SUPPLEMENT ARTICLE

Interventions to Prevent Sexually Transmitted Infections, Including HIV Infection

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The Centers for Disease Control and Prevention (CDC) Sexually Transmitted Disease (STD) Treatment Guidelines were last updated in 2006. To update the "Clinical Guide to Prevention Services" section of the 2010 CDC STD Treatment Guidelines, we reviewed the recent science with reference to interventions designed to prevent acquisition of STDs, including human immunodeficiency virus (HIV) infection. Major interval developments include (1) licensure and uptake of immunization against genital human papillomavirus, (2) validation of male circumcision as a potent prevention tool against acquisition of HIV and some other sexually transmitted infections (STIs), (3) failure of a promising HIV vaccine candidate to afford protection against HIV acquisition, (4) encouragement about the use of antiretroviral agents as preexposure prophylaxis to reduce risk of HIV and herpes simplex virus acquisition, (5) enhanced emphasis on expedited partner management and rescreening for persons infected with *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, (6) recognition that behavioral interventions will be needed to address a new trend of sexually transmitted hepatitis C among men who have sex with men, and (7) the availability of a modified female condom. A range of preventive interventions is needed to reduce the risks of acquiring STI, including HIV infection, among sexually active people, and a flexible approach targeted to specific populations should integrate combinations of biomedical, behavioral, and structural interventions. These would ideally involve an array of prevention contexts, including (1) communications and practices among sexual partners, (2) transactions between individual clients and their healthcare providers, and (3) comprehensive population-level strategies for prioritizing prevention research, ensuring accurate outcome assessment, and formulating health policy.

The landscape of interventions to prevent transmission of sexually transmitted infections (STIs), including human immunodeficiency virus (HIV) infection, has changed considerably since the Centers for Disease Control and Prevention (CDC) Sexually Transmitted Disease (STD) Treatment Guidelines were last updated in 2006 [1]. Major interval developments include (1) licensure and uptake of immunization against genital human papillomavirus (HPV), (2) validation of male circumcision as a potent prevention tool against acquisition of HIV and some STIs, (3) failure of a promising HIV vaccine candidate to afford protection against HIV acquisition, (4) encouragement about the use of antiretroviral agents as both early treatment for HIV-positive persons and preexposure prophylaxis for HIV-negative persons to reduce the risk of HIV and herpes simplex virus (HSV) acquisition, (5) enhanced emphasis on expedited partner management and rescreening for persons infected with *Chlamydia trachomatis* or *Neisseria gonorrhoeae*, (6) recognition that behavioral interventions will be needed to address a new trend of sexually transmitted hepatitis C among men who have sex with men (MSM), and (7) the availability of a modified female condom.

The need for effective prevention of HIV and other STIs remains a high priority, both internationally and domestically. UNAIDS reported in 2010 that although

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the rate of new HIV infections has fallen in several countries, these favorable trends are at least partially offset by increases in new infections in others; moreover, the proportion of infections in women is increasing in several countries, and young persons aged 15–24 years account for 41% of new HIV infections in sub-Saharan Africa [2]. In 2008, the CDC revised its estimates of the annual incidence of new HIV infections in the United States by 40% (an increase from an estimated 40 000 new infections annually to ~56 000) [3]. Moreover, a large proportion of new HIV infections continue to be diagnosed in late stages of the disease [4, 5]. In the United States in 2008, most new HIV infections occurred in MSM, who also continue to sustain the highest incidence of syphilis as part of the resurgence of this resilient STI [6, 7]. Rates of reportable non-HIV STI either have not declined or have actually increased. In 2009, >1.2 million diagnoses of *C. trachomatis* were reported to the CDC, yet rates of appropriate screening in young women remain suboptimal [8]. In 2009, the number of reported cases of gonorrhea remained stable, with increasing concern about advancing antimicrobial resistance, and cases of primary and secondary syphilis comprised the highest number of cases reported since 1995 [6]. Some data suggest that an epidemiologic shift of the syphilis resurgence into heterosexual networks may be underway [9]. Finally, sexual transmission of hepatitis C is increasingly recognized in MSM who reported sexual practices involving exposure to blood or even minimal trauma to the rectal mucosa [10–12].

To update the "Clinical Guide to Prevention Services" section of the 2010 CDC STD Treatment Guidelines, we reviewed the recent science with reference to key questions related to prevention interventions. We have not included community-level behavioral interventions, because these have been extensively reviewed elsewhere [13].

METHODS

We searched the English language literature from January 2005 to December 2010, using the MEDLINE computerized database of the US National Library of Medicine. We used the following MeSH terms: *condom, behavioral counseling, microbicide, diaphragm, spermicide, sexually transmitted diseases, sexually transmitted infections, male circumcision, prevention, HIV, preexposure prophylaxis, postexposure prophylaxis, genital hygiene, douching, vaccines, immunization, hepatitis B, hepatitis A,* and *hepatitis C.* We also searched abstracts from major STD/HIV-related meetings during the same period with the same terms using conference Web sites. We considered their data if the abstracts had not yet resulted in published articles. Abstract authors were contacted for more information if necessary. We also reviewed relevant publications and policy statements from major international organizations, including the World Health Organization (WHO), UNAIDS, and CDC. Key questions were generated by review of these resources and in consultation with experts in the fields of infectious diseases and prevention. We emphasize randomized controlled trials in our review, but methodologically sound observational cohort and cross-sectional studies were also included when data on a particular topic were sparse.

RESULTS

Efficacy of Individual-Level Prevention Methods in Preventing Acquisition and Transmission of STDs and HIV Infection

Vaccination

Preexposure vaccination is one of the most effective methods for preventing transmission of 2 main STDs: HPV infection and hepatitis B (Table 1). In March 2007, the Advisory Committee on Immunization Practices (ACIP) issued guidelines for administration of the quadrivalent HPV vaccine to females aged ≤25 years [14] (details at www.cdc.gov/std/hpv). This vaccine confers protection against HPV types 6/11 (responsible for 90% of genital warts) and 16/18 (responsible for 70% of cervical cancers). In published clinical trials, the quadrivalent HPV vaccine has demonstrated efficacy for prevention of vaccine HPV type-related cervical, vaginal, and vulvar cancer precursor and dysplastic lesions, and external genital warts [15]. Universal vaccination of girls aged 11–12 years is recommended, as is catch-up vaccination for girls and women aged 13–26 years. The vaccine is also efficacious in preventing infection in women aged 24–45 years not already infected with the relevant HPV types. [16] Data on the efficacy of the quadrivalent HPV vaccines in protecting young men from vaccine-type HPV acquisition indicates similarly high levels of protection [17, 18], and the ACIP issued permissive guidance for immunization to prevent genital warts in young men in 2010. Both men and women are also likely to benefit from protection against anal intraepithelial neoplasia afforded by the quadrivalent vaccine. A bivalent vaccine that is effective in preventing cervical neoplasia associated with HPV types 16/18 has also been approved for use in the United States, and is recommended by ACIP [19, 20].

