2005 evidence synthesis.[2] A key reason for this update is the release in September 2006 of revised Centers for Disease Control and Prevention (CDC) recommendations advising routine voluntary HIV screening of most U.S. adolescents and adults.[3] The 2005 USPSTF recommendations differ from the revised CDC recommendations in that they do not recommend for or against routine screening non-pregnant adults and adolescents who do not report risk factors and are not in high-prevalence (>1%) or other high-risk settings.[2] Staff at the CDC have indicated that the agency's expanded screening recommendations are based primarily on new evidence as to the effects of HIV screening on transmission risk. This report focuses on new or "breakthrough" evidence that could affect the 2005 USPSTF recommendations regarding routine screening of low- or average-risk adults and adolescents.

Burden of Condition / Epidemiology

It is estimated that approximately one million persons in the United States are infected with HIV, and approximately 400,000 persons are known to be living with the acquired immunodeficiency syndrome (AIDS) in 2003.[4] Of those infected, 25% (180,000-280,000) are thought to be unaware of their positive status.[4, 5] New surveillance data from the CDC indicates no significant changes in the number of new HIV or AIDS diagnoses between 2001 and 2004.[6] Rates of infection remain highest among non-Hispanic blacks (8.4 times higher than among whites).[7]

Healthcare Interventions

There remains no effective vaccine to prevent HIV infection and no cure for chronic infection. Of the interventions used to treat chronic HIV infection, highly active antiretroviral therapy (HAART) has the greatest impact on clinical outcomes, including survival.[8] Since the USPSTF evidence synthesis was completed in 2005, updated guidelines for antiretroviral therapy have been published.[9, 10]

Prior Recommendations

The USPSTF released updated recommendations for HIV screening in 2005.[2] The USPSTF recommends screening all patients at higher risk for HIV infection (including those reporting risk factors and those in high-prevalence or high-risk clinical settings) and all pregnant women (A recommendations).[2] The USPSTF makes no recommendation for or against routinely screening for HIV non-pregnant adults and adolescents not at higher risk for HIV infection. Although it found fair evidence that screening adolescents and adults not known to be at increased risk for HIV can detect additional individuals with HIV, and good evidence that appropriately timed interventions lead to improved health outcomes for some of those individuals, the USPSTF

concluded that the yield from screening persons without risk factors in low-prevalence settings would be low, and that there may be potential harms[1] of screening as well as additional burdens on clinicians. The USPSTF concluded that the benefits are too small relative to potential harms to justify a general recommendation for routine screening (C recommendation). The USPSTF made no recommendations on the frequency of screening or on methods of pre-test counseling.

The 2005 USPSTF recommendations are generally consistent with the 2001 CDC recommendations, which defined high prevalence of HIV infection as >1%, or an AIDS diagnosis rate of >1 per 1000 hospital discharges.[11] These thresholds were based on prevalence data from 1993. High-risk clinical settings as defined by the 2001 CDC recommendations are shown in Table 1.

The revised 2006 CDC recommendations advise routine voluntary screening for all persons aged 13 to 64 years through opt-out testing (notifying patients that testing will be performed unless they decline), unless prevalence of undiagnosed HIV infection is documented to be <0.1% and no risk factors are identified.[3] The CDC also recommends screening all patients initiating treatment for tuberculosis and those seeking treatment for STDs (including all patients attending STD clinics) at each visit for a new complaint. The CDC recommends testing all persons likely to be at high risk for HIV infection at least annually and encourages testing of patients and prospective partners before initiating a new sexual relationship, but does not provide specific guidance for repeat screening in average or low-risk persons. The 2006 CDC recommendations also differ from previous CDC recommendations in that they advocate more streamlined HIV testing procedures and do not require separate written consent for HIV screening or prevention counseling as part of testing. These changes are intended to help reduce barriers to testing, decrease burdens associated with pre-test counseling, and increase acceptability of screening by patients and clinicians.

Scope of Update

This update reviews new evidence on HIV screening not included in the 2005 evidence synthesis. It focuses on evidence in non-pregnant, adults and adolescents who do not report risk factors and are evaluated in lower-prevalence (<1%), low-risk clinical settings (referred to in this report as 'low-risk' persons), because this is the population for which the USPSTF and the 2006 CDC recommendations are discordant. In the 2005 evidence review, we identified several key areas where additional evidence could strengthen the case for screening in low-risk populations.[1] These include gaps in the research regarding uncertainties about the acceptability of routine voluntary screening in low-risk persons; the yield of targeted versus universal screening and optimal methods of risk assessment in low-risk settings; the impact on test uptake and follow-up of abbreviated or streamlined counseling methods and newer testing or sampling methods; and the effects of screening on HIV transmission rates. We therefore focused on studies that could help fill in these gaps. We also evaluated new evidence on the cost-effectiveness of routine HIV screening and studies on the frequency of testing.

II. METHODS

Literature Search and Strategy

We limited our review to references cited in the revised 2006 CDC recommendations[3] and published in 2004 or later (as the main searches for the 2005 evidence synthesis were conducted through June 2004), and to a list provided by the CDC of other new studies reviewed but not included as references in its revised recommendations.

Inclusion / Exclusion Criteria

A single reader reviewed all citations. Papers were selected for full review if they were about HIV infection and evaluated the effects of screening on high-risk behaviors, rates of sexually transmitted diseases, or HIV transmission rates in adults and adolescents in outpatient, low-risk (i.e., not high risk or high prevalence) settings. High prevalence was defined as >1% and high risk settings were defined as in the 2001 CDC guidelines.[11] We also included studies evaluating the yield of different risk assessment methods; acceptability of HIV screening; impact of streamlined counseling or testing methods on test uptake, clinical stage at diagnosis, and rates of entry into medical care; effects of repeat screening at different intervals; and cost-effectiveness of screening. We included studies performed in the U.S. or Australia, Canada and countries of Western Europe, in which the epidemiology and management of chronic HIV infection are similar. When important new studies for a specific key question had only been performed in other countries, these were reviewed as well.

Data Extraction and Synthesis

We used predefined criteria from the USPSTF to assess the internal validity of included systematic reviews, trials, observational studies, and cost-effectiveness analyses, which we rated as good, fair, or poor.[12, 13] We also rated the applicability of each study to the population likely to be identified by screening and the overall body of evidence for each key question. The rating system was developed by the USPSTF and is described in detail elsewhere and summarized in Appendix 1.[12] For included studies, we abstracted information about setting, patients, interventions, and outcomes.

Size of Literature Reviewed

Investigators reviewed 116 abstracts published in or after 2004. Of these, 6 were already cited in the 2005 evidence synthesis, 67 were excluded because they evaluated high-risk, high-prevalence, pediatric, or prenatal populations or were conducted in Asia or Africa, 10 contained no original data (editorials, letters, or non-systematic reviews), 23 did not address areas relevant to our scope, and 1 did not report interpretable outcomes. Nine full-text articles were retrieved,

including two randomized controlled trials[14, 15] and two systematic reviews.[16, 17] After review of the full-text articles, neither randomized trial met inclusion criteria because they evaluated high-risk patients (STD clinic patients and men who have sex with men). An observational study was also excluded after full-text review because it took place in a high-risk setting.[18] Two systematic reviews met inclusion criteria and evaluated rates of risky behaviors before and after HIV testing.[16, 17] One[17] was an update of a systematic review[19] included in the 2005 evidence synthesis. Other studies meeting inclusion criteria included a survey of the general population that included information on test acceptability,[20] an observational study of outpatients and inpatients evaluating test acceptability,[21] a modeling study estimating effects of HIV screening on sexual transmission,[22] and a cost-effectiveness analysis of screening.[23]

III. RESULTS

Can Risk Factor Assessment Identify Asymptomatic Adolescents and Adults at Increased Risk for HIV Compared to the General Population?

