CLINICAL CARE OPTIONS
HIV

Jointly sponsored by
Northwestern University's Feinberg School of Medicine (NUFSM)
and Clinical Care Options, LLC

New Insights Into Prevention of HIV and Other Sexually Transmitted Infections

Program Director

John P. Phair, MD
Emeritus Professor of Medicine
Division of Infectious Diseases
Northwestern University Feinberg, School of Medicine
Chicago, Illinois

Faculty

King K. Holmes, MD, PhD
Director, Center for AIDS and Sexually Transmitted Diseases
Professor of Medicine
University of Washington, Seattle
Seattle, Washington

Contributor

Walter H. Curioso, MD, MPHc
Contributing Author

Staff

Deanna M. Heier, PhD
Associate Managing Editor
Clinical Care Options, LLC

Edward King, MA
Vice-President, Editorial
Clinical Care Options, LLC

John Hawes
Science Writer and Editor

Bobbi Nodell, MA
Contributing Writer

Release Date

Release Date: July 25, 2005; Valid for credit through July 24, 2006.

Disclosures

John P. Phair, MD, has no significant financial interests to disclose.

King K. Homes, MD, PhD, has disclosed that he has received grants/research support from Roche Pharmaceuticals and has served on the advisory board for Merck. In this activity, Dr. Holmes discusses the unlabeled use of nonoxynol-9 in the prevention of HIV.

Walter H. Curioso, MD, MPHc, has no significant financial relationships to disclose.

Deanna M. Heier, PhD has no significant financial interests to disclose.

Edward King, MA, has no significant financial interests to disclose.

John Hawes has disclosed that he has served as a consultant for Pfizer.

Bobbi Nodell, MA, has no significant financial interests to disclose.

Target Audience

This activity is intended for physicians, nurses, pharmacists, and other healthcare community members providing frontline clinical care for persons with HIV/AIDS.

Purpose

The purpose of this activity is to provide physicians with up-to-date information regarding the prevention of HIV and other sexually transmitted infections.

Learning Objectives

Upon completion of this activity, participants should be able to:

- Describe randomized controlled trials of prevention of STI/HIV transmission
- Discuss the interventions that have been successful to prevent or reduce transmission
- Identify other interventions that appear promising to control the HIV epidemic

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Northwestern University's Feinberg School of Medicine and Clinical Care Options, LLC. Northwestern University's Feinberg School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Physician Continuing Medical Education

Northwestern University's Feinberg School of Medicine Office of Continuing Medical Education designates this educational activity for a maximum of 1.5 category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only credits that he/she actually spent in the activity.

Nursing Continuing Education

Approved for 1.5 contact hours of continuing education for RNs, LPNs LVNs and NPs. This program is cosponsored with Medical Education Collaborative, Inc. (MEC) and Clinical Care Options, LLC. MEC is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. Provider approved by the California Board of Registered Nursing, Provider Number CEP 12990, for 1.5 contact hours.

Pharmacist Continuing Education

Approved for 1.25 contact hours (0.125 CEUs) of credit for pharmacists. Approval of this course for pharmacists is under a cosponsorship agreement between Medical Education Collaborative, Inc. (MEC) and Clinical Care Options, LLC. MEC is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. ACPE # 815-999-05-083-H02. This program is designed for all pharmacists.

Credit Hours Available

Physicians: maximum of 1.5 category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.
Nurses: Approved for 1.5 contact hours of continuing education for RNs, LPNs, LVNs, and NPs.
Pharmacists: Approved for 1.25 contact hours (0.125 CEUs) of credit for pharmacists.

Instructions for Credit

Participation in this self-study activity should be completed in approximately 1.5 hours. To successfully complete this activity and receive credit, participants must follow these steps during the period from July 25, 2005 through July 24, 2006:

1. Register online at http://clinicaloptions.com
2. Read the target audience, learning objectives, and faculty disclosures.
3. Study the educational activity online or printed out.
4. Submit answers to the post-test questions and evaluation questions online.

You must receive a test score of at least 70% and respond to all evaluation questions to receive a certificate. After submitting the evaluation, you may access your online certificate by selecting the certificate link on the post-test confirmation page. Records of all CME activities completed can be found on the "My CME" page. There are no costs/fees for this activity.

This activity is supported by educational grants from:

Abbott Laboratories
Boehringer Ingelheim
Bristol-Myers Squibb Company
GILEAD
gsk GlaxoSmithKline
MERCK
ORTHO BIOTECH
Tibotec Therapeutics
Roche
TRIMERIS

Disclaimer

The materials published on the Clinical Care Options Web site reflect the views of the reviewers or authors of the CCO material, not those of Clinical Care Options, LLC, the CME provider, or the companies providing educational grants. The materials may discuss uses and dosages for therapeutic products that have not been approved by the United States Food and Drug Administration. A qualified health care professional should be consulted before using any therapeutic product discussed. Readers should verify all information and data before treating patients or using any therapies described in these materials.

New Insights Into Prevention of HIV and Other Sexually Transmitted Infections

Contents

Introduction

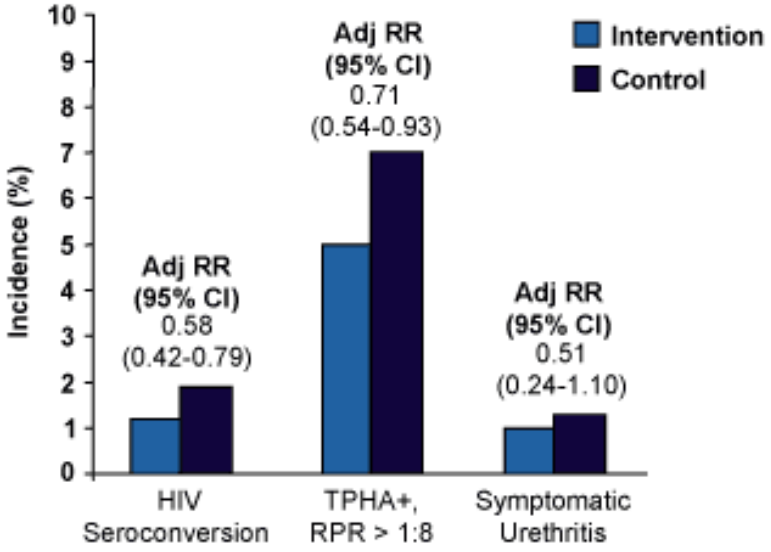
HIV continues to infect 14,000 people per day worldwide[1] despite a variety of prevention efforts. In the United States, the number of new infection cases has hovered around 40,000 per year since 1992,[2] falling far short of the Centers for Disease Control and Prevention (CDC)'s goal of reducing that number to 20,000 per year by 2005.[3] This review will focus on randomized controlled trials of the prevention of HIV in both the general population and individuals known to be HIV-seropositive. It will also examine successful means of preventing HIV acquisition as well as promising efforts to control the HIV epidemic.