Immunization against hepatitis B has been routinely recommended for infants since 1991 and was subsequently recommended for adolescents. Although this has been temporally associated with marked declines in the incidence of hepatitis B virus infection in the United States [21], sexual transmission still accounts for the majority of new infections, which are especially common among unvaccinated MSM. Consequently, hepatitis B vaccination is recommended for all adults who are at risk for sexual infection, including sex partners of persons positive for hepatitis B surface antigen, sexually active persons who are not in a long-term, mutually monogamous relationship, persons seeking evaluation or treatment for a STD, and MSM

[22]. Moreover, all HIV-infected persons should be immunized against hepatitis B, because the natural history of hepatitis B is accelerated in the setting of HIV, and coinfection imposes specific considerations in selection of antiretroviral agents. Hepatitis A vaccine is licensed and is recommended for MSM and illicit drug users (both injecting and noninjecting) [23] (details available at http://www.cdc.gov/hepatitis). Finally, new vaccine approaches aimed at hepatitis C, including peptide, recombinant protein, DNA and vector-based vaccines, have recently reached phase I/II human clinical trials, providing some promise for future control of this infection [24].

Prospects for an effective HIV vaccine remain on the distant horizon. Recent disappointing results from human trials have stimulated a renewed focus on the basic biology of HIV pathogenesis. Two phase III trials of a vaccine aimed at eliciting neutralizing antibodies against the envelope glycoprotein 120 did not find protection against HIV infection [25, 26]. A phase IIB trial of the first T cell vaccine (Merck's MRKAd5 HIV-1 gag/pol/nef trivalent product, using a replication-defective adenovirus type-5 vector with 3 HIV genes) was stopped in September 2007. Interim analysis revealed no protective effect against HIV acquisition and no reduction in initial viral loads among participants infected with HIV [27, 28]. Further analysis showed that preexisting immunity to adenovirus type 5 was directly associated with a significantly higher risk of acquiring HIV and that this untoward effect was further augmented among uncircumcised men. A community-based, randomized, double-blind, placebo-controlled trial performed in >16 000 Thai adults evaluated 4 priming injections of a recombinant canary pox vector vaccine (ALVAC-HIV) plus 2 booster injections of a recombinant glycoprotein 120 subunit vaccine (AIDSVAX B/E) [29]. There was a trend toward prevention of HIV infection in the intention-to-treat analysis (vaccine efficacy, 26.4%; 95% confidence interval [CI], −4.0 to 47.9), but not in the per-protocol analysis (vaccine efficacy, 26.2%; 95% CI, −13.3 to 51.9). Vaccination did not affect HIV viral load or CD4 cell count in participants who acquired HIV infection during the trial.

Male Condoms

The 2006 STD Treatment Guidelines noted that, when used consistently and correctly, male latex condoms are effective in preventing sexual transmission of HIV and other STDs, including chlamydia, gonorrhea, syphilis, genital HPV, and trichomoniasis [1]. By limiting lower genital tract infections, male condoms might also reduce the risk of pelvic inflammatory disease in women [30]. In heterosexual serodiscordant relationships in which condoms were consistently used, HIV-negative partners were 80% less likely to become HIV infected than persons in similar relationships in which condoms were not used [31]. Condom use might also reduce the risk for transmission of HSV-2, although data for this effect are more limited [32, 33]. Finally, condom use reduces the risk of HPV infection [34, 35] and HPV-associated diseases (eg, genital warts and cervical cancer) [36]. Use of condoms has been associated with regression of cervical intraepithelial neoplasia [37] and clearance of HPV infection in women, and with regression of HPV-associated penile lesions in men [38].

Since 2006, available data on male condom efficacy have emerged in several areas: (1) protection against infection with genital HPV, HSV-2, and *C. trachomatis*; (2) the methodology of self-reporting on consistent and correct condom use; and (3) interventions to reduce adolescents' sexual risk behavior and absence of condom use during first sex on adolescents' subsequent sexual risk behavior.

A prospective study among newly sexually active college women demonstrated that consistent condom use was associated with a 70% reduction in risk for genital HPV transmission; a large cross-sectional study supported slightly lower but significant efficacy in men. Investigators followed up 82 female university students who reported their first intercourse with a male partner either during the study period or within 2 weeks before enrollment [35]. Cervical and vulvovaginal samples for HPV DNA testing and Pap smears were collected every 4 months. The incidence of genital HPV infection was 37.8/100 patient-years at risk among women whose partners used condoms for all instances of intercourse during the 8 months before testing, compared with 89.3/100 patient-years at risk in women whose partners used condoms <5% of the time (adjusted hazard ratio [AHR], 0.3; 95% CI, .1–.6). In participants in this study who reported 100% condom use by their partners, no cervical squamous intraepithelial lesions were detected in 32 patient-years at risk, whereas 14 incident lesions were detected during 97 patient-years at risk among women whose partners did not use condoms or used them less consistently. In a separate cross-sectional study from 2 cities in the United States, 393 men were assessed for 37 HPV types from 5 anogenital sites. Report of always using condoms was associated with lower odds of HPV detection (adjusted odds ratio [AOR], 0.50; 95% CI, .30–.83) [34].

Prospective studies continue to support a protective effect of condoms against acquisition of genital herpes, chlamydia, and gonorrhea. In an analysis that pooled data from all published studies that prospectively assessed condom use and HSV-2 incidence, persons who always used condoms had a 30% decreased risk of acquiring HSV-2, compared with those who reported no condom use ($P = .01$). [39] Moreover, the risk of acquiring HSV-2 decreased by 7% for every additional 25% of the time that condoms were used ($P = .01$). Conversely, HSV-2 acquisition rose steadily with report of increasing frequency of unprotected sex acts. These effects were consistent for men and women. Among men who participated in the Kenya circumcision trial, report of condom use at last vaginal intercourse was

independently associated with lower rates of incident chlamydial or gonococcal infection detected during 2 years of follow-up (AHR, 0.64; 95% CI, .50-.82) [40].

Cross-sectional data support the claim that male condoms protect against acquisition of *C. trachomatis.* Three cross-sectional studies addressed risk of chlamydial infection as a function of various correlates of condom use. Data from a public STD clinic database examined chlamydia prevalence among known chlamydia contacts who were consistent versus inconsistent condom users. The AOR for chlamydial infection in consistent relative to inconsistent users was 0.10 (95% CI, .01–.83) [41]. In a database from an Australian STD clinic, condom use was associated with a lower odds of rectal, but not urethral, chlamydia among MSM [42]. In an urban adolescent healthcare clinic, the prevalence of chlamydia or gonorrhea was assessed as a function of reported condom use in 509 predominantly African American adolescent girls. Although consistent and correct use was reported uncommonly (in only 16% of subjects), it was associated with reduced odds of chlamydia (odds ratio [OR], 0.4; 95% CI, .2–1.0) and gonorrhea (OR, 0.1; 95% CI, 0–.7) [43].

