Chapter 12
Public Health and Prevention

Elissa Meites and Kimberly A. Workowski

Introduction

Sexually transmitted diseases (STDs) are a challenging public health problem with tremendous health and economic impacts. In the United States alone, there are approximately 20 million new sexually transmitted infections per year [1], and the estimated annual direct medical cost is $16 billion [2]. Of all the notifiable infectious diseases in the United States, the one most commonly reported is chlamydia [3]. Most sexually active persons will have at least one sexually transmitted infection during their lifetime, though many will never know it [1, 4–6].

STD epidemics encompass behavioral, biomedical, and sociopolitical realities. Although STDs can affect people of all races and ethnicities, ages, and geographic areas, marginalized populations may be particularly vulnerable to the consequences of disease. STD prevention is all the more challenging due to the effects of cultural taboos, stigma, and discrimination. STD outbreaks can reveal vulnerabilities in a community's access to appropriate medical care, quality education and health information, healthy economic and social policies, and other structural failures [7].

E. Meites, MD, MPH, FAAFP (✉)
Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA
e-mail: emeites@cdc.gov

K.A. Workowski, MD, FIDSA, FACP
Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA

Department of Medicine, Infectious Diseases, Emory University, Atlanta, GA, USA

N.S. Skolnik et al. (eds.), *Sexually Transmitted Diseases: A Practical Guide for Primary Care*, Current Clinical Practice, DOI 10.1007/978-1-62703-499-9_12,

Table 12.1 Epidemiology of selected sexually transmitted infections compared with their status as nationally notifiable infectious conditions in the United States

Infection	Nationally notifiable [47]	Epidemiology [1]
Human papillomavirus (HPV)	No	Prevalence: 24 million persons
Herpes simplex virus (HSV) type 2	No	Prevalence: 79 million persons
Trichomoniasis	No	Prevalence: 3.7 million persons
Chlamydia	Yes	Annual incidence: 2.9 million cases
Gonorrhea	Yes	Annual incidence: 820,000 cases
Syphilis	Yes	Annual incidence: 55,000 cases
Chancroid	Yes	Annual incidence: 24 cases [8]

Public Health Information

Public health organizations in the United States include health departments in every state, as well as the Centers for Disease Control and Prevention (CDC) at the national level. Public health activities of particular value to clinicians include surveillance for trends in who is acquiring infections and diseases, or trends in antimicrobial resistance. Local and state health departments may collect case reports of certain diseases, conduct partner notification and contact tracing during investigations of communicable diseases, and provide clinical consultation and education. Nationally, there are federally funded STD control programs for chlamydia, gonorrhea, and syphilis. In addition to providing leadership and financial support, key functions of public health organizations at the state and national levels are to guide research and policy development, and to assess, provide, and interpret timely scientific information regarding STDs.

Information about the epidemiology (prevalence and incidence) of STDs in the US population is derived from several different sources. These include (A) surveillance of reportable diseases; (B) nationally representative surveys; and (C) studies in special populations. Although the most commonly reported diseases are STDs, the most common sexually transmitted infections are not nationally notifiable (Table 12.1).

First, surveillance occurs for certain conditions which are considered to be of public health importance. While state policies vary regarding which conditions are reportable, the nationally notifiable STDs are chancroid, chlamydia, gonorrhea, and syphilis (Table 12.1). In addition, viral hepatitis and HIV are also notifiable conditions but are not always sexually transmitted. Case reports may be generated from a clinician who makes the diagnosis, a laboratory where a clinical test is positive, or a local health department following the case; reports are transmitted to the state health department. Each state health department then provides CDC with the overall numbers of cases to create the national surveillance estimates, which are compiled and published annually [3, 8].

Second, studies conducted on a nationally representative sample can provide helpful estimates of the prevalence of STDs that are common but not reportable. One example

is the National Health and Nutrition Examination Survey (NHANES), a population-based study conducted on a representative sample of the civilian, noninstitutionalized population of the United States. Estimates of the national prevalence of common infections such as human papillomavirus (HPV), genital herpes, and trichomoniasis can be extrapolated from the prevalence detected in NHANES participants [9].