The randomized controlled trials of individual-level, population-level, and multilevel interventions for preventing sexually transmitted infections, including HIV infections, were recently reviewed.[4] Of 85 trials identified, 43 had systematic objective measurements of sexually transmitted disease (STD) outcomes. Although only 1 intervention showed efficacy against sexual transmission of HIV, 22 (51%) showed effectiveness against other STDs.

Examples of Prevention Trials With Different Outcomes: The Mwanza Trial

The only randomized controlled trial that showed efficacy in preventing the transmission of HIV was conducted between 1991 and 1994 in the Mwanza region of Tanzania, Africa. Grosskurth and colleagues[5] estimated that the improved management of persons with STDs resulted in a 42% reduction of HIV incidence (Figure 1). \No other HIV intervention has had such a major effect on infection rates. This trial marked the first demonstration that STD treatment could also succeed in preventing HIV infection in the general population.

Figure 1. Impact of syndromic management on the incidence of HIV and other STDs in the Mwanza community randomized trial.[5]



Adj, adjusted; CI, confidence interval; RPR, rapid plasma reagin; RR, relative risk; TPHA, Treponema pallidum hemagglutination assay.

In this study, HIV incidence was compared in 6 intervention communities and 6 pair-matched comparison communities. A randomly selected cohort of approximately 1000 adults from each community, aged from 15 to 54 years, was surveyed at baseline and at follow-up 2 years later. The intervention consisted of 5 components:

- Establishment of an STD reference clinic and laboratory
- Training of existing staff from health centers and dispensaries in the intervention cities
- Use of syndromic treatment algorithms for the treatment of STDs
- Regular supply of drugs to treat STDs effectively
- Regular supervisory visits to health facilities that provided health education about STDs.

This study showed that simple, replicable STD care activities integrated into primary healthcare services led to a reduction of about 40% in HIV transmission.[5,6] The potential for STD/HIV reduction was the largest among young women (15-24 years). However, the reproducibility and sustainability of this outcome needs to be observed as the quality of health care declines in many developing countries. For example, except where separate distribution systems are established, access to drugs required to treat STDs is primarily a function of the general level of drug access, as was the case in the Mwanza trial.

Examples of Prevention Trials With Different Outcomes: The Rakai and Masaka Trials

The positive results from the Mwanza trial need to be balanced against the negative results of other similar studies involving STD treatment intervention. Shortly after the Mwanza trial, a study that focused on treating all members of 5 clusters of paired communities was conducted in Uganda's Rakai district. The periodic mass treatment in Rakai did not result in any decline in the incidence of HIV infection. One conclusion could be that ongoing syndromic treatment is a more effective strategy than periodic mass treatment. However, the results of a third trial, in the Masaka district of Uganda, which neighbors Rakai, refuted this hypothesis. In the latter trial, syndromic treatment had no effect on the incidence of HIV infection.[7]

Korenromp and associates[7] performed simulation modeling of HIV and STD transmission in these 3 studies and found that the lack of impact of the Rakai and Masaka interventions could be explained by the lower prevalence of curable STDs in Rakai and Masaka, which would be the result of changes in sexual behavior in Uganda since the Mwanza study. The researchers also found that, in the mature HIV epidemics in Uganda, most cases of HIV transmission occurred outside core groups with high STD rates, which would also have contributed to the interventions' lack of impact on HIV incidence.

These researchers concluded that lower-risk behavior and the mature HIV epidemic explained the limited impact of STD treatment on HIV incidence in Uganda in the 1990s; however, in populations with high-risk sexual behavior and high STD rates (ie, much of the world, where HIV epidemics are usually concentrated rather than generalized), STD treatment interventions can still contribute substantially to the prevention of HIV infection.[7]

How Well Have Behavior Change Interventions Worked?

The AIDS case that alarmed health officials in New York City in February 2005 illustrates the challenge and importance of promoting and sustaining changes in sexual behavior. The patient, a 46-year-old man infected with a multidrug-resistant strain of HIV who progressed rapidly to AIDS, reported having engaged in sexual intercourse with a number of men. Some of these encounters were with anonymous partners while the patient was using crystal methamphetamine.[8] This risky pattern of unprotected sex in association with the use of this illegal stimulant now is reportedly common in cities across the United States.[9,10]

The most ambitious effort to develop and test an intervention to reduce HIV transmission rates among gay men at high risk was the EXPLORE project, a randomized controlled trial of a behavioral intervention to prevent HIV infection in men who have sex with men (MSM).[11] In this study, no statistically significant reduction in HIV acquisition was found. The study, which started in 1999, monitored 4296 HIV-1 seronegative MSM who reported having engaged in anal sex with 1 or more partners in the previous year. The men were recruited from 6 US cities: Boston, Chicago, Denver, New York, San Francisco, and Seattle. Half of the men received 10 sessions of one-on-one counseling over 4 to 6 months, and then maintenance sessions were offered every 3 months. The other half received twice-yearly counseling on risk reduction based on the CDC Project RESPECT model.[12] In Project RESPECT, the CDC found that enhanced counseling, defined as 4 interactive counseling sessions based on theories of behavioral science, and “brief counseling”, defined as 2 short interactive counseling sessions based on the CDC client-centered HIV Prevention Counseling model, were more effective in preventing STDs than were didactic messages, ie, the typical form of counseling currently given at many volunteer counseling and testing sites.[12]

In the EXPLORE project, the rate of acquisition of HIV infection, after adjustment for baseline covariates, was 15.7% lower in the intervention group than in the standard group (95% CI, 8.4-34.4). The difference between the standard and intervention groups was not statistically significant. The effect of the intervention appeared to be somewhat more favorable in the first 12 to 18 months of follow-up, but this was not sustained.

Although other behavioral trials are ongoing, few, if any, are adequately powered to demonstrate an objective measure of the intervention’s impact on HIV acquisition. For example, in March 2005, Baptiste and colleagues[13] reported preliminary data on the Chicago HIV Prevention and Adolescent Mental Health Project (CHAMP), a program developed and implemented to decrease HIV and AIDS risk exposure among youth living in a community dramatically affected by HIV/AIDS. In the CHAMP approach, a collaborative partnership between academic researchers from a local university and parents, school staff, agency representatives, and other residents of the neighborhood in which the program was delivered (the community) provided many of the ideas and strategies that helped customize the program for the youths. So far, there are limited outcome data attesting to the effectiveness of the CHAMP Program in decreasing the risk of HIV exposure, but there are encouraging signs. Youths participating in the program reported a decrease in family conflicts and improvement in parental decision-making. They also reported that they were more likely to break off undesirable relationships and that they were less frequently in situations that might lead to sexual activity.