Data support the need for adolescents to receive comprehensive, current, and accessible information on prevention of STDs, HIV infection, and pregnancy, including information on condoms. Data from the 1994 to 2002 National Longitudinal Study of Adolescent Health (Add Health) compared subsequent sexual behaviors and risk of STI among adolescents who did and did not use a condom at their sexual debut [44]. Adolescents who reported condom use at sexual debut were more likely to report condom use at most recent intercourse (on average, 6.8 years after sexual debut), and were half as likely to test positive for chlamydia or gonorrhea (AOR, 0.50; 95% CI, .26–.95). Reported number of lifetime sexual partners did not differ between the 2 groups. A separate analysis of Add Health data included teens enrolled in 2001 who were followed up 1 and 3 years later; teens who took a virginity pledge reported a longer time until sexual debut than teens who did not [45]. However, overall sexual behaviors subsequent to pledging, including patterns of condom use, did not differ between these groups. A more recent analysis demonstrated that teens who took the pledge and who did have sex were less likely to use condoms at sexual debut [46].

Estimating true condom efficacy requires that measures of consistent and correct use must be developed, understood, and used. Multiple problems with condoms occurred among 1152 participants who completed a supplemental questionnaire as part of Project RESPECT, a counseling intervention trial conducted at 5 publicly funded STD clinics in the 1990s [47]. Nearly half (41%) of respondents reporting condom use indicated that condoms broke, slipped off, leaked, or were not used throughout intercourse in the previous 3 months. Nearly 9% of acts in which condoms were used resulted in potential STI exposure because of delayed application of condoms, breakage, early removal, slippage, or leakage. Critically, use problems were significantly associated with reporting inconsistent condom use, multiple partners, and other condom problems. Among 130 participants who were tested for gonorrhea and chlamydia at the time of the questionnaire completion and 3 months prior, no infections were detected among consistent users reporting no use problems. A significant dose-response relationship occurred between measures of increased protection from condom use and reduced gonorrhea and chlamydia rates.

Nonlatex condoms provide an acceptable alternative for persons unable to tolerate latex condoms. Two general categories of nonlatex condoms exist. The first type is made of polyurethane or other synthetic material and provides protection against STDs, HIV infection, and pregnancy equal to that of latex condoms. These condoms provide an acceptable alternative for persons unable to use latex condoms. A Cochrane review concluded that although one nonlatex condom (eZon) did not protect against pregnancy as well as its latex comparison condom, no differences were found in the typical use efficacy between the Avanti and the Standard Tactylon condoms and their latex counterparts [48]. The nonlatex condoms had higher rates of clinical breakage than latex comparison condoms (OR for clinical breakage, 2.64 [95% CI, 1.63–4.28] to 4.95 [95% CI, 3.63–6.75]). The contraceptive efficacy of nonlatex condoms could not be estimated, and will require more research [48]. The Food and Drug Administration (FDA) has published draft guidelines modifying the labeling on male latex condoms to reflect these findings [49].

Female Condoms

Laboratory studies indicated that the original version of the female condom (Reality), is an effective mechanical barrier to viruses and semen. If used consistently and correctly, the female condom might substantially reduce the risk for STI. Female condoms are safe to use repeatedly if proper care procedures are followed. Since the last guideline review, relatively few studies have been completed to evaluate the efficacy of female condoms in providing protection from STIs, including HIV infection. The new evidence uses postuse markers of semen to measure more precisely the mechanical barrier provided by this method. Other in vitro data assess a new formulation of the female condom.

Two systematic reviews supported the potential effectiveness of female condoms. The first reviewed 137 articles and abstracts on various aspects of the female condom and 5 randomized controlled trials on its effectiveness [50]. The review concluded that although the evidence is limited, ''the female condom is effective in increasing protected sex and decreasing STI incidence among women.'' A second systematic review concluded that ''randomised controlled trials provide evidence that female condoms confer as much protection from STIs as male condoms'' [51].

The comparative effectiveness of the male condom and female condom was assessed in a randomized controlled trial that assigned women to sequential use of 10 male latex condoms, then 10 female polyurethane condoms. [52] The association between frequency and types of self-reported mechanical failure and semen exposure was measured based on prostate-specific antigen (PSA) levels. Moderate to high postcoital PSA levels were detected in 3.5% of male condom users and 4.5% of female condom users (difference, 1.4; 95% CI, 1.6–3.7). PSA levels were more frequent with mechanical problems and less frequent with other problems or correct use with no problems. Although mechanical problems were more common with the female condom, the risk of semen exposure was probably similar.

The FDA held an advisory meeting in December 2008 to review evidence in support of a new version of the female condom [53]. The new version has a slightly modified shape and no seam and is made from nitrile (as opposed to polyurethane, the material used for the first version). Modifications to the manufacturing process as a result of this shift have resulted in considerable cost reductions to the product. The advisory panel voted to support FDA approval of the new female condom, and it became available in 2009. The new female condom is already in use in many countries outside the United States and has been endorsed by WHO after a similar review process. This new design should theoretically afford protection similar to the polyurethane female condom and allows for lower manufacturing cost. The female condom also has been evaluated for protection against HIV infection and other STIs protection during receptive anal intercourse [54]. Although it might provide some protection, no new data are available to help to define its efficacy in this setting.

Male Circumcision

Three randomized controlled trials performed in healthy African men showed that male circumcision was effective in preventing HIV acquisition. In studies performed in Uganda, South Africa, and Kenya, men were randomized to be offered immediate or delayed (at 24 months) circumcision and followed up for 2 years for acquisition of HIV infection and other STDs [55–58]. The summary rate ratio for reduction of HIV acquisition in the men who underwent immediate circumcision for the 3 trials was 0.42 (95% CI, .31–.57), identical to that obtained from observational studies, which translates into a protective effect of male circumcision of 58% [56]. On the basis of these findings, a WHO and UNAIDS consultation in March 2007 recommended that circumcision be recognized as an effective intervention for preventing heterosexual HIV acquisition in men [59]. WHO and UNAIDS also recommended that male circumcision be offered to HIV-negative men in addition, but not as a substitute, to other HIV risk-reduction strategies.