Risk factors for HIV infection are unchanged since the USPSTF first issued recommendations for HIV screening in 1996.[24] Persons at higher risk for HIV infection include those seeking treatment for sexually transmitted diseases; men who have had sex with men after 1975; past or present injection drug users; persons who exchange sex for money or drugs, and their sex partners; women and men whose past or present sex partners were HIV-infected, bisexual individuals, or injection drug users; and persons with a history of transfusion between 1978 and 1985.[24] The CDC also considers persons who themselves or whose sex partners have had more than one sex partner since their most recent HIV test as high risk.[3]

Updated surveillance data from the CDC indicates that from 2001 through 2004, 61% of new diagnoses of HIV or AIDS in U.S. males were associated with male-to-male sex, 17% with heterosexual contact, 16% with intravenous drug use, 5% with intravenous drug use by men who have sex with men, and 1% with other risk factors.[7] Among females, the most prevalent exposure categories were heterosexual contact (76%) and injection drug use (21%). Non-Hispanic blacks account for 68% of new HIV diagnoses in females and 44% in males.[7]

In the 2005 evidence synthesis, we summarized evidence suggesting that a significant proportion of American adults and adolescents report behaviors that could put them at risk for HIV infection.[25, 26] New data from the National Center for Health Statistics estimates that 11.9% of persons between 15 and 44 years of age had engaged in sexual or drug use behaviors in the past year that put them at increased risk of HIV, or had been treated for a sexually transmitted disease.[27] About one-third had never been tested for HIV. Results from the Youth Risk Behavior Surveillance System found that in 2005, 47% of high school students reported ever having sexual intercourse, and 37% of sexually active high school students had not used a condom during last sexual intercourse.[28] A small proportion (2.1%) of high school students reported ever using a needle to inject an illegal drug into their body.

We found no new studies evaluating willingness to disclose high risk behaviors in low-prevalence or primary care settings. Previous studies included in the 2005 evidence synthesis indicate that most adolescents[29] and adults[30] are willing to discuss and disclose high risk

behaviors when asked about them.[31, 32] Even in settings with good access to medical care, however, high-risk behaviors frequently remain undetected and do not necessarily lead to testing even when identified.[33, 34]

We found no new studies evaluating the proportion of HIV-positive patients reporting risk factors in low-risk settings. One new retrospective study found that 28% (33/120) of newly diagnosed HIV-infected persons in the Denver public health system had an HIV clinical indicator condition or sexually transmitted infection, but it did not assess for the presence of HIV risk factors.[18] In the 2005 evidence synthesis, we reviewed data from the largest U.S. study on HIV testing, which found that 20% of HIV-positive clients at federally funded HIV testing sites with a prevalence of 0.1% to 2.0% reported no risk factors.[35] The rate of HIV positivity in patients reporting no risk factors ranged from 0.2% to 0.8% in these sites.

We found no new studies comparing the proportion of HIV-infected persons diagnosed using targeted versus universal screening strategies in low-risk or other settings. In the only prospective study included in the 2005 evidence synthesis, screening only those patients in an STD clinic setting reporting risky behaviors (5.8% of the population) would have resulted in missed diagnoses in 74% (79/107) of cases.[36] A strategy that also included testing of all patients from higher-prevalence demographic groups (black males and age >30 years) would have resulted in fewer (7%) missed diagnoses, but substantially more testing (70% of the population). However, this study did not include unprotected sexual intercourse with partners not known to be at high risk for HIV infection as a risk factor. Multiple retrospective and cross-sectional studies in diverse settings that were reviewed in the 2005 evidence synthesis also found that significant proportions of HIV-infected persons reported no risk factors, though estimates ranged from 7% to 51%.[1] Factors that could explain some of the variation in rates of identifiable risk factors include population differences, varying stringency of risk factor ascertainment, or use of different definitions for HIV risk factors (such as whether more than one sexual partner or any unprotected heterosexual intercourse were considered risk factors).

We also found no new studies evaluating the effects of implementation of routine voluntary screening in low-risk settings. In one older study at an average-risk hospital, 51% (4535/8868) patients agreed to voluntary testing, and 0.26% (12 of 4535) tested positive.[37] Ten of the twelve HIV-positive persons (83%) were considered high-risk. Several other studies included in the 2005 evidence synthesis reported increased numbers of new HIV diagnoses after the implementation of routine voluntary screening in higher-risk settings (prevalence >1%).[38-41]

Is Routine Voluntary Screening Acceptable to Patients?

Approximately half of U.S. adults report having been tested at least once for HIV.[20, 42] In one new national survey, 21% had been tested within the last 12 months.[20] The proportion of adolescents tested for HIV infection is substantially lower than for those aged 18 or older.[43]

We identified no new studies evaluating the acceptability of routine, voluntary HIV antibody testing in low-risk settings. One new study of routine voluntary HIV testing in four high-prevalence (2%) urgent care centers found that 67% of 9,129 patients refused testing.[44] Of those who gave one reason for test refusal, 43% refused because they did not feel that they were high

risk, 1% felt that the information was too personal, and 4% felt testing would take too long. The site with the longest-standing routine testing policy had the lowest rate of test refusal (47% versus 75-87% at the other three sites). One potential explanation for this finding is that HIV test uptake rates may increase over time, as routine testing becomes normalized in a particular setting. However, such a hypothesis needs to be confirmed, as numerous other factors could affect testing rates across sites.

One older, good-quality systematic review of 62 studies on the acceptability of HIV antibody testing in the U.S., included in the 2005 evidence synthesis, found lower prevalence settings associated with lower acceptance rates, though estimates varied widely.[45] For example, in family planning clinics, test uptake rates ranged from 14% to 67%. Several recent studies included in the 2005 evidence synthesis evaluated the implementation of routine voluntary HIV testing policies in higher risk settings. In one study, testing rates increased approximately three-fold (to 6.4%) in an inpatient urban hospital.[40] However, the proportion of patients offered and refusing testing were not reported. In studies evaluating routine testing policies in urgent care and emergency room settings, testing rates ranged from 1.8% to 32%.[38, 39, 41]

CDC's 2001 guidelines for HIV testing recommended fairly extensive pre-test counseling.[11] A new, national survey by the Kaiser Family Foundation found that approximately two-thirds of 2,517 respondents agreed with a statement that HIV testing should be treated just like routine screening for other diseases.[20] On the other hand, about one-quarter agreed with a statement that HIV testing should require special procedures, such as written permission from the patient. Data on the effects of streamlined counseling on uptake rates remains sparse. No new studies evaluated the acceptability or effects of 'opt-out' testing policies (notifying people that an HIV test is routine and performing it unless refused) in non-pregnant, low-risk adults or adolescents in the U.S. One study from a low-prevalence STD clinic in the U.K., included in the 2005 evidence synthesis, found that test uptake increased from 35% to 65% after implementing opt-out testing.[46] We found no new studies assessing the effects of anonymous versus confidential or name-based testing.

The use of more convenient, less invasive, or rapid tests could improve HIV testing acceptability. One new randomized trial of outpatients and inpatients found a trend towards a higher rate of test uptake in patients randomized to a rapid HIV test versus conventional testing (60/101 or 59%, versus 42/102 or 41%, p=0.07).[21] In this trial, more than 90% of patients reported at least one risk factor (including unprotected heterosexual intercourse). A recent Kaiser Family Foundation survey found that 62% of respondents would prefer to be tested for HIV in a doctor's office or clinic, versus 26% at home.[20] We found no other new studies in low-risk settings evaluating preferences for home sample collection kits, telephone-based counseling, rapid tests, on-site testing, or non-invasive tests compared to standard office-based blood testing. These methods were generally preferred over standard office-based testing in studies, most in higher-risk settings, reviewed in the 2005 evidence synthesis. One new study in a mobile sexually transmitted disease/HIV clinic found that 64% of subjects offered rapid or standard testing chose the former.[47]

Does Routine Voluntary Screening Increase the Proportion of HIV-Positive Patients Entering Care or Result in Earlier Diagnosis?