How Effective Are Male Condoms in Preventing HIV?

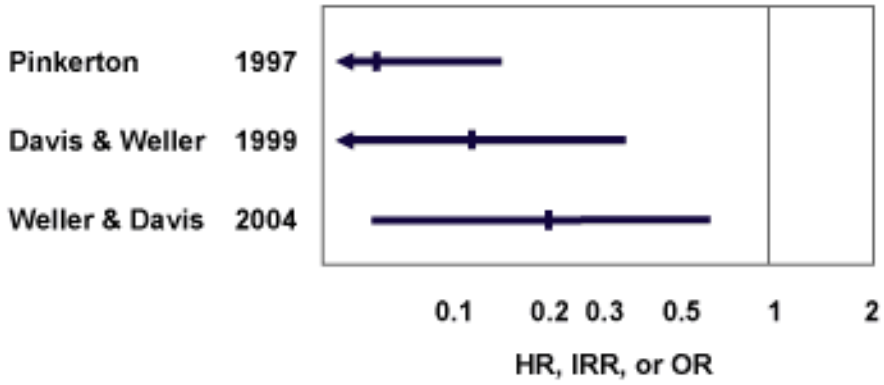
Condom promotion has been associated with a substantial reduction in HIV incidence in many studies, particularly in countries, such as Thailand, where both transmission and condom promotion are concentrated in commercial sex.[14]

Even in Uganda, where President Yoweri Museveni has strongly advocated fidelity and abstinence while not advocating condom use, and where ecologic data have suggested that abstinence and fidelity have been particularly important in reducing HIV incidence in the general population, according to a recent survey in the Rakai region of Uganda, condom use also contributed to lowering HIV transmission.[15]

A series of meta-analyses of published longitudinal studies has estimated that consistent condom use was 80% to 95% effective in preventing HIV transmission.[16] However, the studies included in the meta-analyses did not report on whether condoms were used correctly at every intercourse. Because a randomized trial to document the actual effectiveness of using condoms for HIV infection prevention in high risk persons would be unethical, these meta-analyses provide the best information available on the extent to which male condoms prevent transmission of HIV.

Recent prospective observational studies have shown that couple fidelity and condom use (Figure 2) have been associated with decreased risk of acquisition of virtually all STDs examined.[4]

Figure 2. Effectiveness of male condom use in preventing HIV infection.[4]



HR, hazard ratio; IRR, incidence rate ratio; OR, odds ratio.

How Effective Are Female Condoms in Preventing HIV?

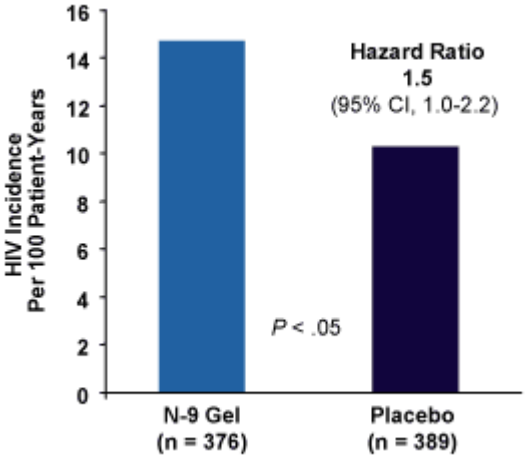
No conclusive evidence exists on the use of the female condom in reducing the rate of HIV infection, but studies are ongoing. In Thai brothels where male or female condoms were randomly distributed, a nonsignificant (16%) decrease in incident STDs was observed compared with brothels that received male condoms only.[17] On Kenyan plantations where intensive information, education, and communication programs on HIV prevention were accompanied with a distribution of both female and male condoms or of male condoms only, no difference in incidence of STDs was observed between the 2 groups.[18]

However, a large prospective follow-up study of women at high risk for STDs found the female condom to be at least as effective as the male condom in preventing gonorrhea and chlamydia infection when used correctly and consistently.[19] The clinic-based intervention used in this study led to increased female condom use among women attending STD clinics. The authors noted that use of the female condom allows women to control contraception and HIV prophylaxis, whereas more traditional HIV prevention interventions which focus on the use of male condoms do not because they require the cooperation of the male partners.[19]

How Effective Are Topical Microbicides?

Since 1990, 4 randomized controlled trials of the use of nonoxynol-9 (N-9) to prevent HIV infection in women at high risk have shown no benefit.[20-24] In fact, in one of the trials, it was associated with significantly increased rates of HIV infection. In that trial, Van Damme and colleagues[24] reported that the use of COL-1492, a 3.5% N-9 gel, significantly increased the risk of HIV-1 seroconversion among 765 female sex workers from 4 countries (Figure 3). A meta-analysis restricted to these and other randomized controlled trials concluded that N-9 trials showed no significant reduction in risk of STD or HIV infection, but, instead, some evidence of harm through the induction of genital lesions, and, in the Van Damme trial, an actual increase in rates of HIV acquisition.[25] Other types of topical microbicides are being developed, and some have recently entered phase 2b randomized clinical trials for HIV prevention.

Figure 3. Lack of effectiveness of the nonoxynol-9 (N-9) gel COL-1492 on HIV-1 acquisition by female sex workers.[24]



Is Male Circumcision Effective in Preventing HIV Acquisition?

Strong evidence from cross-sectional studies suggests that male circumcision decreases the risk of acquiring HIV and chancroids.[26-29] Three randomized trials of male circumcision for HIV prevention are currently in progress in Kenya, Uganda, and South Africa, but none has any outcome data yet.

Belated Attention to Preventive Interventions for HIV-Seropositive Persons

Studies of HIV-infected persons have repeatedly shown that between 25% and 35% of those living with HIV/AIDS continue unprotected sexual practices.[30] Although their sexual contacts are often with other HIV-seropositive individuals ("sero-sorting"), contacts can also occur with partners who are HIV negative or of unknown HIV status. For example, in a survey of 3723 HIV-infected persons in clinics and community-based agencies in Los Angeles, Milwaukee, New York City, and San Francisco from June 2000 to January 2002, Weinhardt and associates[31] found that approximately 19% of women, 15.6% of MSM, and 13.1% of heterosexual men engaged in unprotected vaginal or anal intercourse with partners who were HIV negative or whose serostatus was unknown.