Third, special studies are useful to measure STDs in specific at-risk or minority populations, such as adolescents, pregnant women, men who have sex with men, and others. These types of studies are also useful to learn about less common conditions such as neonatal herpes, pelvic inflammatory disease (PID), or lymphogranuloma venereum. All research studies involving human subjects receive additional oversight from institutional review boards (IRBs) to ensure that the research conducted is ethical and its methods are sound.

Public Health and Clinicians

To improve population health, however, public health efforts rely on the foundation of the clinical encounter. Clinicians observe and assess symptoms and signs, request laboratory tests, make a diagnosis, and offer interactive counseling for individual patients. Primary care providers in particular play a unique and important role in routine sexual history-taking, risk assessment, and risk reduction counseling.

To help guide clinicians, CDC produces national STD treatment guidelines, which offer recommendations on the prevention, diagnosis, and treatment of STDs and sexually transmitted infections [10]. Clinically, the prevention and control of STDs are based on five major strategies:

- Education and counseling of persons at risk on ways to avoid STDs through changes in sexual behaviors and use of recommended prevention strategies (e.g., condoms).
- Screening and identification of asymptomatically infected persons and of symptomatic persons unlikely to seek diagnostic and treatment services.
- Effective diagnosis, treatment, and counseling of infected persons.
- Evaluation, treatment, and counseling of sex partners of persons who are infected with an STD.
- Pre-exposure vaccination of persons at risk for vaccine-preventable STDs (e.g., hepatitis A, hepatitis B, HPV).

Public Health Problems in STD Control and Prevention

The following examples of major public health problems will highlight the crucial role of clinicians and discuss how the above strategies can help prevention and control of STDs. Major problems include antimicrobial-resistant gonorrhea, STD-related cancers, STD-related HIV acquisition and transmission, STD-related infertility, and STD-related adverse outcomes of pregnancy.

Antimicrobial-Resistant Neisseria gonorrhoeae

There are estimated to be over 820,000 new cases of gonorrhea in the United States each year [1]. The epidemiology of gonorrhea varies greatly among communities, and disproportionately affects certain populations, including adolescents and young adults, blacks, and men who have sex with men [8]. Untreated gonorrheal infections can lead to PID and infertility. Most of the time, gonorrhea can be treated successfully using a third-generation cephalosporin antimicrobial. However, gonorrhea treatment has been complicated by the ability of *N. gonorrhoeae* to develop resistance to many antimicrobials over the past several decades. From 2006 through 2010, the minimum concentrations of cefixime needed to inhibit the growth of gonorrhea strains in the United States and many other countries increased, suggesting that the effectiveness of this medication may be waning [11]. These patterns may indicate the impending development of clinically significant gonococcal resistance to cephalosporins [11].

Priorities for clinicians include treating all cases of gonorrhea with the most effective available antimicrobial regimen, as well as offering male latex condoms, risk-reduction counseling and testing for other STDs. Due to the possibility of reinfection, repeat gonorrhea testing 3 months following appropriate treatment at the anatomic site of infection is recommended [10]. In addition, providers should ensure that all sex partners from the preceding 60 days are promptly evaluated and treated. Primary screening should be targeted and offered to persons who are considered to be at increased risk, taking into consideration the local prevalence of gonorrhea [12, 13]. Due to the widespread use of nucleic acid amplification tests for gonorrhea diagnosis, laboratory capacity to isolate *N. gonorrhoeae* by culture has been declining; healthcare systems should support continued access to culture or develop partnerships with laboratories that can perform culture. Local, state, and national public health organizations can provide helpful consultation.

STD-Related Cancers

Cervical cancers are caused by certain types of HPV, particularly HPV types 16 and 18. In addition, many anal cancers, oropharyngeal cancers, vulvar, and penile cancers are caused by HPV, although the natural history and epidemiology of these cancers have been less fully described [14].