HIV-positive patients who qualify for interventions may not receive them. In a large study of publicly funded testing sites across the U.S., 44% of all tested patients and 38% of those with a positive test result did not have a post-test counseling session.[48] The proportion of patients informed of test results could be increased by the use of rapid tests, which provide results within 10 to 30 minutes. Although positive results need to be confirmed by further testing,[49] patients can be given initial results prior to leaving the testing site. One recent randomized trial of inpatients and outpatients at a public health hospital found that more patients randomized to rapid testing were informed of their results compared to those randomized to standard testing (95% vs. 43%, $p<0.001$).[21] We identified no other new studies evaluating the proportion of HIV-positive persons learning their serostatus in low-risk settings. In studies of patients in high-risk settings included in the 2005 evidence synthesis, rapid testing was consistently associated with a higher rate of HIV-positive persons learning their serostatus, compared to standard testing.[47, 50, 51]

HIV-positive patients may delay entry into medical care or not receive care at all.[52] In 1996, only an estimated 36% to 63% of patients with known or unknown HIV infection were seeing a provider outside an emergency room at least once every 6 months.[53] We found no new studies evaluating the proportion of newly diagnosed patients in low-risk settings who entered into care. One study included in the 2005 evidence synthesis found that only 35% (26/74) of newly diagnosed HIV-infected persons identified through a routine voluntary screening program in a high-prevalence urgent care center had entered care within four months.[39]. However, in another study, at least 70% (42/60) of newly diagnosed HIV-infected persons had one or more documented follow-up visits.[38] Rates of entry into care are likely to vary across different settings, in part due to population characteristics and differences in the resources and models used to enhance rates of follow-up.

Studies summarized in the 2005 evidence synthesis indicate that a high proportion of HIV-infected patients are diagnosed at late stages of disease.[1] We identified no new studies estimating the effects of screening on the proportion of patients with HIV infection identified shortly before being diagnosed with AIDS or concurrently with their AIDS diagnosis.

How Effective Is Repeat Testing in Identifying Additional Cases of HIV Infection and Improving Clinical Outcomes?

We identified no new studies evaluating the effectiveness of repeat testing, or determining optimal testing intervals,,for identifying new cases of HIV infection in non-pregnant adults and adolescents in low-risk or other settings. The optimal frequency of testing will vary depending on the incidence of undetected HIV infection in the group being tested (prevalent cases would be identified on initial screening).[54] Two good-quality cost-effectiveness analyses included in the 2005 evidence synthesis found screening every five years in a population with 1% prevalence cost less than $50,000 per quality-adjusted life-year only when secondary transmission benefits were included and annual incidence was at least 0.09%.[55, 56] In low-prevalence (0.1% undiagnosed HIV infection) settings, one of these studies found repeat screening at any interval cost more than $100,000 per quality-adjusted life-year at all plausible incidences.[56] This study also found that in a high-risk setting (incidence 1.20% per year and prevalence 3.0%), screening every five years cost $50,000 per quality-adjusted life year relative to one-time screening, and

screening every three years or annually cost more than $60,000 per quality-adjusted life-year compared to less frequent screening strategies.

How Effective Is HIV Screening in Reducing Transmission Rates of HIV or Other Sexually Transmitted Diseases?

Theoretically, HIV testing and counseling could reduce HIV transmission rates through a reduction in risky behaviors. However, direct evidence on the impact of HIV testing and counseling on HIV transmission rates remains sparse. We identified no new studies comparing rates of HIV transmission from tested and untested persons. An epidemiologic study included in the 2005 evidence synthesis estimated that the annual HIV transmission rate from HIV-seropositive persons in the United States declined from 13% in 1987 (the year zidovudine was introduced) to 5.5% in 1989, but has remained steady at approximately 4.2% from 1990 through 2000.[57] The 2005 evidence synthesis also included one prospective U.S. study of 144 serodiscordant heterosexual couples who received counseling and reported reduced risky behaviors. The study found no seroconversion after 193 couple-years of follow-up.[58] However, because of possible underlying factors impeding transmission, data from monogamous serodiscordant couples may not be applicable to the general population of patients with HIV infection. An older, prospective African study found a rate of seroconversion among uninfected female partners of HIV-positive men of 6-9/100 person-years, compared to 22/100 person-years among uninfected women with untested partners.[59]

HIV counseling and testing could also reduce HIV transmission indirectly, by identifying additional patients who meet criteria for antiretroviral therapy. HAART could decrease the spread of HIV from infected persons by reducing viral loads.[60] On the other hand, increases in risky behaviors by patients on HAART could attenuate or offset the beneficial effects of viral suppression.[61] We identified no new studies estimating effects of HAART on horizontal transmission rates. In the 2005 evidence synthesis, we included one good-quality meta-analysis of 25 studies that found no association between receipt of HAART or having an undetectable viral load and an increased likelihood of unprotected sex, but among seronegative and seropositive persons, unprotected intercourse was associated with optimistic beliefs about HAART or an undetectable viral load (OR 1.82, 95% CI, 1.52-2.17).[62]

One fair-quality systematic review of observational studies (an update of a study included in the 2005 evidence synthesis[19]) included an analysis of rates of sexually transmitted diseases (a clinical marker for risky behaviors) following HIV testing, based on searches conducted through November 2003 (Evidence Table 1).[17] It did not assess the quality of the included studies (Evidence Table 2). Data on sexually transmitted disease rates could only be pooled from two studies.[63, 64] The incidence of new sexually transmitted diseases decreased modestly among individuals testing HIV-positive (standardized effect size [d+] = 0.18, 95% CI 0.08 to 0.28), but increased modestly among individuals testing negative (d+ = -0.12, 85% CI -0.22 to -0.02) and those untested (d+ = -0.05, 95% CI -0.09 to -0.01). A third study, which could not be pooled, was a retrospective cohort study of primarily young (ages 15 to 25 years) black persons in a sexually transmitted disease clinic setting. This study found an increase in gonorrhea rates relative to pre-test rates among those who tested HIV-negative and received post-test counseling (RR 1.27, 95% CI 1.09 to 1.48), and no significant difference in gonorrhea rates among those

testing positive (RR 0.53, 95% CI 0.17 to 1.60).[65] All three studies were retrospective and had unclear rates of loss to follow-up.

More intensive or targeted HIV counseling could be more effective than standard counseling in reducing sexually transmitted diseases or HIV infection rates, but would require additional resources. We identified no new studies evaluating the effectiveness of more intensive or targeted HIV counseling in reducing sexually transmitted diseases or HIV infection rates in HIV-positive persons. In the single randomized controlled trial of HIV-positive persons included in the 2005 evidence synthesis, more intensive counseling was associated with fewer sexually transmitted diseases than standard counseling in 366 infected women.[66] One new randomized trial (RESPECT-2) found no differences in the risk for new sexually transmitted diseases in HIV-negative persons at STD clinics, following counseling and testing with a rapid versus a standard HIV test (RR 1.11, 95% CI 0.96 to 1.29).[15] Another new trial (the EXPLORE study) found a trend towards a lower rate of HIV infection among 4,295 HIV-negative men who have sex with men, among those receiving more intensive versus less intensive individualized counseling after 48 months (rate difference 18.2%, 95% CI -4.7 to 36.0%), with the largest effects in the first 12 to 18 months.[14] A large trial (n=5,758) of heterosexual, HIV-negative persons, included in the 2005 evidence synthesis, found interactive HIV counseling and testing associated with 20% fewer sexually transmitted diseases after twelve months than standard non-interactive didactic counseling and testing; however, no significant difference was found between the counseling groups in the rate of new HIV infections (eight total).[67]

How Effective Is HIV Screening in Reducing Rates of Risky Behaviors?