Interviews of HIV-infected persons in various settings suggest that more than 70% are sexually active after being diagnosed with HIV infection, and that many have not told their partners about their infection.[32] Comprehensive updates on preventive interventions for seropositive persons have been published in the October 2004 issue of JAIDS, and in the February 2005 issue of AIDS Prevention and Care.[33]

Relaxed Attitudes About the Need for Safer Sex Practices in the HAART Era

Optimism about the effectiveness of highly active antiretroviral therapy (HAART) for HIV infection may be contributing to relaxed attitudes about the need for safer sex practices, leading to increased sexual risk-taking by some HIV-infected persons.[34-40] For example, Lightfoot and coworkers[40] compared behaviors among 349 HIV-seropositive adolescents in Los Angeles, San Francisco, New York City, and Miami from 1994 to 1996 with 175 HIV-seropositive adolescents in the same cities from 1999 to 2000. The authors found that adolescents infected with HIV were more likely to engage in risky sex practices and drug use during the more recent period than they were in the earlier period, when HAART was not yet widely used.

Are Prevention Programs for HIV-Seropositive Persons Working?

Most HIV prevention programs have been directed at HIV-negative persons;[41-44] until recently, there were few prevention programs for HIV-seropositive persons and even fewer whose effectiveness was formally evaluated.[44-46] But the focus may be shifting. In July 2003, the CDC, the Health Resources and Services Administration (HRSA), the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America released evidence-based guidelines on incorporating HIV prevention into the health care of persons with HIV/AIDS, bringing new attention to prevention in persons who tested positive.[2]

These guidelines deal with several broad areas for behavioral prevention in HIV-infected persons and recommend the following: risk screening (Table 1 and Table 2); behavioral interventions (Table 3); partner notification and counseling; and screening for STDs that reflect risk taking and increased risk for HIV transmission.

Table 1. Recommendations for Screening of HIV-Infected Persons for HIV Transmission Risk[2]

- HIV-infected patients should be screened for behaviors associated with HIV transmission by using a straightforward, nonjudgmental approach. This should be done at the initial visit and subsequent routine visits or periodically, as the clinician feels necessary, but at a minimum of yearly. Any indication of risky behavior should prompt a more thorough assessment of HIV transmission risks.
- At the initial and each subsequent routine visit, HIV-infected patients should be questioned about symptoms of STDs (eg, urethral or vaginal discharge; dysuria; intermenstrual bleeding; genital or anal ulcers; anal pruritus, burning, or discharge; and, for women, lower abdominal pain with or without fever). Regardless of reported sexual behavior or other epidemiologic risk information, the presence of such signs or symptoms should always prompt diagnostic testing and, when appropriate, treatment.
- At the initial visit:
  - All HIV-infected women and men should be screened for laboratory evidence of syphilis. Women should also be screened for trichomoniasis. Sexually active women aged ≤ 25 years and other women at increased risk, even if asymptomatic, should be screened for cervical chlamydial infection.
  - Consideration should be given to screening all HIV-infected men and women for gonorrhea and chlamydial infections. However, because of the cost of screening and the variability of prevalence of these infections, decisions about routine screening for these infections should be based on epidemiologic factors (including prevalence of infection in the community or the population being served), availability of tests, and cost. (Some HIV specialists also recommend type-specific serologic testing for herpes simplex virus type 2 for both men and women.)
- Screening for STDs should be repeated periodically (ie, at least annually) if the patient is sexually active or if earlier screening revealed STDs. Screening should be done more frequently (eg, at 3- to 6-month intervals) for asymptomatic persons at higher risk.
- At the initial and each subsequent routine visit, HIV-infected women of childbearing age should be questioned to identify possible current pregnancy, interest in future pregnancy, or sexual activity without reliable contraception. They should be referred for appropriate counseling, reproductive health care, or prenatal care, as indicated. Women should be asked whether they suspect pregnancy or have missed their menses and, if so, should be tested for pregnancy.

Table 2. Examples of Screening Strategies to Elicit Patient-Reported Risk for HIV Transmission*[2]

Open-ended question by clinician, similar to one of the following:

- "What are you doing now that you think may be a risk for transmitting HIV to a partner?"
- "Tell me about the people you've had sex with recently."
- "Tell me about your sex life."

Screening questions (checklist) for use with a self-administered questionnaire; computer-, audio-, or video-assisted questionnaire; or a face-to-face interview:†‡

"Since your last checkup here," or, if first visit, "Since you found out you were infected with HIV,":

- "Have you been sexually active; that is, have you had vaginal, anal, or oral sex with a partner?"

  If yes

  — "Have you had vaginal or anal intercourse without a condom with anyone?"

  If yes

  — "Were any of these people HIV-negative, or are you unsure about their HIV status?"

  — "Have you had oral sex with someone?"

  If yes

  — (For a male patient) "Did you ejaculate into your partner's mouth?"

- "Have you had a genital sore or discharge, discomfort when you urinate, or anal burning or itching?"
- "Have you been diagnosed or treated for a sexually transmitted disease (STD), or do you know if any of your sex partners have been diagnosed or treated for an STD?"
- "Have you shared drug-injection equipment (needles, syringes, cotton, cooker, water) with others?"

  If yes

  — "Were any of these people HIV negative, or are you unsure about their HIV status?"

** Adapted from CDC. Revised guidelines for HIV counseling, testing, and referral. MMWR Morb Mortal Wkly Rep. 2001;50(RR-19).*

† This checklist can be administered by the patient or clinician and should take approximately 4 minutes.

‡ A positive response to any of the screening questions should cue the clinician to have a more in-depth discussion to ensure that specific risks are clearly understood.

Table 3. Recommendations for Behavioral Interventions to Reduce HIV Transmission Risk[2]