Circumcision also affords a similar level of protection against acquisition of other STIs, particularly nonulcerative pathogens, such high-risk genital HPV infection, and also against acquisition of genital herpes [60–62]. In South Africa, after 21 months of follow-up, circumcision protected against high-risk HPV infection (OR, 0.57; 95% CI, 0.43–0.75), but not gonorrhea [60]. The association between trichomoniasis and male circumcision remained borderline when age, ethnic group, number of lifetime partners, marital status, condom use, and HIV status were controlled for (AOR, 0.48; $P = .069$). In the as-treated analysis, this association became significant (OR, 0.49 [$P = .030$]; AOR, 0.41 [$P = .03$]). The authors concluded that male circumcision reduces incident trichomoniasis among men. Men in Uganda were also followed up for acquisition of STDs for 2 years. At 24 months, the cumulative probability of HSV-2 seroconversion was 7.8% in men randomized to circumcision (1684 men who were initially HSV-2 seronegative) and 10.3% in the control group (1709 men who were initially HSV-2 seronegative) (AHR, 0.72; 95% CI, .56–.92; $P = .008$) [62]. The prevalence of high-risk HPV genotypes was 18.0% in the intervention group and 27.9% in the control group (adjusted risk ratio, 0.65; 95% CI, .46–.90; $P = .009$). However, no significant difference between the 2 study groups was observed in the incidence of syphilis (AHR, 1.10; 95% CI, .75–1.65; $P = .44$). Among men enrolled in the Kenya study, circumcision afforded no protection against incident gonorrhea, chlamydia, or trichomoniasis [40].

No randomized controlled trials of circumcision have been performed among men in the United States However, a cross-sectional analysis reported that among 394 heterosexual African-American men attending a Baltimore STD clinic who reported known HIV exposure, circumcision was significantly associated with lower HIV prevalence (10.2% vs 22.0%; adjusted prevalence rate ratio [PRR], 0.49; 95% CI, .26–.93). No such association was seen for men with unknown HIV exposure [63].

The benefits of circumcision to MSM are unproved. A meta-analysis of studies reported that overall, circumcised MSM had lower odds of being infected with HIV (OR, 0.86; 95% CI, .65–1.10), an association that did not reach statistical significance and that was similar among men who reported primarily engaging in insertive anal sex [64]. Among the 4889 participants in the VaxGen rgp 120 HIV vaccine study (87.4% of whom were circumcised), 342 men (7.0% of all participants) acquired HIV while enrolled; being uncircumcised was not associated with incident HIV infection (AHR, 0.97; 95% CI, .56–1.68) among men who reported unprotected insertive anal sex with HIV-infected partners [65]. However, studies conducted prior to the introduction of highly active antiretroviral therapy demonstrated a significant inverse association of circumcision with HIV infection (OR, 0.47; 95% CI, .32–.69) [64]. No significant effects were seen for non-HIV STIs, and the investigators concluded that more data were needed.

Unfortunately, the benefits of male circumcision in reducing HIV acquisition in men do not extend to women; however,

other benefits may occur. Female sex partners of men who participated in the Uganda circumcision trial were followed up to assess effects on their genital symptoms and vaginal infections [66]. Among women with normal vaginal flora scores at enrollment, rates of bacterial vaginosis (BV) at follow up were significantly lower in wives of men who had been circumcised compared with men who had not (prevalence risk ratio [PRR], 0.80; 95% CI, .65–.97). In women with BV at enrollment, persistent BV at 1 year was significantly lower in the intervention arm than control arm women (PRR 0.83; 95% CI, .72–.96). The adjusted prevalence risk ratio of genital ulcer disease among wives of circumcised men compared with uncircumcised men was 0.78 (95% CI, .61–.99), consistent with circumcision efficacy of 22%. The adjusted prevalence risk ratio for trichomoniasis in intervention arm wives relative to controls was 0.55 (95% CI, .34–.89; efficacy 45%). The authors concluded that male circumcision may have direct benefits for prevention of genital ulceration, trichomoniasis, and BV in female partners and that this should be considered when plans are made to scale up of male circumcision programs to prevent HIV infection.

Implementation of male circumcision as a strategy for preventing HIV infection remains to be fully defined. Concerns include possible disinhibitory effects on sexual risk behaviors, complications from unsafe or inexperienced providers, and acceptability by substantial numbers of men at highest risk for HIV infection [67]. Male circumcision is a complement to, not a substitute for, other HIV risk-reduction strategies. WHO and UNAIDS recommend that countries with hyperendemic and generalized HIV epidemics and low prevalence of male circumcision expand access to safe male circumcision services within the context of ensuring universal access to comprehensive HIV infection programs, including prevention, treatment, care, and support.

Nonspecific Topical Agents

In general, results of topical agents with nonspecific antimicrobial activity for the prevention of HIV and other STDs have been disappointing [67, 68]. A randomized controlled trial comparing vaginal application of 0.5% PRO 2000 (a synthetic polyanionic polymer that blocks attachment of HIV to the host cell) with BufferGel (a vaginal buffering agent), placebo gel, and condom use only found that PRO 2000 was associated with a 30% reduction in risk of HIV acquisition relative to no gel use (AHR, 0.70; 95% CI, .46–1.08; $P = .10$) or placebo gel use (AHR, 0.67; 95% CI, .44–1.02; $P = .06$) [69]. However, a considerably larger study (the MDP301 trial, conducted in 4 sub-Saharan African countries) assessing 0.5% PRO2000 relative to placebo gel found no protective effect [70].

Other topical polyanion agents have not fared well either. A randomized controlled trial compared coitally dependent use of Carraguard (a carrageenan derivative with in vitro activity against HIV) with methylcellulose gel placebo among South African women at high risk for HIV infection. After 2 years follow-up, the incidence of HIV infection in the Carraguard group (n = 3011) was 3.3/100 woman-years, compared with 3.8/100 woman-years in the placebo group (n = 2994) (AHR, 0.87; 95% CI, .69–1.09). Applicator dye testing—one means of measuring actual vaginal insertion of the product—indicated that adherence to product was low (42% of sex acts overall). Self-reported product use was substantially higher than the estimate obtained from applicator testing, and some investigators have reported low accuracy for applicator dye testing [71, 72].

Two randomized controlled trials compared daily 6% cellulose sulfate (an HIV entry inhibitor) vaginal gel with corresponding placebo. A multicountry trial enrolled 1398 African women at high risk for HIV infection. Twenty-five newly acquired HIV infections occurred in the cellulose sulfate group, and 16 in the placebo group, with an estimated hazard ratio (HR) of infection for the cellulose sulfate group of 1.61 ($P = .13$). This result, which is not significant, is in contrast to the interim finding that led to the trial's being stopped prematurely (HR, 2.23; $P = .02$) and the suggestive result of a preplanned secondary (adherence-based) analysis (HR, 2.02; $P = .05$). Compared with placebo, cellulose sulfate had no significant effect on the risk of gonorrhea (HR, 1.10; 95% CI, .74–1.62) or chlamydia (HR, 0.71; 95% CI, .47–1.08). The authors concluded that cellulose sulfate did not prevent and may have increased the risk of HIV acquisition [73]. A second randomized, placebo-controlled trial of cellulose sulfate in Nigeria was stopped prematurely after the data safety monitoring board of the multicountry trial concluded that cellulose sulfate might be increasing the risk of HIV acquisition [73, 74]. With the limited data available, cellulose sulfate gel appeared not to prevent transmission of HIV, gonorrhea, or chlamydial infection.