In the 2005 evidence synthesis, we summarized evidence indicating that a significant proportion of HIV-infected persons engage in ongoing behaviors that increase the risk of transmitting the disease, such as using condoms inconsistently, having multiple sexual partners, engaging in injection drug use, or trading sex for drugs or money.[52] For example, one recent survey found that 13-19% of HIV-infected persons (n=3723) reported unprotected vaginal or anal intercourse with partners HIV-negative or of unknown serostatus.[25] Another survey of HIV-positive persons (n=1,421) found that 13% reported unprotected anal or vaginal intercourse without disclosure of HIV status.[68] In several epidemiological studies (with data collected through 2002), risky behaviors and STD rates appeared resurgent among certain highly tested populations of men who have sex with men.[25, 69-75]

We identified one new systematic review comparing the rates of self-reported unprotected anal or vaginal intercourse of HIV-positive persons aware and unaware of their status (Evidence Table 1).[16] Four of the eight studies that were included (no randomized trials) evaluated men who have sex with men, and another primarily evaluated female intravenous drug users. The systematic review was rated only fair quality, because it did not assess the quality of included studies or report reasons for excluding studies (Evidence Table 2). In addition, unpublished data from four studies was used in the analysis, but there was insufficient detail about methods to judge their quality. The meta-analysis found self-reported rates of unprotected anal or vaginal intercourse with any partner an average of 53% lower (95% CI 45% to 60%) in patients aware of their HIV-positive status, compared to those unaware. There was a 68% reduction (95% CI 56%

to 76%) when the analysis was adjusted to focus on unprotected intercourse with serodiscordant partners.

We also identified an update of an earlier systematic review[19] (included in the 2005 evidence synthesis) that included 23 observational studies published in November 2003 or earlier, on the effects of HIV counseling and testing on risky behaviors in patients testing HIV-positive or -negative and in untested persons (Evidence Table 1).[17] This update also did not assess the quality of included studies (Evidence Table 2). It found self-reported reductions in unprotected intercourse greater for persons testing HIV-positive (standardized effect size [d+] = 0.44, 95% CI 0.37 to 0.51) and for serodiscordant couples (d+ = 0.85, 95% CI 0.71 to 0.99) than for untested persons (d+ = 0.13, 95% CI 0.07 to 0.18) or those testing HIV-negative (d+ = 0.18, 95% CI 0.12 to 0.23). The number of self-reported sexual partners decreased more in persons testing HIV-positive (d+ = 0.34, 95% CI 0.20 to 0.47) or -negative (d+=0.24, 95% CI 0.15 to 0.34) than in untested persons (d+ = 0.07, 95% CI 0.03 to 0.18). These estimates are similar to earlier estimates based on studies published through 1997.[19]

Two other older systematic reviews were included in the 2005 evidence synthesis.[76, 77] Both found testing and counseling most effective in reducing risky behaviors (primarily rates of unprotected intercourse or condom use) among serodiscordant heterosexual couples and those testing HIV-positive, with less evidence for beneficial effects in other populations.

Interpreting the results of all the systematic reviews is difficult because the primary studies evaluated diverse populations, employed different counseling interventions, and frequently had methodological shortcomings. Reasons for testing were not reported, and it is not clear if the results are generalizable to asymptomatic patients who would be identified by screening. In addition, all the studies were conducted when guidelines recommended extensive pre-test counseling prior to HIV testing, and may not be generalizable to streamlined HIV screening without prevention counseling as recommended in the 2006 CDC recommendations. The content and duration of counseling was generally poorly described and varied dramatically between studies, and in some cases may have varied within studies.[17] Most studies used older counseling approaches and measured self-reported behavior changes, which could lead to over-reporting of socially desirable responses (reductions in risky behaviors).[78] None of the studies reported attempts to verify self-reported behaviors (by methods such as checking concordance with partners' reports or with rates of sexually transmitted diseases). Other methodological shortcomings also may have led to overestimates of changes in risky behaviors. For example, in two of the four published studies included in a new meta-analysis,[16] approximately 30% of patients failed to return for follow-up, and persons lost to follow-up were not considered when estimating rates of behavior changes.[79, 80] A third study reported no clear inception cohort.[81] Most studies did not adequately report methods for ascertaining risky behaviors or state whether investigators assessing rates of risky behaviors were blinded to testing status of subjects. In addition, in the two systematic reviews that pooled data, some estimates were associated with significant heterogeneity,[17] or heterogeneity was not reported.[16] In addition to the fact that the studies evaluated diverse populations and counseling interventions, another factor that could explain a portion of between-study heterogeneity is that studies evaluated changes in risky behavior at different times following testing.[17]

We found no new studies comparing the efficacy of different counseling methods on risky behaviors in HIV-infected persons. However, several[66, 82-84] trials reviewed in the 2005 evidence synthesis found targeted counseling (tailored to participants) or more intensive counseling associated with greater reductions in risky behaviors than standard or less intensive counseling.

Have Self-reported Reductions in Risky Behaviors Been Shown to Reduce Spread of Disease?

Using a mathematical formula, one new study using data from a new meta-analysis (reviewed above[16]) calculated an HIV transmission risk 3.5 times lower in HIV-positive patients aware of their status (6.9%) compared to those unaware (2.0%).[22] It estimated a 31% decline in new sexual infections per year (from 32,000 to 22,150) if all HIV-positive patients unaware of their status became aware. However, the reliability of these estimates is uncertain because studies included in the meta-analysis relied on self-reported behavior changes and had methodological flaws (such as attrition bias, lack of clearly defined inception cohorts, and unclear blinding of outcome assessors). Even if estimates of decreased risky behaviors are accurate, rates of HIV transmission are affected by a variety of factors (such as type of risky behaviors, number of risky behavior episodes, number of sexual partners, viral load, use of antiretroviral therapy, presence of other sexually transmitted diseases, CD4 count, and time since diagnosis),[85] many of which are not captured in the formula used in this study. The estimate of reductions in the number of new sexual infections also assumes that all patients who are HIV-positive will be tested and reduce behaviors accordingly. However, patients who are at highest risk for transmitting infection may not be equally likely to be tested or reduce risky behaviors compared to those at lower risk for transmitting infection. The formula also does not consider potential effects of testing in those with negative results, who had higher rates of subsequent STD's in some studies.[64, 65]

We identified no other new studies evaluating the association between changes in risky behaviors in HIV-positive persons and reduced risk of horizontal transmission. A systematic review included in the 2005 evidence synthesis found that consistent use of condoms, defined as use of a condom for all acts of penetrative vaginal intercourse, resulted in an 80% reduction in heterosexual transmission of HIV.[86] Another pooled analysis found condoms 90% to 95% effective when used consistently, and consistent condom users 10 to 20 times less likely to become infected when exposed to the virus than inconsistent or non-users.[87]

What Is the Cost-Effectiveness of Screening for HIV Infection in the General Population?

We identified no new cost-effectiveness analyses of HIV screening in the general population. In two good-quality studies included in the 2005 evidence synthesis, the cost-effectiveness of one-time HIV screening compared to no screening in outpatients with 1% prevalence of unidentified HIV infection was $38,000 to $42,000 per quality-adjusted life-year gained, when secondary transmission benefits were not included.[55, 56] Neither study included long-term cardiovascular harms associated with HAART when calculating cost-effectiveness.[88] In one of the studies, cost remained <$50,000 per quality-adjusted life-year at a prevalence of 0.5%.[55] After incorporating estimates of beneficial effects on secondary transmission, cost-effectiveness remained less than

$50,000 per quality-adjusted life-year at HIV prevalences substantially lower than seen in the general population (0.05%).[55] The other study, which did not directly incorporate secondary transmission benefits into its model, estimated an incremental cost-effectiveness of one-time screening in the general population (prevalence of unknown HIV infection 0.1%, corresponding to an overall HIV prevalence of about 0.4%) greater than $100,000 per quality-adjusted life-year.[56]