- Clinics or office environments where patients with HIV infection receive care should be structured to support and enhance HIV prevention.
- Within the context of HIV care, brief general HIV prevention messages should be regularly provided to HIV-infected patients at each visit or periodically, as determined by the clinician, and at a minimum of twice yearly. These messages should emphasize the need for safer behaviors to protect their own health and the health of their sex or needle-sharing partners, regardless of perceived risk. Messages should be tailored to the patients' needs and circumstances.
- Patients should have adequate, accurate information regarding factors that influence HIV transmission and methods for reducing the risk for transmission to others, emphasizing that the most effective methods for preventing transmission are those that protect noninfected persons against exposure to HIV (eg, sexual abstinence; consistent and correct use of condoms made of latex, polyurethane, or other synthetic materials; and sex with only a partner of the same HIV status). HIV-infected patients who engage in high-risk sexual practices (ie, capable of resulting in HIV transmission) with persons of unknown or negative HIV serostatus should be counseled to use condoms consistently and correctly.
- Patients' misconceptions regarding HIV transmission and methods for reducing risk for transmission should be identified and corrected. For example, ensure that patients know that (1) per-act estimates of HIV transmission risk for an individual patient vary according to behavioral, biological, and viral factors; (2) highly active antiretroviral therapy (HAART) cannot be relied upon to eliminate the risk of transmitting HIV to others; and (3) nonoccupational postexposure prophylaxis is of uncertain effectiveness for preventing infection in HIV-exposed partners.
- Tailored HIV prevention interventions, using a risk-reduction approach, should be delivered to patients at highest risk for transmitting HIV.
- After initial prevention messages are delivered, subsequent longer or more intensive interventions in the clinic or office should be delivered, if feasible.
- HIV-infected patients should be referred to appropriate services for issues related to HIV transmission that cannot be adequately addressed during the clinic visit.
- Persons who inject illicit drugs should be strongly encouraged to cease injecting and enter into substance abuse treatment programs (eg, methadone maintenance) and should be provided referrals to such programs.
- Persons who continue to inject drugs should be advised to always use sterile injection equipment and to never reuse or share needles, syringes, or other injection equipment and should be provided information regarding how to obtain new, sterile syringes and needles (eg, syringe exchange program).

How Effective Are Behavioral Interventions for HIV-Seropositive Persons?

Evidence for the efficacy of multisession interventions for HIV-infected patients, individually or in groups, is limited to a few randomized controlled trials that have mainly measured intervention impact through self-reported risk behaviors (Table 4). None have evaluated the impact on HIV transmission (which would, of course, be difficult to assess), and few have assessed the impact on acquisition of other STDs that could serve as surrogate markers for unprotected sex.

Table 4. Summary of Randomized Trials of Preventive Interventions in HIV-Infected Persons With Objective Measures of HIV-Related Outcomes

Study	Population Sample	Intervention Method	Outcomes
Wingood et al. 2004[47]	366 HIV-positive women in Alabama and Georgia	Gender pride, maintaining current and identifying new network members, HIV transmission knowledge, communication and condom use skills, and healthy relationships	Unprotected vaginal intercourse
Richardson et al. 2004[54]	585 HIV-seropositive persons, sexually active attending 6 HIV clinics in California	Counseling from medical providers supplemented with written information	Self-reported unprotected anal or vaginal intercourse
Kalichman et al. 2001[45]	322 HIV-seropositive men and women	Five-session group intervention focused on strategies for practicing safer sexual behavior	Sexual-risk and protective behaviors (number of sex partners, unprotected vaginal and anal intercourse, total vaginal and anal intercourse, percentage of condom use for vaginal and anal intercourse, unprotected oral sex)

However, in 2004, Wingood and colleagues[47] reported on the first trial—the WiLLOW Program— to evaluate postintervention reductions in risky sexual behavior and objective postintervention measures of STD acquisition. This trial randomized 366 women with HIV infection receiving care at health departments or HIV/AIDS clinics in Alabama and Georgia and attending group sessions that emphasized risk reduction, gender pride, and enhanced social networks. Compared with women in the control group (who attended group sessions on nutrition and adherence), women in the study group experienced an 81% decrease in incidence of bacterial STDs. This trial was small, but nonetheless showed that interventions conducted in the context of HIV clinical management may decrease subsequent unprotected sex, as reflected by the decreased incidence of STDs.

Kalichman and associates[45] conducted one of the first randomized controlled trials to evaluate HIV transmission risk reduction resulting from a behavioral intervention tailored for persons with HIV/AIDS. The results published in 2001 showed that a behavioral intervention grounded in social cognitive theory reduced unprotected sexual intercourse among men and

women living with HIV infection, and that the greatest reductions in risk behaviors occurred with HIV-negative sex partners. The intervention consisted of 5 group sessions that used exercises to develop stress management; coping skills to enhance motivation; assertiveness; efficacy regarding decision-making and disclosure; and problem-solving skills regarding transmission and risk behavior. The intervention used scenes from popular films to encourage open discussion and role-playing about sensitive issues. Results indicated that this combination of activities, conducted in a supportive group format in a community-based setting, led to decreased use of behaviors with transmission risk.

Kalichman and associates[48] also developed and tested an intervention for HIV risk reduction in HIV-seropositive men and women that melded elements of mental health and public health models. These interventions, which had failed independently, led to self-reported risk reduction when used together by these researchers.

The public health model used by Cleary and coworkers[49] found no significant changes in sexual risk behaviors after a structured 6-session intervention among HIV-seropositive men and women. The intervention used educational and skill-building techniques and was delivered in a health care setting. Similarly, a meta-analysis of the long-term effects of risk-reduction counseling that followed testing of HIV-infected persons suggested limited effects on risk behavior for many people living with HIV/AIDS.[50] Mental health or other approaches to risk reduction for people living with HIV warrant further study.[51-53]

In 2004, Richardson and colleagues reported that brief counseling by the medical provider emphasizing the negative consequences of unsafe sex reduced self-reported risky behaviors in HIV-seropositive patients who had presented with high-risk behavioral profiles.[54] This trial randomized 6 HIV clinics in California. Two clinics used a gain-frame approach (stressing the positive consequences of protective behavior), 2 used a loss-frame approach (stressing the negative consequences of not using protection), and 2 were attention-control clinics (stressing adherence to antiretroviral therapy). Interventions were given to all 585 HIV-infected, sexually active patients who attended the clinics for 10 to 11 months in 1999 and 2000. The cohort was reassessed for up to 7 months after the study interventions ended. An incentive sum was paid at each interview. Among participants who had 2 or more sex partners at baseline, self-reported unprotected anal or vaginal intercourse decreased by 38% ($P < .001$) among those who received the loss-frame intervention but not among those who received the gain-frame approach. The benefits of the loss-frame approach may apply only to behavior change among MSM with multiple partners, since no benefit was seen in MSM who had 1 partner at baseline. No significant changes were seen in the gain-frame arm.