Two trials of the effectiveness of 1.0% C31G (Savvy; a surfactant) in preventing HIV acquisition were similarly disappointing. In the first, more women in the SAVVY group than in the placebo group reported reproductive tract adverse events [75]. In the second, 33 seroconversions (21 in the SAVVY group and 12 in the placebo group) occurred in the 2153 participants. The cumulative probability of HIV seroconversion was 2.8% in the SAVVY group and 1.5% in the placebo group ($P = .121$), with an HR of 1.7 for SAVVY versus placebo (95% CI, .9–3.5). [76]. The trials indicated that SAVVY did not reduce the incidence of HIV infection and may have been associated with increased risks. Taken together, these studies do not support further testing of polyanion-type compounds with nonspecific activity against STDs and HIV.

Vaginal Diaphragms

Observational studies demonstrate that diaphragm use protects against cervical gonorrhea, chlamydia, and trichomoniasis [51].

The MIRA trial examined the effect of a diaphragm plus polycarbophil (Replens) lubricant on HIV acquisition in women in Zimbabwe and South Africa. The authors found no additional protective effect of latex diaphragm, lubricant gel, and condoms on HIV acquisition compared with condoms alone [77]. A subsequent analysis of data from this study evaluated outcomes of chlamydia and gonorrhea. [78] Median follow-up time was 21 months, and the retention rate was >93%. A total of 471 first chlamydia infections occurred, 247 in the intervention arm and 224 in the control arm, with an overall incidence of 6.2/100 woman-years (relative hazard [RH], 1.11; 95% CI, .93–1.33) and 192 first gonococcal infections, 95 in the intervention arm and 97 in the control arm with an overall incidence of 2.4/100 woman-years (RH, 0.98; 95% CI, .74–1.30). Per-protocol results indicated that when diaphragm adherence was defined as ''always use'' since the last visit, a significant reduction in gonorrhea incidence occurred among women randomized to the intervention (RH, 0.61; 95% CI, .41–.91). The authors concluded that, although no difference by study arm was found in the rate of acquisition of chlamydia or gonorrhea, per-protocol, results suggested that consistent use of the diaphragm may reduce acquisition of gonorrhea.

Another analysis from the MIRA trial estimated the diaphragm's effect on the incidence and clearance of HPV infection in women in Zimbabwe [79]. There was no overall difference in incidence at the first postenrollment visit or at 12 months, or in HPV clearance at 12 months among women who were HPV positive at enrollment. However, clearance of HPV type 18 was lower in the diaphragm group at the exit visit (relative risk[RR], 0.55; 95% CI, .33–.89) but not at 12 months. Women reporting diaphragm and gel use at 100% of prior sex acts had a lower likelihood of having ≥1 new HPV type detected at 12 months (RR, 0.75; 95% CI, .58–.96). The authors concluded that diaphragms did not reduce the incidence of HPV infection or increase clearance. Diaphragms should not be relied on as the sole source of protection against STIs or HIV infection. Diaphragms used with nonoxynol-9 (N-9) spermicides have been associated with an increased risk for bacterial urinary tract infections in women.

Rectal Use of Spermicides

Although no new data directly address the effects of human rectal use of N-9, new data regarding N-9 disruption of vaginal mucosa mitigate against its use in the rectum, where mucosal disruption is even more profound [80]. Therefore, N-9 should not be used as a microbicide or lubricant during anal intercourse. Since the last treatment guidelines review, preclinical and clinical assessment of microbicides has expanded to include the rectum, and several studies are planned or underway [81].

Effects of Nonbarrier Contraception, Surgical Sterilization, Hysterectomy, and Genital Hygiene on Acquisition and Transmission of STDs and HIV Infection

Nonbarrier Contraception, Surgical Sterilization, and Hysterectomy

Exogenous hormones may modulate mucosal immunity to STDs and HIV infection, and additional evidence suggests that some types of hormonal contraception (primarily injectable depot medroxyprogesterone acetate [DMPA]) may increase risk of HIV acquisition. Importantly, hormonal contraceptives do not provide protection against STD or HIV acquisition and need to be used in conjunction with barrier methods of protection (condoms) in women at risk. The WHO has called for high-quality studies to assess the potential role of hormonal contraception in increasing the risk of HIV-1 infection [66, 67].

The most recent analysis of data on the possible association between hormonal contraception and HIV acquisition question provides an example of the observational studies to date [82]. The study team followed up 1314 HIV-discordant couples in which the HIV-1 seronegative partner was female. They found HIV-1 acquisition rates of 6.61 and 3.78/100 person-years, respectively, in women who self-reported using or not using hormonal contraception at least once during the study (adjusted HR [AHR], 1.98; 95% CI, 1.06–3.68; $P = .03$). Among 2476 couples in which the HIV-1 seronegative partner was male, HIV-1 transmission rates from women to men were 2.61/100 person-years and 1.51/100 person-years, respectively, for men whose partners currently used hormonal contraception and those whose partners did not. (AHR, 1.97; 95% CI, 1.12–3.45; $P = .02$). In subgroup analysis, injectable contraceptive users had a significantly higher increased risk of acquiring and transmitting HIV-1 to their partners than those using no hormonal contraception. In addition, HIV-1 seropositive women using injectable contraception had higher genital HIV-1 RNA concentrations, suggesting a mechanism for increased transmission risk. The elevated genital viral load was observed in users of both injectable (AHR, 2.05; $P = .04$) and oral (AHR, 1.80; $P = .33$) contraceptives.

The relationship between hormonal contraception and HIV acquisition was more closely examined in 2 prospective observational studies in which contraceptive use was carefully documented. The largest one followed up 6109 HIV-uninfected women from family planning clinics in Uganda and Zimbabwe to assess risk of HIV acquisition over the course of 15–24 months [83]. The original analysis used a Cox statistical approach and found that neither combined oral contraceptives (HR, 0.99; 95% CI, .69–1.42) nor DMPA (HR, 1.25; 95% CI, .89–1.78) was associated with significant risk of HIV acquisition overall, including among participants with cervical or vaginal infections. However, hormonal contraceptive users who were HSV-2 seronegative had an increased risk of HIV acquisition

(HR for combined oral contraceptive use, 2.85 [95% CI, 1.39–5.82]; HR for DMPA, 3.97 [95% CI, 1.98–8.00]). A subsequent reanalysis of the same data base used a marginal structural modeling statistical approach to reduce bias and found significantly higher risks of HIV acquisition for DMPA use [84].