HPV is a common infection in both men and women, and first infection can occur soon after sexual debut [15, 16]. Virtually all sexually active persons will be infected with at least one type of HPV at some point during their lives [4, 5]. An estimated 79 million persons in the United States are currently infected with at least one type of HPV [1]; among 14–59-year-old women, the prevalence of any type of HPV is 42.5 % [17]. Most HPV infections resolve spontaneously without any treatment—about 70 % clear within 1 year, and 90 % within 2 years—however, those

that persist can develop into intraepithelial lesions and cancers [18, 19]. The most common kind of HPV-associated cancer is cervical cancer, which affects an estimated 12,000 women each year in the United States; globally, the vast majority of cervical cancer deaths occur in women in developing countries [14, 20]. Men who have sex with men appear to be at particularly high risk for HPV-associated diseases; their incidence of anal cancer is estimated to be 37 times higher than that among men who have sex with only women [21, 22].

Since 2006, HPV vaccine has been routinely recommended in the United States for females at a target age of 11 or 12 years; since 2011, vaccine has been recommended for males at this age as well [23, 24]. Before a vaccine can be used in the United States, it must be licensed by the US Food and Drug Administration (FDA), which requires safety and efficacy data for the vaccine. Next, national vaccine policy is made by the Advisory Committee on Immunization Practices (ACIP), a panel of independent experts organized by the CDC with formal meetings three times a year. ACIP recommendations are based on the best available scientific evidence on the use of the vaccine in populations, such as vaccine efficacy and safety, epidemiology, and burden of disease in the United States, cost and cost-effectiveness, vaccine acceptability, and implementation plans. HPV vaccine is covered by most insurance plans as well as the Vaccines for Children Program in the United States [25]. Vaccination is one of the most effective methods for preventing HPV infection; clinicians should make strong recommendations and vaccinate adolescents on time.

STD-Related HIV Acquisition and Transmission

Not only is the diagnosis of a new sexually transmitted infection an objective marker of unprotected sexual activity, but in addition, certain STDs can increase plasma HIV viral load and genital HIV shedding, which may also increase the risk of sexual and perinatal HIV transmission [10, 26, 27].

Identification of sexual risk behaviors, risk reduction counseling, appropriate diagnosis, and treatment are important in the prevention and management of specific STDs that can increase HIV acquisition and transmission. In particular, STDs that cause ulceration or inflammation (e.g., syphilis, herpes, trichomoniasis, and chancroid) can increase the transmissibility of HIV [28–30]. In the United States, the most common etiologies of genital, anal, or perianal ulceration are genital herpes or syphilis. These infections can be easily confused on physical exam, and laboratory testing is warranted to confirm a specific diagnosis, in order to ensure the correct course of treatment [10].

Genital herpes is a common cause of genital ulceration; in addition, many persons may have mild or unrecognized infection yet shed the virus intermittently. An estimated 24 million people in the United States are infected with herpes simplex virus (HSV) type 2 [1]; more than 80 % of these infections are undiagnosed [31]. A particularly high burden of disease has been observed among non-Hispanic blacks, with a seroprevalence of 39.2 % [31]. The majority of genital herpes infections are

transmitted by persons who are unaware of their infection or are asymptomatic when transmission occurs.

Syphilis in the United States tends to cluster geographically and within sexual networks. There are an estimated 55,000 new cases of syphilis annually in the United States [1]; rates among men were more than 7 times higher than among women, and two-thirds of primary and secondary syphilis in men occurred among men who have sex with men [8]. The resurgence of syphilis in patients with HIV infection underscores the importance of primary prevention of syphilis in this population, which should include client-centered risk reduction messages and discussions of specific actions that can reduce the risk of acquiring syphilis and of acquiring or transmitting HIV infection.

Trichomoniasis is quite common, affecting an estimated 3.7 million people in the United States [1], including 3.1 % of women aged 14–49 years [32]. *Trichomonas vaginalis* infection can cause local inflammation that has been associated with an increased risk of HIV acquisition and transmission [32].