It is still not clear which counseling strategy, based on self- or partner-protection, is the best source of motivation for behavior change. Until this is clarified, and because motivations may vary among patients, it has been argued that counseling strategies should include both messages.[54]

Fisher and associates[55] in this “Options Project,” conducted research on the dynamics of risk behaviors among HIV-seropositive patients in clinical care and used this research to design a clinician-based prevention initiative for HIV-seropositive patients (Figure 4). These researchers sampled 20 HIV-seropositive patients in New Haven, Connecticut, who

participated in 1 of 4 focus groups depending on sex and mode of HIV acquisition (eg, male injection-drug users). The findings from the focus groups revealed important deficits in HIV prevention information, motivation, and behavioral skills, and risky sexual behavior among HIV-infected patients. The findings were integrated into a theory-based HIV prevention approach that was initiated by clinicians and proved acceptable to both clinicians and patients.[55]

Figure 4. Information-motivation-behavioral skills model of HIV prevention behavior.[55]

At present, several larger studies designed to evaluate the effectiveness of group-based cognitive behavioral stress management interventions for persons living with HIV/AIDS are ongoing. One project by the HRSA known as the Prevention with Positives Initiative is evaluating the effectiveness of a behavioral prevention intervention program for HIV-seropositive persons seen in a clinical care setting. The program is being funded for 15 demonstration sites and an Evaluation and Technical Support Center.[56]

Other grants involving HIV prevention can be accessed through the Computer Retrieval of Information on Scientific Abstracts (CRISP) database, a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other research institutions. It is available at http://crisp.cit.nih.gov.

Is Risk Behavior Screening and Partner Notification Working?

No randomized controlled trials of differing approaches to risk-behavior screening appear to have been reported recently. Kurth and coworkers[57] conducted a study to compare reporting of sexual risk behaviors by audio computer-assisted self-interview (ACASI) vs clinician-administered sexual histories to explore the usefulness of ACASI for risk assessment in STD clinics. The authors found that sexual histories obtained by ACASI may help to identify persons at risk for STDs. This approach warrants further evaluation in HIV/AIDS clinics. Partners can be reached and informed of their exposure to HIV infection by health department staff, clinicians in the private sector, or by the infected person. In the only randomized controlled trial conducted to date,[58] 35 HIV-infected persons were asked to notify their partners themselves (the “patient-referral group”), and only 10 of 153 partners (7%) were notified. Another 39 HIV-infected persons were assigned to health department referral (the “provider-referral group”); and for these, 78 of 157 partners (50%) were notified. Thus, notification by the health department in this study was substantially more effective than notification by the infected person. Other studies with less rigorous designs have demonstrated similar results.[59,60]

Conclusions

After more than 20 years of research on prevention of sexual transmission of HIV infection, with over 35,000 related publications—based on a search of PubMed using terms “prevention and (HIV OR STD OR STI)”—only about 85 citations represent randomized controlled trials of prevention of sexual transmission of STDs including HIV infection, with only 45 having systematic measures of HIV or other outcomes. Of these, only 1 (the Mwanza trial) reported a significant reduction in sexual acquisition of HIV, and only 1 that involved HIV seropositive persons (WiLLOW) showed a significant reduction of bacterial STDs.

The medical community also needs to do its part, even if funding for HIV prevention is not available. When we, as clinicians, talk to HIV-infected patients and others at risk, we need to discuss the importance of avoiding unprotected sex with persons who are not infected or do not know if they are infected. We need to stay current on the latest approaches to change behavior and to use the methods that have proven most successful. HIV clinics should provide HIV prevention counseling during their primary care visit. A cross-sectional survey examined whether HIV care providers were talking with their HIV-infected patients about safer sex and disclosure. The random survey performed in 1998 and 1999 at 6 HIV clinics in California (N = 839) found that 71% of the patients reported that a provider had talked with them at least once about safer sex; the range, however, varied widely between clinics (52% to 94%), and discussion of safer sex was more prevalent with physicians than with other clinic staff. The researchers concluded that care providers should assess and overcome barriers to providing prevention messages to patients.[32]

At the Nathan Smith Clinic of the Yale–New Haven Hospital (New Haven, Connecticut), Fisher and colleagues[55] found that clinicians self-reported that they rarely discussed risk reduction with their HIV-infected patients, although most recognized the importance of doing so. In addition to time constraints, these clinicians indicated that other barriers included financial constraints (no reimbursement), discomfort in talking about sex and drug use, concerns that interventions could require them to interact with their patient and the patient’s partner, the belief that they cannot influence patients’ behavior, and lack of knowledge about sex and drug use and how to assess and address these issues.

In 2004, Myers and associates[61] reported the results of a survey in which 614 HIV-infected patients leaving a primary care visit at 16 clinics in 9 states were asked whether they received HIV prevention counseling. Clinics were coded as clinics with written procedures, clinics where individual providers initiated counseling, and clinics with no procedures. The HIV-infected patients in clinics with written procedures were significantly more likely to report receiving HIV prevention counseling in the last 6 months than were patients in clinics with no procedures (odds ratio, 3.17; 95% confidence interval, 1.2-8.1; $P < .002$).

The neglect of HIV prevention research in HIV-infected persons and of HIV prevention interventions in clinical practices has been tragic. The current political and religious environments are making HIV prevention research ever more difficult. The rate of HIV infections—40,000 per year in the United States and 14,000 new infections per day globally—are unacceptable and cannot simply be taken in stride. Clinicians and health care professionals must become as familiar with the HIV prevention literature as with the HIV treatment literature and become capable of implementing formal policies and procedures for prevention services in the context of clinical HIV management and care.

To receive free CME credit for this article,
Please complete the following Post-test online at:
http://clinicaloptions.com/hiv/conf/cco2005/

Post Test

1. What impact did the intervention used in the Mwanza trial (which involved STD treatment and care) have on the incidence of HIV and other STDs?

A. This intervention had no impact on the incidence of HIV seroconversion or syphilis
B. This intervention resulted in significant reduction in the incidence of BOTH HIV seroconversion and syphilis
C. This intervention resulted in a significant reduction in the incidence of syphilis, but had no impact on the incidence of HIV seroconversion
D. This intervention resulted in a significant reduction in the incidence of HIV seroconversion, but had no impact on the incidence of syphilis

2. According to studies by Korenromp and associates, which of the following is a likely reason for the lack of impact on HIV acquisition of the preventative interventions used in the Rakai and Masaka trials in Uganda?

A. Lower prevalence of curable STDs in Rakai and Masaka
B. Changes in sexual behavior in Uganda
C. High prevalence of HIV transmission occurring outside core groups with high STD rates in these regions
D. All of the above

3. According to randomized controlled trials on topical microbicides, which of the following statements regarding nonoxynol-9 (N-9) is TRUE?

A. Four randomized controlled trials that examined prevention of HIV acquisition with use of N-9 found no benefit.
B. Van Damme and colleagues reported that use of N-9 gel significantly reduced the risk of HIV-1 seroconversion among female sex workers from 4 countries.
C. A meta-analysis of randomized controlled trials of N-9 concluded that use of N-9 conferred a significant and consistent reduction in risk of certain STDs other than HIV infection.
D. None of the above are true.