A second study accounted for HSV-2 serostatus in a prospective cohort study of 1206 HIV seronegative sex workers from Mombasa, Kenya, who were followed up monthly. In this study, 233 women acquired HIV (8.7/100 person-years). HSV-2 prevalence (81%) and incidence (25.4/100 person-years) were high. In multivariate analysis, including adjustment for HSV-2, HIV acquisition was associated with use of oral contraceptive pills (AHR, 1.46; 95% CI, 1.00–2.13) and DMPA (AHR, 1.73; 95% CI, 1.28–2.34). The effect of contraception on HIV susceptibility did not differ significantly between HSV-2 seronegative and seropositive women. HSV-2 infection was associated with elevated HIV risk (AHR, 3.58; 95% CI, 1.64–7.82). These authors concluded that in this group of high-risk African women, hormonal contraception and HSV-2 infection were both associated with increased risk for HIV acquisition. HIV risk associated with hormonal contraceptive use was not related to HSV-2 serostatus [85].

A systematic review of data from 1966 through early 2005 concluded that studies of combined oral contraceptive and DMPA use generally found positive associations with cervical chlamydial infection, although not all associations were statistically significant. For other STIs, the findings suggested no association between hormonal contraceptive use and STI acquisition, or the results were too limited to draw any conclusions. Evidence was generally limited in both amount and quality, including inadequate adjustment for confounding, lack of appropriate control groups and small sample sizes. Thus, observed positive associations may be due to a true association or to bias, such as differential exposure to STI by contraceptive use or increased likelihood of STI detection among hormonal contraceptive users [86]. A retrospective cohort study at a US university clinic assessed STI incidence among 304 HIV-infected women, 82 of whom received DMPA and 222 who did not. There were no significant differences in trichomoniasis, chlamydial infection, or gonorrhea between women receiving and those not receiving DMPA [87].

Genital Hygiene

Vaginal douching does not protect against acquisition of STDs or HIV, and increases the risk of certain vaginal infections, notably BV. A large meta-analysis of individual participant data from 13 prospective cohort studies involving 14 874 women, of whom 791 acquired HIV infection during 21 218 woman-years of follow-up, found that intravaginal use of cloth or paper (pooled AHR, 1.47; 95% CI, 1.18–1.83), insertion of products to dry or tighten the vagina (AHR, 1.31; 95% CI, 1.00–1.71), and intravaginal cleaning with soap (AHR, 1.24; 95% CI, 1.01–1.53) remained associated with HIV acquisition after controlling for age, marital status, and number of sex partners in the past 3 months [88]. Among HIV-uninfected Kenyan female sex workers, increased frequency of vaginal washing was associated with a higher likelihood of BV, as were vaginal lubrication with petroleum jelly (OR, 2.8; 95% CI, 1.4–5.6), lubrication with saliva (OR, 2.3; 95% CI, 1.1–4.8), and bathing less than the median for the cohort (14 times/week; OR, 4.6; 95% CI, 1.2–17.5). The authors concluded that modification of intravaginal and general hygiene practices should be evaluated as potential strategies for reducing the risk of BV [89]. Genital hygiene methods for washing after sexual exposure, including vaginal washing and douching, are ineffective in protecting against HIV and STD and may increase the risk of bacterial vaginosis, some STDs, and HIV infection [90].

Preexposure Prophylaxis to Prevent STDs and HIV Infection

HIV Infection

Since the last review, the field of preexposure prophylaxis (PrEP) has been galvanized by the results from clinical trials of antiretroviral therapy (ART) to reduce transmission and acquisition of HIV. In HIV-infected persons, ART reduces viral load and presumably reduces infectiousness, a concept illustrated by its efficacy in breast-feeding [91]. A recent trial, HPTN 052, provided more optimism about the use of ART for prevention when given to persons already infected with HIV early in the course of their disease [92]. Focusing on the HIV-infected partner of discordant couples, HPTN 052 was a randomized, multicenter, clinical trial to evaluate the effectiveness of ART in preventing sexual transmission. To be eligible, the HIV-infected partner needed to have a CD4 cell count of 350–550 cells/mm^3, above the level of current WHO recommendations to initiate therapy. Couples were randomized to 1 of 2 study arms: (1) immediate initiation of ART the index case patient on enrollment or (2) delayed initiation of ART until the patient had 2 consecutive CD4 cell counts $<$250 cells/mm^3 or an AIDS-defining illness. The HPTN 052 results were striking and validated findings from 7 previous observational studies [93]. Participants in the immediate-ART initiation arm had a 96% lower risk of acquiring HIV than those in the delayed arm. Moreover, the HIV-infected partner in the immediate-treatment arm also suffered fewer HIV-related complications than those in the delayed arm.

In HIV-uninfected persons, ART reduces susceptibility to infection, a concept initially supported by animal studies and by a study of safety and acceptability in West African women. The first trials to provide proof of concept for both topical and oral PrEP were the CAPRISA 004 and the iPrEX studies [94–96]. CAPRISA 004 randomized 889 women in South Africa to coitally dependent use of 1% tenofovir gel inserted vaginally (up to 12 hours before and within 2 hour after intercourse, not to exceed 2 administrations in 1 day) or to corresponding placebo

gel, for a median of 30 months. Women randomized to the tenofovir gel group had a significantly reduced rate of HIV acquisition: 5.6/100 woman-years, compared with 9.1/100 woman-years (incidence rate ratio, 0.61; 95% CI, .40–.94). The risk of HSV-2 acquisition was also reduced in the tenofovir group (by 51%; $P = .003$).

In the first clinical trial reporting on the efficacy of oral PrEP (iPrEx), nearly 3000 men at high risk for HIV acquisition through sex with other men were randomized to daily oral tenofovir-emtricitabine or placebo and followed up for a median of 1.2 years [97]. Men in the tenofovir-emtricitabine arm experienced a 42% reduction in incidence of HIV (95% CI, 18%–60%) [98]. A nested case-control analysis compared drug levels in men randomized to the tenofovir-emtricitabine group. Among men with a detectable drug level, compared with those without a detectable level, the odds of HIV infection were lower by nearly 13-fold (OR, 12.9; 95% CI, 1.7–99.3), corresponding to a relative reduction in HIV acquisition risk of 92% (95% CI, 40%–99%). Of note, adherence among men randomized to the active study product as estimated by tenofovir or emtricitabine levels in peripheral blood mononuclear cells was ~50%. More recently, the iPrEx investigators reported that daily oral tenofovir-emtricitabine use for 2 years in HIV-uninfected men was associated with a small but significant loss of bone mineral density at the femoral neck (net effect, −1.1% (95% CI, −0.4 to 1.9) [99]. The encouraging findings from the iPrEx study prompted the CDC to publish interim guidance on the use of tenofovir-emtricitabine for PrEP in MSM [100]. Planning is underway to issue full guidelines, expected sometime in 2011.