Chancroid, an ulcerative STD caused by the bacteria *Haemophilus ducreyi*, has been associated with HIV acquisition [29]. In the United States, prevalence is low: in 2010, only 24 cases of chancroid were reported from nine different states [8].

Because of the likelihood of co-infection, patients who are diagnosed with one STD (or HIV) should also be offered screening for other STDs including HIV, and their sexual partners should be tested and treated as well [10]. In the United States, men who have sex with men may be at particularly high risk of co-infection with both HIV and other STDs. Prompt recognition and appropriate treatment of STDs are important strategies for reducing HIV risk [10].

Studies conducted internationally in high-prevalence areas have shown that male circumcision can also reduce the risk of HIV acquisition in heterosexual men [33]. In addition, recent data has shown effectiveness of antiretroviral therapy for either pre- or postexposure prophylaxis (PrEP and PEP) in reducing acquisition and transmission of HIV [34, 35]. In a double-blind randomized controlled trial, pericoital use of 1 % tenofovir gel reduced HIV-1 acquisition by 39 %, and HSV-2 acquisition by 51 % [36]. Although topical microbicides have been a subject of some interest, trials of agents with nonspecific antimicrobial activity have not proved particularly useful for STD prevention to date [37]. The spermicide nonoxynol-9 (or “N-9”) can injure anal and vaginal mucosal tissue and may even enhance HIV transmission [38]. Clinicians can counsel patients on primary prevention methods, including using condoms consistently and correctly, minimizing the number of sexual partners, and avoiding concurrent sexual partnerships [10].

STD-Related Infertility

Gonorrheal and chlamydial infections, even when asymptomatic, can lead to PID and complications including infertility.

Chlamydia is the most commonly reported STD in the United States. Chlamydial infections are usually asymptomatic in women, but can cause significant reproductive health sequelae including acute PID, an important infectious cause of infertility, ectopic pregnancy, and chronic pelvic pain. There are an estimated 2.9 million new cases of chlamydia annually in the United States [1]. Particularly high rates of chlamydia are seen among adolescent girls and women, blacks, and persons in high-risk settings such as juvenile detention facilities, jails, or prisons, as well as STD and family planning clinics [8].

When chlamydial or gonorrheal infections ascend into a woman's upper genital tract, they can induce a host immune response that causes inflammation and tissue damage, which can lead to PID and/or scarring of the fallopian tubes. Long-term consequences can include infertility, ectopic pregnancy, or chronic pelvic pain. An estimated 10 % of women with untreated chlamydia may develop PID, and a proportion of these may go on to develop infertility [39].

Public health programs aim to prevent these reproductive problems before they can occur. Most public health efforts focus on at-risk women, although treating affected male partners is also clinically important. Overlapping public health paradigms focus on (a) preventing initial infections; (b) providing primary screening and treatment for existing infections; and (c) conducting secondary screening for repeat infections [28]. Clinicians play an important role in counseling patients about prevention methods such as using latex condoms consistently and correctly throughout every sexual encounter, and minimizing numbers of sexual partners. In addition, prompt screening and appropriate treatment for chlamydia reduces the risk of PID.

STD-Related Adverse Outcomes of Pregnancy

Many sexually transmitted infections can cause adverse outcomes of pregnancy, including spontaneous abortion, stillbirth, premature delivery, and congenital infections.

Syphilis remains an important cause of infant mortality and morbidity during pregnancy despite availability of serologic screening tests and recommendations for routine prenatal screening and counseling. Thus, each case of congenital syphilis can be seen as a sentinel event, signaling missed opportunities within a health care system. In the United States, congenital syphilis is uncommon, with a total of 377 cases reported from 28 states, the District of Columbia, and one outlying area in 2010 [8].