Neither cost-effectiveness analysis evaluated incremental cost-effectiveness ratios of a strategy of screening only persons reporting risk factors, as suggested by the 2005 USPSTF recommendations, compared with a strategy of universal screening in low-prevalence settings. In addition, in the study that included secondary transmission benefits, cost-effectiveness in low-prevalence settings was sensitive to estimates of beneficial effects of screening on transmission.[55] The other cost-effectiveness analysis did not directly incorporate secondary transmission benefits, but estimated that screening 100,000 persons in the general population would prevent 10 of the 780 to 1,060 expected secondary transmissions.[56] A subsequent analysis based on the model used in the latter study found that increasing rates of test notification and entry into care had a greater impact on cost-effectiveness than similar increases in rates of testing.[23]

IV. DISCUSSION

After reviewing new studies on HIV screening, we found insufficient evidence to change the main conclusions of our 2005 evidence synthesis. Specifically, the 2005 evidence synthesis found no direct evidence on the effects of HIV screening on clinical outcomes. However, it found good evidence that HIV screening can accurately identify infected persons and screening appears acceptable to most patients, though a significant proportion of persons are likely to decline routine screening, frequently because of a low perception of risk. Many patients are currently diagnosed at advanced stages of HIV disease, and a significant proportion does not receive test results or enter into medical care. Identification and treatment of asymptomatic HIV infection at immunologically advanced stages of disease can result in marked reductions in clinical progression and mortality, particularly with the use of HAART. Risk factor assessment can identify persons at increased risk of infection, though targeted screening would miss a significant number of infected persons with unidentified or unreported risk factors. The 2005 USPSTF and 2006 CDC recommendations are generally in agreement on each of these points.

For this brief update, we found no new studies directly evaluating the effects of HIV screening on transmission risk. The major difference between the 2005 USPSTF and the 2006 CDC recommendations appears related to conflicting interpretations of the strength of indirect evidence on effects of screening on HIV transmission. To support recommendations for routine HIV testing in most adolescents and adults, the CDC cites a new meta-analysis[16] that found that HIV-infected persons reduce their sexual high-risk behaviors substantially when they become aware of their infection, and a modeling study[22] predicting significant reductions in new HIV infections based on these estimates. However, we identified flaws in the studies included in the meta-analysis cited by the CDC, including reliance on self-reported changes in behavior, lack of defined inception cohorts, significant attrition, poorly described methods for assessing sexual risk behaviors, and unclear blinding status of outcomes assessors. These methodological

shortcomings probably led to overestimates of reductions in sexual risky behaviors. The reliability of models for estimating effects of reductions in risky sexual behaviors on transmission is also unknown, because of the difficulty of capturing accurately all the factors that can affect transmission, such as sustainability of behavior changes, effects on different types of behaviors, differences in baseline risk that could affect likelihood of testing and subsequent behavior changes, and effects of screening on those testing negative).

We also found that the cost-effectiveness of universal screening in low-risk, low-prevalence (<=0.3%) settings remains uncertain because cost estimates may be sensitive to transmission benefits. Excluding transmission benefits, one study found one-time screening in the general population cost >$100,000 per quality-adjusted life-year.[56] In addition, although routine screening appears cost-effective (<$50,000 per quality-adjusted life-year) relative to no screening when population prevalence of undiagnosed HIV infection is >=0.5%, the incremental cost-effectiveness of routine screening relative to targeted screening based on risk factors in low-prevalence settings has not been evaluated. Studies in federally-funded testing sites indicate that most patients at higher risk for HIV infection are likely to be identifiable through risk factor assessment even in lower-prevalence settings.[35] Studies that assess cost-effectiveness of routine versus targeted screening would be substantially more informative for a comparison of these strategies in low-prevalence settings. In addition, future cost-effectiveness analyses should include estimates of long-term harmful cardiovascular effects of HAART, which appear to increase over time.[88]

Although the 2006 CDC recommendations advise screening high-risk persons at least annually and testing patients and prospective partners before they initiate new sexual relationships, we found no new clinical studies evaluating optimal frequency of screening. A cost-effectiveness analysis, however, suggests that repeat screening at any interval costs more than $100,000 per quality-adjusted life-year in low-prevalence and low-incidence settings; however, the study did not incorporate potential beneficial effects on transmission.[56] Annual screening was not cost-effective (≥$100,000 per quality-adjusted life year) even in high-risk settings (prevalence of undiagnosed HIV infection 3% and incidence 1.20%). Screening every three years may be cost-effective (<$50,000 per quality-adjusted life-year) when prevalence is at least 1%, incidence is at least 0.09%, and potential transmission benefits are included.[55]

We also found no new studies evaluating the effects of routine screening in low-risk populations on the proportion of HIV-infected persons diagnosed at later stages of disease, on test notification rates, entry into care, or uptake of recommended interventions. Nor did we find new studies evaluating the effects of opt-out testing without prevention counseling in non-pregnant, low-risk persons, as advised in the 2006 CDC recommendations. One reason this is important is because currently available studies on the effects of HIV screening on risky behaviors have included standard pre-test counseling and risk assessment as suggested in previous CDC recommendations. The effects of eliminating routine prevention counseling on risky behaviors (either positive or negative) are unknown. The lack of data on screening uptake, linkage to care, and stage of diagnosis in low-risk, low-prevalence settings may be explained in part by the fact that, until recently, recommendations for HIV testing centered on high-risk and high-prevalence settings, with prenatal screening the major exception. Although opt-out testing appears acceptable to most pregnant women, it is not clear if such data are applicable to non-pregnant

persons, because a high value is placed on preventing HIV infection in newborns and there is strong evidence that interventions are effective for preventing mother-to-child transmission.[89]

In summary, there remains no direct evidence on benefits of screening for HIV infection in the general population. In the 2005 evidence synthesis, we found screening likely to be beneficial in average-risk patients , based on the effects of HAART in patients meeting criteria for treatment; however, a large number of patients would need to be screened to prevent one case of HIV disease progression or death. We estimated that the numbers needed to screen to prevent one case of clinical progression or death after three years ranged from 1,210 to 13,800 in the general population (Table 2).[1] At that time, we were unable to estimate effects of HIV screening on rates of secondary transmission. We concluded that evidence showing decreased secondary transmission following screening would greatly strengthen the case for routine screening in the general population. This is particularly important because expanded screening programs are likely to identify more HIV-infected patients at earlier stages of disease. In such patients, who are less likely to qualify for HAART, other beneficial effects—such as decreased transmission rates—assume greater relative importance when considering net benefits from screening.

After reviewing new evidence available since June 2004, we still cannot estimate the effects of screening on HIV transmission rates. Studies directly linking screening to decreased rates of transmission would require very large populations with long duration of follow-up, and are difficult to perform. Not surprisingly, no such studies have been published since the 2005 evidence synthesis was completed. Although reductions in risky behaviors are reported following HIV testing and counseling, self-reported behavior changes (an intermediate outcome) may be unreliable, and studies have probably overestimated reductions in risky sexual behaviors. In addition, even if estimates of changes in self-reported behaviors are accurate, predicting their effect on transmission rates remains problematic because of the complex relationships between risky behaviors, HAART use, differential effects in those testing negative compared to those testing positive, and other factors that affect transmission.