Most recently, the first evidence that oral PrEP is effective in heterosexual populations was provided by 2 studies done in Sub-Saharan Africa. The Partners PrEP Study included 4747 HIV serodiscordant couples in Kenya and Uganda in which the HIV-negative partner was randomized to daily oral tenofovir-emtricitabine, oral tenofovir, or oral placebo. Of the overall study population, 1785 (38%) were women and 2692 (62%) were men [101]. The study was stopped ahead of schedule by its Data Safety Monitoring Board when both drugs were found to significantly reduce the risk of HIV acquisition. Efficacy was 62% among those randomized to daily oral tenofovir (HR, 0.38; 95% CI, .34–.78; $P = .0003$), and 73% among those randomized to daily oral tenofovir-emtricitabine (HR, 0.27; 95% CI, .49–.85). Of note, adherence in this study was remarkably and consistently high throughout the study; the motivation to be highly adherent may be heightened in the setting of discordant partnerships. The TDF2 Study enrolled 1200 heterosexuals (46% women) in Botswana who were randomized to daily oral tenofovir-emtricitabine or placebo [102]. The study was discontinued before planned cessation when it was deemed that it would not accrue enough time on product to reach its objectives; however, the data that were collected showed a 62.6% efficacy (CI, 21.5–83.4; $P = .013$) for the intervention in reducing risk of HIV acquisition. Neither of these studies showed a differential effect of the PrEP regimens by sex.

Although the results of the trials above are extremely encouraging, a phase III, double-blind, randomized, placebo-controlled trial of daily oral tenofovir-emtricitabine among African women at high risk for HIV acquisition was stopped early when its Independent Data and Monitoring Committee concluded that the study would be unable to determine whether oral Truvada is effective in preventing HIV infection in high-risk women [103]. An equal number of HIV infections ($n = 28$) were observed in each arm among the 1951 women enrolled to that point. The study had planned to enroll 3900 women and follow them up for 1 year. Complete analysis of the final data set must occur before a plausible explanation for this disappointing result can be offered, and such analysis is anticipated in the next several months. In the interim, another randomized controlled trial of PrEP, the VOICE study (MTN 003), is still underway and is slated to complete follow-up of participants in mid-2012. The VOICE study is examining the efficacy of daily use of vaginal 1% tenofovir gel, oral tenofovir, or oral tenofovir-emtricitabine among reproductive-age women in South Africa, Uganda, and Zimbabwe. Information on all of these studies is available at www.avac.org.

Non-HIV STDs

Two studies examined suppression of HSV infection as a means of reducing acquisition or transmission of HIV. Infection with HSV-2 is a significant risk for acquisition and transmission of HIV [104]. A meta-analysis of 19 prospective observational studies found that infection with HSV-2 increased risk of HIV acquisition 2.7-fold in men and 4.4-fold in women [105]. However, 2 studies of daily suppressive acyclovir therapy in HIV-uninfected adults in Africa did not show a reduction in risk of HIV acquisition, despite high rates of reported adherence and excellent retention in one of them [106]. [107] A similar study among HIV-infected persons showed that although acyclovir treatment reduced the frequency of genital ulcers by 73% and HIV plasma viral load by 40% (0.25 $\log_{10}$ copies/mL) compared with placebo, it did not reduce the risk of HIV acquisition [108, 109]. Notably, participants treated with acyclovir had a small but significant reduction in risk of progression to HIV-related disease including decline of CD4 cell counts to <200 cells/mm^3, initiation of ART, or death.

Regarding PrEP for other STDs, as described earlier, an unexpected finding from the CAPRISA 004 trial was the protective effect of 1% tenofovir gel on HSV-2 acquisition [110]. Earlier work had shown that oral tenofovir did not produce drug levels in the vagina necessary to reach the median effective concentration against herpes. However, topical tenofovir allows local drug concentrations nearly 1000 times higher than oral dosing. In CAPRISA 004, the higher level of tenofovir in

cervicovaginal fluid was associated with significantly reduced rates of HSV-2 acquisition. The relationship between vaginal tenofovir gel use and HSV-2 acquisition will also be assessed in heterosexual women participating in the ongoing VOICE study, with results expected in early 2013.

Another randomized trial of PrEP for STIs evaluated other vaginal infections. It assessed the effect of directly observed oral treatment with 2 g of metronidazole plus 150 mg of fluconazole compared with metronidazole placebo plus fluconazole placebo administered monthly in reducing vaginal infections among Kenyan women at risk for HIV-1 acquisition. Of 310 HIV-1–seronegative female sex workers enrolled (155 per arm), 303 were included in the primary end points analysis. Compared with control subjects, women receiving the intervention had fewer episodes of BV (HR, 0.55; 95% CI, .49–.63) and more frequent vaginal colonization with any *Lactobacillus* species (HR, 1.47; 95% CI, 1.19–1.80) and hydrogen peroxide-producing *Lactobacillus* species (HR, 1.63; 95% CI, 1.16–2.27). The incidences of vaginal candidiasis (HR, 0.84; 95% CI, .67–1.04) and trichomoniasis (HR, 0.55; 95% CI, .27–1.12) among treated women were less than those among control subjects, but the differences were not statistically significant. The authors concluded that periodic presumptive treatment reduced the incidence of BV and promoted colonization with normal vaginal flora [111]. Another trial randomized women with asymptomatic BV to observation or treatment and prophylaxis with twice-weekly intravaginal metronidazole gel. Women in the metronidazole gel arm had fewer chlamydial infections during the subsequent 6 months [112].

Postexposure Prophylaxis to Prevent STDs, HIV Infection, and Unintended Pregnancy

Data continue to support implementation of postexposure prophylactic approaches to prevent STD, HIV and unintended pregnancy. In the United States, an emergency contraceptive pill with the brand name Plan B is available over the counter to women aged ≥17 years and to younger women by prescription. Plan B contains 2 tablets of levonorgestrel (each 0.75 mg), which may be taken 12 hours apart as labeled or together as a single dose. If Plan B is not readily accessible, oral emergency contraception also may be provided using many commonly available brands of oral contraceptive pills by instructing the woman to take a specified number of tablets at once. Emergency insertion of an IUD up to 7 days after sex can reduce pregnancy risk by >99%. However, this method is not advisable for a woman who may have untreated cervical gonorrhea or chlamydia, who is already pregnant, or who has other contraindications to IUD use. All oral emergency contraceptive regimens are most efficacious when initiated as soon as possible after unprotected sex but have some efficacy as long as 5 days later. Emergency contraception is ineffective (but is also not harmful) if the woman is already pregnant. [113] More information is available in the 19th edition of *Contraceptive Technology* [114] or at http://core.arhp.org.