4. According to a survey taken by Weinhardt and colleagues, approximately what proportion of HIV-infected men who have sex with men (MSM) in major US cities reported engaging in unprotected vaginal or anal intercourse with partners who were HIV negative or whose serostatus was unknown?

A. 5%
B. 15%
C. 25%
D. 35%

5. Which of the following statements regarding effective behavioral interventions for HIV-seropositive persons is TRUE?

A. Behavioral intervention grounded in social cognitive theory reduced unprotected sexual intercourse among men and women living with HIV infection.
B. Brief provider counseling emphasizing the negative consequences of unsafe sex reduced self-reported HIV transmission behaviors in HIV-seropositive patients presenting with risky behavioral profiles.
C. HIV-infected patients in clinics with written procedures were significantly more likely to report receiving HIV prevention counseling in the last 6 months than were patients in clinics with no procedures.
D. All of the above are true.

References

1. UNAIDS. 2004 Report on the Global AIDS Epidemic: UNAIDS; July 2004.

2. CDC. Incorporating HIV prevention into the medical care of persons living with HIV. Recommendations of CDC, the Health Resources and Services Administration, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR 2003;52(RR12):1-24. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5212a1.htm. Accessed July 13, 2005.

3. CDC. HIV Prevention Strategic Plan Through 2005. Available at: http://www.cdc.gov/hiv/partners/PSP/National_Goal.htm. Accessed July 13, 2005.

4. Manhart LE, Holmes KK. Randomized controlled trials of individual-level, population-level, and multilevel interventions for preventing sexually transmitted infections: what has worked? J Infect Dis. 2005;191(suppl 1):S7-S24.

5. Grosskurth H, Mosha F, Todd J, et al. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. Lancet. 1995;346:530-536.

6. Laga M. STD control for HIV prevention--it works! Lancet. 1995;346:518-519.

7. Korenromp EL, White RG, Orroth KK, et al. Determinants of the impact of sexually transmitted infection treatment on prevention of HIV infection: a synthesis of evidence from the Mwanza, Rakai, and Masaka intervention trials. J Infect Dis. 2005;191(suppl 1):S168-S178.

8. Markowitz M, Mohri H, Mehandru S, et al. Infection with multidrug resistant, dual-tropic HIV-1 and rapid progression to AIDS: a case report. Lancet. 2005;365:1031-1038..

9. Colfax GN, Mansergh G, Guzman R, et al. Drug use and sexual risk behavior among gay and bisexual men who attend circuit parties: a venue-based comparison. J Acquir Immune Defic Syndr. 2001;28:373-379.

10. Rusch M, Lampinen TM, Schilder A, Hogg RS. Unprotected anal intercourse associated with recreational drug use among young men who have sex with men depends on partner type and intercourse role. Sex Transm Dis. 2004;31:492-498.

11. Koblin B, Chesney M, Coates T. Effects of a behavioural intervention to reduce acquisition of HIV infection among men who have sex with men: the EXPLORE randomised controlled study. Lancet. 2004;364:41-50.

12. RESPECT. Project RESPECT. Available at: http://www.cdc.gov/hiv/projects/respect Accessed: July 13, 2005.

13. Baptiste DR, Paikoff RL, McKay MM, Madison-Boyd S, Coleman D, Bell C. Collaborating with an urban community to develop an HIV and AIDS prevention program for black youth and families. Behav Modif. 2005;29:370-416.

14. Hearst N, Chen S. Condom promotion for AIDS prevention in the developing world: is it working? Stud Fam Plann. 2004;35:39-47.

15. Roehr B. Abstinence programmes do not reduce HIV prevalence in Uganda. BMJ. 2005;330:496.

16. Weller S, Davis K. Condom effectiveness in reducing heterosexual HIV transmission. Cochrane Database Syst Rev. 2004:CD003255.

17. Feldblum PJ, Kuyoh MA, Bwayo JJ, et al. Female condom introduction and sexually transmitted infection prevalence: results of a community intervention trial in Kenya. AIDS. 2001;15:1037-1044.

18. Fontanet AL, Saba J, Chandelying V, et al. Protection against sexually transmitted diseases by granting sex workers in Thailand the choice of using the male or female condom: results from a randomized controlled trial. AIDS. 1998;12:1851-1859.

19. Artz L, Macaluso M, Kelaghan J, et al. An intervention to promote the female condom to sexually transmitted disease clinic patients. Behav Modif. 2005;29:318-369.

20. Kreiss J, Ngugi E, Holmes K, et al. Efficacy of nonoxynol 9 contraceptive sponge use in preventing heterosexual acquisition of HIV in Nairobi prostitutes. JAMA. 1992;268:477-482.

21. Roddy RE, Zekeng L, Ryan KA, Tamoufe U, Weir SS, Wong EL. A controlled trial of nonoxynol 9 film to reduce male-to-female transmission of sexually transmitted diseases. N Engl J Med. 1998;339:504-510.

22. Richardson BA, Lavreys L, Martin HL, Jr., et al. Evaluation of a low-dose nonoxynol-9 gel for the prevention of sexually transmitted diseases: a randomized clinical trial. Sex Transm Dis. 2001;28:394-400.

23. Roddy RE, Zekeng L, Ryan KA, Tamoufe U, Tweedy KG. Effect of nonoxynol-9 gel on urogenital gonorrhea and chlamydial infection: a randomized controlled trial. JAMA. 2002;287:1117-1122.

24. Van Damme L, Ramjee G, Alary M, et al. Effectiveness of COL-1492, a nonoxynol-9 vaginal gel, on HIV-1 transmission in female sex workers: a randomised controlled trial. Lancet. 2002;360:971-977.

25. Wilkinson D, Tholandi M, Ramjee G, Rutherford GW. Nonoxynol-9 spermicide for prevention of vaginally acquired HIV and other sexually transmitted infections: systematic review and meta-analysis of randomised controlled trials including more than 5000 women. Lancet Infect Dis. 2002;2:613-617.

26. Cameron DW, Simonsen JN, D'Costa LJ, et al. Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. Lancet. 1989;2:403-407.

27. Nasio JM, Nagelkerke NJ, Mwatha A, Moses S, Ndinya-Achola JO, Plummer FA. Genital ulcer disease among STD clinic attenders in Nairobi: association with HIV-1 and circumcision status. Int J STD AIDS. 1996;7:410-414.

28. Quinn TC. Viral load, circumcision and heterosexual transmission. Hopkins HIV Rep. 2000;12:1,5,11.

29. Weiss HA, Quigley MA, Hayes RJ. Male circumcision and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis. AIDS. 2000;14:2361-2370.

30. Kalichman SC, Rompa D, Cage M. Sexually transmitted infections among HIV seropositive men and women. Sex Transm Infect. 2000;76:350-354.