The 2005 USPSTF recommendations for HIV screening consist of testing based on individual risk factors as well as testing based on clinical setting, including criteria based on local prevalence of infection. For risk-based testing to be maximally effective, more studies are needed on effective and efficient methods of risk assessment and on ways of improving testing rates in those assessed as being at high risk. With regard to prevalence-based testing, the 2005 USPSTF recommendations cite the 2001 CDC threshold of 1% to routinely test, though recent cost-effectiveness studies suggest that a significantly lower threshold may be appropriate. Even if the threshold for testing is lowered, a persistent challenge for prevalence-based testing is that local prevalence data are often not readily available for practicing clinicians. One approach could be for clinicians to institute routine testing unless local prevalence data is available to guide further testing—a strategy advocated by the 2006 CDC recommendations.[3]

By eliminating the need for risk assessment or local prevalence information, universal testing is theoretically less burdensome for clinicians and easier to put into practice, though studies assessing implementation of routine opt-out testing in low-risk, low-prevalence settings are not yet available. Another potential effect of routine testing is to decrease the stigma associated with HIV screening and misperceptions about who may be at risk. However, the acceptability of

routine testing and rates of test uptake in low- or average-risk adults and adolescents has not been evaluated. Even in higher-risk settings, less than one-third of patients were tested after implementation of routine voluntary screening programs.[34, 38, 39, 41] Though difficult to quantify and based primarily on anecdotal evidence, potential harms from implementing routine screening in low-prevalence settings have also been identified,[1] including anxiety, labeling, adverse effects on close relationships, and a higher proportion of false-positive results. For example, rapid HIV tests are suggested in the 2006 CDC recommendations as a method for increasing test result notification rates, particularly in settings in which continuing relationships with patients do not exist.[3] However, based on the sensitivity and specificity of rapid tests, the calculated positive predictive value prior to confirmatory testing in a population with an HIV prevalence of 0.2% is 50%,[90] though actual false-positive rates may vary and in some settings are substantially lower than predicted.[91, 92] Laws in certain states, mandating specific informed consent or extensive pretest counseling, constitute an important barrier to implementing the 2006 CDC recommendations for streamlined, routine voluntary testing..[93]

Despite continuing educational efforts and longstanding recommendations for screening of high-risk persons and settings, HIV incidence remains steady in the U.S. Reducing the rate of new HIV infections is an important public health goal, and more effective implementation of screening programs could be an integral method for achieving this aim.[94] Studies comparing outcomes between general and targeted HIV screening in low-prevalence settings are urgently required to help clarify the advantages and disadvantages of these alternative approaches. To increase the success of all screening programs, more studies are also needed on methods for increasing HIV test uptake rates, particularly among high-risk persons, and for improving entry into care, reducing risky behaviors, and increasing use of recommended interventions in those testing positive.[23]

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Appendix 1. Quality Rating Criteria

Randomized Controlled Trials (RCTs) and Cohort Studies

Criteria

- Initial assembly of comparable groups**:** RCTs—adequate randomization, including concealment and whether potential confounders were distributed equally among groups; cohort studies—consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
- Maintenance of comparable groups (includes attrition, cross-overs, adherence, contamination)
- Important differential loss to follow-up or overall high loss to follow-up
- Measurements: equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- Important outcomes considered
- Analysis: adjustment for potential confounders for cohort studies, or intension-to-treat analysis for RCTs

DEFINITION OF RATINGS BASED ON ABOVE CRITERIA

Good: Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (follow-up at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; important outcomes are considered; and appropriate attention to confounders in analysis.

Fair: Studies will be graded "fair" if any or all of the following problems occur, without the important limitations noted in the "poor" category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred in follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for.

Poor: Studies will be graded "poor" if any of the following major limitations exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention.

Case Control Studies

Criteria

- Accurate ascertainment of cases
- Nonbiased selection of cases/controls with exclusion criteria applied equally to both
- Response rate
- Diagnostic testing procedures applied equally to each group
- Measurement of exposure accurate and applied equally to each group
- Appropriate attention to potential confounding variable

Definition of ratings based on criteria above

Good: Appropriate ascertainment of cases and nonbiased selection of case and control participants; exclusion criteria applied equally to cases and controls; response rate equal to or greater than 80 percent; diagnostic procedures and measurements accurate and applied equally to cases and controls; and appropriate attention to confounding variables.

Fair: Recent, relevant, without major apparent selection or diagnostic work-up bias but with response rate less than 80 percent or attention to some but not all important confounding variables.

Poor: Major selection or diagnostic work-up biases, response rates less than 50 percent, or inattention to confounding variables.

Quality ratings criteria for randomized controlled trials, cohort studies, and case-control studies based on methods developed by the USPSTF.[1]

Systematic Reviews

Criteria

- Were the search methods reported?
- Was the search comprehensive?
- Were the inclusion criteria reported?
- Was selection bias avoided?
- Were the validity criteria reported?
- Was validity assessed appropriately?
- Were the methods used to combine studies reported?
- Were the findings combined appropriately?
- Were the conclusions supported by the reported data?
- What was the overall scientific quality of the overview?

DEFINITION OF RATINGS BASED ON ABOVE CRITERIA

Good: Recent, comprehensive review that uses explicit criteria to identify and select studies for inclusion, uses appropriate methods to assess quality of primary studies appropriately, and uses appropriate methods for synthesizing or combining results

Fair: Systematic methods for identifying studies but doesn't meet one or more of the criteria listed above.

Poor: No systematic methods for identifying studies, major selection bias, or inappropriate methods for combining or pooling data

Quality criteria for systematic reviews are based on those developed by the USPSTF [1] and by Oxman and Guyatt.[2]

Cost-effectiveness Studies

Criteria

- Are interventions and populations compared appropriate?
- Is the study conducted from the societal perspective?
- Is the time horizon clinically appropriate and relevant to the study question?
- Are all important drivers of effectiveness included?
- Are key harms included?
- Is the best available evidence used to estimate effectiveness?
- Are long-term outcomes used?
- Do effects measured capture preferences or utilities?
- Are all appropriate downstream costs included?
- Are charges converted to costs appropriately?
- Are the best available data used to estimate costs?
- Are incremental cost-effectiveness ratios (ICERs) presented?
- Are appropriate sensitivity analyses performed?

Quality criteria for cost-effectiveness studies are based on those developed by the USPSTF for evaluation of cost effectiveness analyses.[3] We used these criteria to guide our categorization of studies as good, fair, or poor. Quality grades were assigned based on a subjective assessment of study design and quality of data inputs.

References

1. Harris RP, Helfand M, Woolf SH, et al. Current methods of the third U.S. Preventive Services Task Force. *Am J Prev Med.* 2001;20(3S):21-35.
2. Oxman AD, Guyatt GH. Validation of an index of the qulaity of review articles. *Journal of Clinical Epidemiology.* 1991;44(11):1271-1278.
3. Saha S, Hoerger TJ, Pignone MP, Teutsch SM, Helfand M, Mandelblatt JS. The art and science of incorporating cost effectiveness into evidence-based recommendations for clinical preventive services. *Am J Prev Med.* 2001;20(3S):36-43.

Table 1. 2001 CDC Recommendations for Counseling and Testing for HIV Infection*

Recommended screening	Examples
All clients in settings serving populations at increased behavioral or clinical HIV risk (regardless of setting HIV prevalence)	Adolescent or school-based health clinics with high rates of sexually transmitted diseases Clinics serving men who have sex with men Correctional facilities, prisons, juvenile detention centers Drug or alcohol prevention and treatment programs Freestanding HIV test sites Homeless shelters Outreach programs (e.g., syringe exchange programs) Sexually transmitted diseases clinics Tuberculosis clinics (only persons with confirmed or suspected tuberculosis and their contacts)
Individual clients in setting with <1% HIV prevalence who have: -Clinical signs or symptoms suggesting HIV infection -Diseases suggesting increased risk for HIV infection -Self-report HIV risks -Specifically request an HIV test	Fever or illness of unknown origin Opportunistic infection (including active tuberculosis disease) without known reason for immune suppression Another sexually transmitted disease or bloodborne infection Injection drug use with shared injection equipment (e.g., needles, syringes, cotton, water) Unprotected intercourse with someone suspected of being infected (partner injects drugs, diagnosed or treated for a sexually transmitted disease or hepatitis, has had multiple or anonymous sex partners, or has exchanged sex for drugs or money) Unprotected vaginal or anal intercourse with more than one sex partner Diagnosed or treated for a sexually transmitted disease, hepatitis, or tuberculosis
All clients in settings with a $\geq$1% HIV prevalence	Specific inpatient and outpatient settings with known high prevalence
Regardless of setting prevalence or behavioral or clinical risk: -All pregnant women -All clients with possible acute occupational exposure -All clients with known sexual or needle-sharing exposure to an HIV-infected person	