A Cochrane review summarized the efficacy, safety, and convenience of various methods of emergency contraception. The review concluded that mifepristone middle dose (25–50 mg) was superior to other hormonal regimens. Mifepristone low dose (<25 mg) could be more effective than levonorgestrel 0.75 mg (2 doses) but this was not conclusive. Levonorgestrel proved more effective than the Yuzpe regimen [115]. The copper IUD was another effective emergency contraceptive that can provide ongoing contraception [113]. CDC guidelines for the use of postexposure prophylaxis with antiretroviral therapy aimed at preventing HIV acquisition as a result of sexual exposure are available [116], as are recommendations for STI prophylaxis after sexual assault [117].

Counseling to Prevent STDs and HIV Infection

New data continue to support the use of individual client-centered counseling to reduce recipients' risk of acquiring HIV infection or other STDs. The US Preventive Services Task Force (USPSTF) recently reviewed the evidence base on this topic [118, 119], and concluded with the following summary statement: "The USPSTF recommends high-intensity behavioral counseling to prevent sexually transmitted infections (STIs) for all sexually active adolescents and for adults at increased risk for STIs. This is a grade B recommendation. The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of behavioral counseling to prevent STIs in non–sexually active adolescents and in adults not at increased risk for STIs" [118].

Since the last guideline revision, training modules continue to become available to help providers develop skills in this area; one consolidated resource is at www.stdhivprevention-training.org. Patient-centered counseling can have a beneficial effect on the likelihood of patients' assuming new or enhancing current risk-reduction practices. All providers should routinely obtain a sexual history from their patients and address management of risk reduction as indicated [120, 121]. This is particularly important for routine care of HIV-infected persons and for adults and adolescents at risk for acquiring STIs.

Rescreening for Incident STIs

No new randomized controlled trials have evaluated the effect of rescreening for chlamydia or gonorrhea in preventing recurrent infection. However, findings of 3 observational studies published since 2006 support continued emphasis on this strategy. Among 272 men followed up for 4 months after a diagnosis of chlamydial infection in Baltimore, Denver, or San Francisco,

Table 1. Individual-Level Biomedical Approaches to Prevention of Sexually Transmitted Infections, Including HIV Infection, by Level of Adherence Required[a]

Level of adherence	Intervention	Effectiveness (level of evidence)[b] in men	Effectiveness (level of evidence)[b] in women
Single-time; susceptible individual	Male circumcision	Prevents acquisition of HIV, genital HPV, genital herpes; may prevent acquisition of trichomoniasis (level I/RCTs in heterosexual men)	Reduces incidence of bacterial vaginosis, trichomoniasis, genital ulcer disease (level 1/RCT)
Several times; time-limited (months)	Vaccines	Prevents acquisition of hepatitis A, hepatitis B (level I/RCTs; ecological data)	Prevents acquisition of HPV, hepatitis A, hepatitis B (level I/RCTs)
Situationally timed with sexual behaviors	Male condom	Prevents acquisition of gonorrhea, chlamydia, syphilis, genital HPV, trichomoniasis, HIV, genital herpes (level II-2); facilitates regression of HPV associated penile lesions (level II-2)	Prevents acquisition of gonorrhea, chlamydia, syphilis, genital HPV, trichomoniasis, HIV, genital herpes, PID (level II-2); facilitates regression of cervical intraepithelial neoplasia and clearance of genital HPV infection (level II-2)
	Female condom	Unknown	Prevents acquisition of gonorrhea, chlamydia, trichomoniasis, syphilis (level III)
	Diaphragm	Unknown	May prevent acquisition of gonorrhea (RCT; level I, subanalysis of self-reported use)
	Topical microbicides	Unknown	PRO2000 did not prevent acquisition of HIV-1 (RCT; level I); coitally dependent use of 1% tenofovir gel prevented acquisition of HIV-1 and HSV-2 (RCT; level I)
Daily use	Suppressive therapy for genital herpes	Prevents transmission of genital HSV-2 (RCT; level I); does not prevent transmission or acquisition of HIV (RCT; level I)	Prevents transmission of genital HSV-2 (RCT; level I); does not prevent transmission or acquisition of HIV (RCT; level I)
	Oral and topical antiretroviral drugs	Prevents transmission of HIV in men who have sex with men and men in heterosexual serodiscordant couples	Oral agents prevent transmission of HIV in women in serodiscordant couples; under study for HIV prevention in larger populations of women[c]

Abbreviations: HIV, human immunodeficiency virus; HPV, human papillomavirus; HSV-2, herpes simplex virus, type 2; PID, pelvic inflammatory disease. RCT, randomized controlled trial.

[a] Adapted from reference 61, with authors' permission.

[b] Levels of evidence are summarized using the classification scheme of the US Preventive Services Task Force (available at http://www.ahrq.gov/CLINIC/uspstfix.htm).

[c] See www.avac.org for details on ongoing clinical trials.

recurrent infection occurred in 13% (incidence, 45.4 infections/100 person-years) [122]. Among 897 female adolescents attending school-based health centers, 236 had ≥1 subsequent positive tests for a cumulative incidence of reinfection in 1 year of 26.3% (95% CI, 23.4–29.2) [123]. Project RESPECT data were used to determine the incidence of new infections during the year after a visit to a STD clinic. Among 1236 women, 25.8% had ≥1 new infection (*C. trachomatis* in 11.9%, *N. gonorrhoeae* in 6.3%, and *T. vaginalis* in 12.8%); among 1183 men, 14.7% had ≥1 new infection (*C. trachomatis* in 9.4% and *N. gonorrhoeae* in 7.1%). The authors concluded that individuals who receive diagnoses of any of these STIs should return in 3 months for rescreening [124]. Rescreening several months after a diagnosis of chlamydia, gonorrhea, or trichomoniasis detects substantial numbers of new infections and can be recommended as a population-level prevention method.

CONCLUSIONS

A range of preventive interventions is needed to reduce the risks of acquiring STIs , including HIV infection, among sexually active persons (Table 1). A flexible approach targeted to specific populations should integrate combinations of biomedical, behavioral, and structural interventions. These would ideally involve an array of prevention contexts, including (1) communications and practices among sexual partners; (2) transactions between individual clients and their healthcare providers; and (3) comprehensive population-level strategies for prioritizing prevention research, ensuring accurate outcome assessment, and formulating health policy.

Notes

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