31. Weinhardt LS, Kelly JA, Brondino M, et al. HIV transmission risk behavior among men and women living with HIV in 4 cities in the United States. J Acquir Immune Defic Syndr. 2004;36:1057-1066..

32. Marks G, Richardson JL, Crepaz N, et al. Are HIV care providers talking with patients about safer sex and disclosure?: a multi-clinic assessment. AIDS. 2002;16:1953-1957.

33. Gordon CM, Stall R, Cheever L. Prevention interventions with persons living with HIV/AIDS. J Acquir Immune Defic Syndr. 2004;37(suppl 2): S53-S141.

34. Stall RD, Hays RB, Waldo CR, Ekstrand M, McFarland W. The Gay '90s: a review of research in the 1990s on sexual behavior and HIV risk among men who have sex with men. AIDS. 2000;14(suppl 3):S101-S114.

35. Kelly JA, Otto-Salaj LL, Sikkema KJ, Pinkerton SD, Bloom FR. Implications of HIV treatment advances for behavioral research on AIDS: protease inhibitors and new challenges in HIV secondary prevention. Health Psychol. 1998;17:310-319.

36. Kelly JA, Hoffman RG, Rompa D, Gray M. Protease inhibitor combination therapies and perceptions of gay men regarding AIDS severity and the need to maintain safer sex. AIDS. 1998;12:F91-F95.

37. Kravcik S, Victor G, Houston S, et al. Effect of antiretroviral therapy and viral load on the perceived risk of HIV transmission and the need for safer sexual practices. J Acquir Immune Defic Syndr Hum Retrovirol. 1998;19:124-129.

38. Dilley JW, Woods WJ, McFarland W. Are advances in treatment changing views about high-risk sex? N Engl J Med. 1997;337:501-502.

39. Van de Ven P, Kippax S, Knox S, Prestage G, Crawford J. HIV treatments optimism and sexual behaviour among gay men in Sydney and Melbourne. AIDS. 1999;13:2289-2294.

40. Lightfoot M, Swendeman D, Rotheram-Borus MJ, Comulada WS, Weiss R. Risk behaviors of youth living with HIV: pre- and post-HAART. Am J Health Behav. 2005;29:162-172.

41. DiClemente RJ, Wingood GM. A randomized controlled trial of an HIV sexual risk-reduction intervention for young African-American women. JAMA. 1995;274:1271-1276.

42. Kelly JA, St Lawrence JS, Diaz YE, et al. HIV risk behavior reduction following intervention with key opinion leaders of population: an experimental analysis. Am J Public Health. 1991;81:168-171.

43. Kelly JA, St Lawrence JS, Stevenson LY, et al. Community AIDS/HIV risk reduction: the effects of endorsements by popular people in three cities. Am J Public Health. 1992;82:1483-1489.

44. Kamb ML, Fishbein M, Douglas JM, Jr., et al; Project RESPECT Study Group. Efficacy of risk-reduction counseling to prevent human immunodeficiency virus and sexually transmitted diseases: a randomized controlled trial. JAMA. 1998;280:1161-1167.

45. Kalichman SC, Rompa D, Cage M, et al. Effectiveness of an intervention to reduce HIV transmission risks in HIV-positive people. Am J Prev Med. 2001;21:84-92.

46. Janssen RS, Holtgrave DR, Valdiserri RO, Shepherd M, Gayle HD, De Cock KM. The serostatus approach to fighting the HIV epidemic: prevention strategies for infected individuals. Am J Public Health. 2001;91:1019-1024.

47. Wingood GM, DiClemente RJ, Mikhail I, et al. A randomized controlled trial to reduce HIV transmission risk behaviors and sexually transmitted diseases among women living with HIV: the WiLLOW program. J Acquir Immune Defic Syndr. 2004;37:S58-S67.

48. Kalichman SC, Rompa D, Cage M. Group intervention to reduce HIV transmission risk behavior among persons living with HIV/AIDS. Behav Modif. 2005;29:256-285.

49. Cleary PD, Van Devanter N, Steilen M, et al. A randomized trial of an education and support program for HIV-infected individuals. AIDS. 1995;9:1271-1278.

50. Weinhardt LS, Carey MP, Johnson BT, Bickham NL. Effects of HIV counseling and testing on sexual risk behavior: a meta-analytic review of published research, 1985-1997. Am J Public Health. 1999;89:1397-1405.

51. Coates TJ, McKusick L, Kuno R, Stites DP. Stress reduction training changed number of sexual partners but not immune function in men with HIV. Am J Public Health. 1989;79:885-887.

52. Hedge B, Glover LF. Group intervention with HIV seropositive patients and their partners. AIDS Care. 1990;2:147-154.

53. Kelly JA, Murphy DA, Bahr GR, et al. Outcome of cognitive-behavioral and support group brief therapies for depressed, HIV-infected persons. Am J Psychiatry. 1993;150:1679-1686.

54. Richardson JL, Milam J, McCutchan A, et al. Effect of brief safer-sex counseling by medical providers to HIV-1 seropositive patients: a multi-clinic assessment. AIDS. 2004;18:1179-1186.

55. Fisher JD, Cornman DH, Osborn CY, Amico KR, Fisher WA, Friedland GA. Clinician-initiated HIV risk reduction intervention for HIV-positive persons: Formative Research, Acceptability, and Fidelity of the Options Project. J Acquir Immune Defic Syndr. 2004;37(suppl):S78-S87.

56. Health Resources and Services Administration. Prevention with Positives Initiative. Available at: http://hab.hrsa.gov/special/%5CSPNS05RPT%5Cprevention.htm. Accessed July 13, 2005.

57. Kurth AE, Martin DP, Golden MR, et al. A comparison between audio computer-assisted self-interviews and clinician interviews for obtaining the sexual history. Sex Transm Dis. 2004;31:719-726.

58. Landis SE, Schoenbach VJ, Weber DJ, et al. Results of a randomized trial of partner notification in cases of HIV infection in North Carolina. N Engl J Med. 1992;326:101-106.

59. Oxman AD, Scott EA, Sellors JW, et al. Partner notification for sexually transmitted diseases: an overview of the evidence. Can J Public Health. 1994;85(suppl 1):S41-S47.

60. Macke BA, Maher JE. Partner notification in the United States: an evidence-based review. Am J Prev Med. 1999;17:230-242.

61. Myers JJ, Steward WT, Charlebois E, Koester KA, Maiorana A, Morin SF. Written clinic procedures enhance delivery of HIV "Prevention With Positives" counseling in primary health care settings. J Acquir Immune Defic Syndr. 2004;37(suppl 2):S95-S100.