*Source: Centers for Disease Control and Prevention. Revised guidelines for HIV counseling, testing, and referral. *MMWR*. 2001;50(RR-19):1-57.[11]

Table 2. Outcomes Table of Counseling and One-time Screening for HIV Infection After Three Years in 10,000 Asymptomatic Adolescents and Adults

Variable	Average-risk population	Prevalence 1%	High-risk	Source*
Base-case Assumptions				
Prevalence of HIV infection	0.3%	1%	5-15%	CDC, 2002 McQuillan, 1997 Valleroy, 2000 Holmberg, 1996
Yield of partner notification (newly diagnosed HIV per index patient)	0.08-0.23	0.08-0.23	0.08-0.23	Macke, 1999 CDC, 2003
Accuracy of standard testing	99%+	99%+	99%+	Weber, 1995 McAlpine, 1994 CDC, 1990 CDC, 1988
Proportion of HIV-positive patients who receive test results	79-93%	79-93%	79-93%	Erickson, 1990 Hightow, 2003 CDC, 2004 Molitor, 1999
Proportion of patients who would qualify for treatment (assuming only patients with CD4 count <200 cells/mm3 treated)	12-43%	12-43%	12-43%	Samet, 2001 Katz, 1992 Luby, 1994 Hutchinson, 1991 Klein, 2003
Proportion of patients qualifying for antiretroviral therapy who would receive it	53-85%	53-85%	53-85%	Stall, 2001 Cunningham, 2000 Kaplan, 1999 McNaghten, 2003

Table 2. Outcomes Table of Counseling and One-time Screening for HIV Infection After Three Years in 10,000 Asymptomatic Adolescents and Adults

Variable	Average-risk population	Prevalence 1%	High-risk	Source*
Base-case Assumptions continued				
3-year risk of clinical progression or death in untreated patients with CD4 count <200 cells/mm3	86% (95% CI 77%-93%)	86% (95% CI 77%-93%)	86% (95% CI 77%-93%)	Mellors, 1997
Relative risk for clinical progression or death with HAART compared to no treatment	0.35 (95% CI 0.25-0.47)	0.35 (95% CI 0.25-0.47)	0.35 (95% CI 0.25-0.47)	Calculated from Jordan 2002 using random effects model
Background rate of myocardial infarction (cases per 3 person-years)	0.00158 (95% CI 0.000508-0.00487)	0.00158 (95% CI 0.000508-0.00487)	0.00158 (95% CI 0.000508-0.00487)	Calculated from Friis-Moller 2003, Figure 1
Relative risk for myocardial infarction with HAART after 2-4 years compared to no treatment	7.73 (95% CI 2.42-24.71)	7.73 (95% CI 2.42-24.71)	7.73 (95% CI 2.42-24.71)	Calculated from Friis-Moller 2003, Figure 1
Background rate of cardio- or cerebrovascular (myocardial infarction, stroke, or invasive cardiovascular procedure) events (cases per 3 person-years)	0.00368 (95% CI 0.00175-0.00770)	0.00368 (95% CI 0.00175-0.00770)	0.00368 (95% CI 0.00175-0.00770)	Calculated from Writing Group of the DAD Study 2004, Figure 1
Relative risk for cardio or cerebrovascular events with HAART after 2-4 years compared to no treatment	5.00 (95% CI 2.31-10.82)	5.00 (95% CI 2.31-10.82)	5.00 (95% CI 2.31-10.82)	Calculated from Writing Group of the DAD Study 2004, Figure 1
Relative risk for spread of disease	Unable to estimate	Unable to estimate	Unable to estimate	

Results on next page

Table 2. Outcomes Table of Counseling and One-time Screening for HIV Infection After Three Years in 10,000 Asymptomatic Adolescents and Adults

Variable	Average-risk population	Prevalence 1%	High-risk
Results			
Number screened	10000	10000	10000
Number identified as positive	30	100	500-1500
Number receiving test results	23.7-27.9	79-93	395-1395
Partners identified as HIV-positive	1.90-6.42	6.3-21.4	31.6-321
Total number of HIV-positive patients identified	25.6-34.3	85-114	426-1716
Number with CD4 count <200 cells/mm^3	3.07-14.8	10.2-49.2	51-738
Number with CD4 count <200 cells/mm^3 who would progress without treatment after 3 years	2.6 (95% CI 2.4-2.9) - 12.6 (95% CI 11.5-13.8)	8.8 (95% CI 8.0-9.6) - 42 (95% CI 38-46)	44 (95% CI 40-49) - 636 (95% CI 576-692)
Number receiving antiretroviral treatment	1.63-12.5	5.4-41.8	27-627
Clinical progression or death prevented over 3 years with HAART	0.9 (95% CI 0.7-1.1) - 7.0 (95% CI 5.6-8.2)	3.0 (95% CI 2.4-3.6) - 23.3 (95% CI 18.6-27.5)	15.1 (95% CI 12.1-17.8) - 350 (95% CI 279-412)
Number needed to screen to prevent 1 clinical progression or death over 3 years	1430 (95% CI 1213-1792) - 11018 (95% CI 9348-13804)	429 (95% CI 364-538) -3306 (2804-4145)	29 (95% CI 24-36) - 661 (95% CI 560-829)
Number needed to treat with HAART to prevent 1 clinical progression or death over 3 years	1.8 (95% CI 1.5-2.2)	1.8 (95% CI 1.5-2.2)	1.8 (95% CI 1.5-2.2)
Numbers need to counsel, screen, or treat to prevent 1 horizontal transmission over 3 years	Unable to calculate	Unable to calculate	Unable to calculate
Background number of myocardial infarctions in patients receiving antiretroviral therapy over 3 years	0.003 (95% CI 0.0008-0.008) - 0.020 (95% CI 0.006-0.06)	0.008 (95% CI 0.003-00026) - 0.066 (95% CI 0.02-0.20)	0.04 (95% CI 0.01-0.13) - 0.99 (95% CI 0.3-3.1)

Table 2. Outcomes Table of Counseling and One-time Screening for HIV Infection After Three Years in 10,000 Asymptomatic Adolescents and Adults

Variable	Average-risk population	Prevalence 1%	High-risk
Results continued			
Myocardial infarctions caused by HAART over 3 years	0.02 (95% CI 0.002-0.09) - 0.13 (95% CI 0.02-0.73)	0.06 (95% CI 0.008-0.31) - 0.44 (95% CI 0.06-2.43)	0.28 (95% CI 0.04-1.6) - 6.55 (95% CI 1.0- 36)
Number needed to screen to cause 1 myocardial infarction over 3 years	76330 (95% CI 13730-507100) - 588080 (95% CI 105790-3907130)	22850 (95% CI 4100-152950) - 176050 (95% CI 31580-1178480)	1520 (95% CI 270-10250) - 35250 (95% CI 6340-236880)
Number needed to treat with HAART to cause 1 myocardial infarction over 3 years	96 (95% CI 17-636)	96 (95% CI 17-636)	96 (95% CI 17-636)
Background number of cardio- or cerebrovascular events in patients receiving antiretroviral therapy over 3 years	0.006 (95% CI 0.003-0.01) - 0.05 (95% CI 0.02-0.10)	0.02 (95% CI 0.01-0.04) - 0.15 (95% CI 0.07- 0.3)	0.1 (95% CI 0.05-0.2) - 2.3 (95% CI 1.1-4.8)
Cardio- or cerebrovascular events caused by HAART over 3 years	0.02 (95% CI 0.006-0.08) - 0.2 (95% CI 0.05-0.6)	0.08 (95% CI 0.02-0.26) - 0.6 (95% CI 0.2-2.0)	0.4 (95% CI 0.1-1.3) - 9.13 (95% CI 2.4-30)
Number needed to screen to cause 1 cardio- or cerebrovascular event over 3 years	54740 (95% CI 16860-205130) - 421770 (95% CI 129890-1580520)	16410 (95% CI 510-61570) - 126450 (95% CI 39030-474410)	1100 (95% CI 340-4110) - 25310 (95% CI 7790-94980)
Number needed to treat with HAART to cause 1 cardio- or cerebrovascular event over 3 years	69 (95% CI 21-257)	69 (95% CI 21-257)	69 (95% CI 21-257)

*Reprinted from Chou R, Huffman LH, Fu R, Smits AK, Korthuis PT. Screening for human immunodeficiency virus in adolescents and adults (Evidence Synthesis Number 38); July 2005. Available at: *http://www.ahrq.gov/downloads/pub/prevent/pdfser/hivrevsyn.pdf* . Accessed September 22, 2006.[1]

Evidence Table 1. Systematic Reviews Published Since 2004 on Effects of HIV Testing on Rates of Risky Behaviors or New Sexually Transmitted Infections

Author, year	Purpose of study	Databases searched, date of last search	Number of studies	Types of studies included/limitations of primary studies
Marks, 2005[16]	To compare the prevalence of high-risk sexual behaviors in HIV+ persons aware of their serostatus with that in HIV+ persons unaware of their status in the U.S. and to discuss implications for HIV prevention programs	MEDLINE, PubMed, PsycINFO, AIDSLINE, Sociofile (through January 2004) Language: not specified. English only assumed	4 studies, 4 multi-site data sets. 11 findings described as independent.	4 studies from peer-reviewed journals and 4 multisite data sets. Meta-analysis of 11 findings described as independent: 6 comparing HIV+ aware persons with independent groups of HIV+ unaware persons (between-group comparisons) and 5 comparing seroconverting persons before and after HIV+ status notification (within-subject comparisons). Outcomes: self-reported unprotected anal or vaginal intercourse (UAV) during specified recall periods. Limitations: lack of clearly defined inception cohorts, risk of attrition bias, no assessment of quality, no report of reasons studies were excluded, self-reported outcomes.
Weinhardt, 2005[17]	To review and synthesize empirical evidence of effects of HIV diagnosis on sexual risk behavior to determine: 1) What is the magnitude of reduction in sexual risk behavior resulting from an HIV diagnosis? 2) How long do reductions in risk behavior persist? 3) What needs to be done to maximize beneficial effects of an HIV diagnosis on transmission risk behavior?	MEDLINE, PsycINFO (through November 2003) Language: not specified. English only assumed	23	Included studies provided an assessment of when at least some participants received an HIV+ diagnosis relative to data collection, sexual behavior outcome data or a proxy measure, $\geq$ 2 assessments with the same participants, data from a sample independent from earlier included studies, summary or inferential statistics sufficient for calculation of within-group effect sizes. Limitations: self-reported sexual risk behaviors, lack of distinction between high risk sexual behavior and sexual behavior, no assessment of quality, risk of attrition bias, lack of information on study inclusion, poorly described content and duration of counseling.

Evidence Table 1. Systematic Reviews Published Since 2004 on Effects of HIV Testing on Rates of Risky Behaviors or New Sexually Transmitted Infections

Author, year	Methods for rating quality of primary studies	Methods for synthesizing results of primary studies	Number of patients (treatment and control)	Interventions
Marks, 2005[16]	Quality not rated	A mathematical formula was used to calculate HIV transmission risk. Effect sizes were estimated with a prevalence ratio and a random-effects model was used for aggregating individual effect sizes. Sensitivity analyses were used for outliers and stratified analyses to control for type of comparison (between group vs within subject) and gender. An adjustment factor was applied to studies that assessed self-reported sexual behavior with any partner, and the analysis was conducted with and without this adjustment. This adjustment focused the analysis on behavior with partners at risk for infection.	Between group comparisons: 12,468 HIV+ aware vs 894 HIV+ unaware Within subject comparisons: 343 HIV+ aware	Notification of HIV+ serostatus
Weinhardt, 2005[17]	Quality not rated	Effect sizes calculated (standardized mean difference index, d+) for sexual risk behaviors before and after HIV testing and counseling. These behaviors included: unprotected intercourse, condom use, and number of sexual partners. Effect size was estimated when only *n* and significance levels were available. Pooled standard deviation was used when only the mean and standard deviation were available.When dichotomous outcomes were reported, proportions were used as means and pooled standard deviations were derived. A correction for bias due to sample size was applied to calculated effect size. For each study, within-group effect sizes were computed separately for each sexual behavior outcome for each group (HIV+, HIV-, untested, serodiscordant couples, and mixed samples).Effect sizes for serodiscordant couples and mixed samples were calculated separately. Each participant was included in only 1 effect size for each outcome to avoid violating the assumption of independence of effect sizes. Fixed-effect procedures were used for analyses. The homogeneity of variance statistic *Q* was computed.	Final set of 62 effect sizes derived from 23 studies with a total population of 28,786. couples, HIV+ men: n=962 couples, HIV+ women: n=1120 couples, HIV+: n=310 couples, HIV-: n=970 couples, HIV status discordant: n=622 HIV+ individuals: 3686 HIV- individuals: 10,915 untested individuals: 10,201	Notification of HIV serostatus

Evidence Table 1. Systematic Reviews Published Since 2004 on Effects of HIV Testing on Rates of Risky Behaviors or New Sexually Transmitted Infections

Author, year	Results	Adverse events	Quality rating
Marks, 2005[16]	HIV+ aware versus HIV+ unaware Prevalence unprotected anal or vaginal intercourse with any partner: 53% lower (95% CI 45% to 60%) Prevalence unprotected anal or vaginal intercourse with partners not HIV+: 68% lower (95% CI 59% to 76%)	Not reported	Fair
Weinhardt, 2005[17]	All results reported as standardized effect sizes (d+); positive effect sizes indicate reduction in risky behaviors <u>Unprotected intercourse:</u> Tested, HIV+: d+=0.44*; 95% CI, 0.37 to 0.51 Serodiscordant couples: d+=0.85; 95%CI, 0.71 to 0.99 Untested: d+=0.13; 95% CI, 0.07 to 0.18 Tested, HIV-: d+=0.18*; 95% CI, 0.12 to 0.23, p<.001 <u>Condom use:</u> Tested, HIV+: d+=0.59; 95% CI, 0.38 to 0.81 Serodiscordant couples: d+=1.31*; 95% CI, 1.14 to 1.48 Untested: d+=0.49*, 95% CI 0.37 to 0.61 Tested, HIV-: d+=0.26, 95% CI 0.11 to 0.41 <u>Number of sexual partners:</u> Tested, HIV+: d+=0.34; 95% CI, 0.20 to 0.47 Tested, HIV-: d+=0.24*; 95% CI, 0.15 to 0.34 Untested: d+=0.07; 95% CI, 0.03 to 0.18 <u>HIV and STD incidence:</u> Tested, HIV+: d+=0.18, 95% CI; 0.08 to 0.28 Tested, HIV-: d+=-0.12, 95% CI, -0.22 to -0.02 Untested: d+=-0.05, 95% CI, -0.09 to -0.01 **Indicates significant (p<0.05) test for heterogeneity*	Not reported	Fair

Evidence Table 2. Quality Rating of Systematic Reviews Published Since 2004 on Effects of HIV Testing on Rates of Risky Sexual Behaviors or Sexually Transmitted Diseases

Author, year	Search methods reported	Search compre-hensive	Inclusion criteria reported	Selection bias avoided	Validity criteria reported	Validity assessed appropriately	Methods used to combine studies reported	Findings combined appropriately	Conclusions supported by reported data	Overall scientific quality of review
Marks, 2005[16]	Yes	Yes	Yes	Cannot tell - specific study exclusion reasons not provided	No (no QR)	No (sensitivity analysis, but no QR)	Yes	Cannot tell	Cannot tell	2 - 3 major flaws
Weinhardt, 2005[17]	Yes	Yes	Yes	Cannot tell - reason for exclusion provided for 2 studies - not clear if others were also excluded	No (no QR)	No (no QR)	Yes	Cannot tell	Cannot tell	2 - 3 major flaws