Genital herpes can also be associated with poor fetal outcomes, especially after primary maternal genital infection acquired in late pregnancy [40]. Neonatal herpes infection is a rare but serious condition caused by HSV; incidence estimates in the United States range from 5.6 to 28.2 per 100,000 births [41, 42]. Guidelines from the American College of Obstetricians and Gynecologists (ACOG) recommend cesarean delivery for women with active genital lesions in order to prevent transmission of HSV to neonates [43]. Although primary prevention is important for women

with herpes lesions at the time of delivery, most mothers of infected neonates had asymptomatic HSV infections [44]. Thus, neonatal herpes mitigation also relies on postnatal testing in infants with a compatible clinical presentation, as well as provision of acyclovir antiviral therapy promptly and for an appropriate course of treatment [45, 46].

Other STDs that can result in adverse pregnancy outcomes include gonorrhea, chlamydia, bacterial vaginosis, and trichomoniasis, although data regarding the effects of these infections on pregnancy are more limited. Health care providers can educate and screen pregnant women for gonorrhea and chlamydia per existing guidelines, and also offer treatment and partner services when appropriate [10].

Conclusion

Clinicians can play an important role in the promotion of sexual health and the prevention and control of STDs through the effective use of five major strategies: education and counseling; screening; diagnosis and treatment; partner treatment; and vaccination. Support for clinicians is available from public health organizations at the local, state, and national levels. Communities across the United States rely on multidisciplinary collaboration between clinicians and public health agencies for the prevention and control of major STD-related public health problems.

References

1. Satterwhite CL, Torrone E, Meites E, Dunne EF, Mahajan R, Ocfemia MCB, Su J, Xu F, Weinstock H. Sexually Transmitted Infections among U.S. Women and Men: Prevalence and Incidence Estimates, 2008. Sexually Transmitted Diseases. 2013; 40(3): 187–193. [Research Support, U.S. Gov't].
2. Owusu-Edusei K, Chesson HW, Gift TL, Tao G, Mahajan R, Ocfemia MC, Kent CK. The estimated direct medical cost of selected sexually transmitted infections in the United States, 2008. Sexually Transmitted Diseases. 2013; 40(3):197-201. [Research Support, U.S. Gov't].
3. Centers for Disease Control and Prevention. Summary of notifiable diseases—United States, 2010. MMWR Morb Mortal Wkly Rep. 2012;59(53):1–111.
4. Koutsky L. Epidemiology of genital human papillomavirus infection. Am J Med. 1997;102(5A):3–8 [Review].
5. Myers ER, McCrory DC, Nanda K, Bastian L, Matchar DB. Mathematical model for the natural history of human papillomavirus infection and cervical carcinogenesis. Am J Epidemiol. 2000;151(12):1158–71 [Research Support, U.S. Gov't, P.H.S.].
6. Forhan SE, Gottlieb SL, Sternberg MR, Xu F, Datta SD, McQuillan GM, et al. Prevalence of sexually transmitted infections among female adolescents aged 14 to 19 in the United States. Pediatrics. 2009;124(6):1505–12 [Research Support, U.S. Gov't].
7. Institute of Medicine (U.S.). Committee on Prevention and Control of Sexually Transmitted Diseases, Eng TR, Butler WT. The hidden epidemic: confronting sexually transmitted diseases. Washington DC: National Academy Press; 1997.

8. Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2010. Atlanta: U.S. Department of Health and Human Services; 2011. http://www.cdc.gov/std/stats/
9. Ezzati TM, Massey JT, Waksberg J, Chu A, Maurer KR. Sample design: Third National Health and Nutrition Examination Survey. Vital Health Stat 2. 1992;113:1–35.
10. Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. MMWR Recomm Rep. 2010;59:1–110. http://www.cdc.gov/std/treatment/2010
11. Bolan GA, Sparling PF, Wasserheit JN. The emerging threat of untreatable gonococcal infection. N Engl J Med. 2012;366(6):485–7 [Review].
12. Workowski KA, Berman SM, Douglas Jr JM. Emerging antimicrobial resistance in Neisseria gonorrhoeae: urgent need to strengthen prevention strategies. Ann Intern Med. 2008;148(8):606–13 [Review].
13. Meyers D, Wolff T, Gregory K, Marion L, Moyer V, Nelson H, et al. USPSTF recommendations for STI screening. Am Fam Physician. 2008;77(6):819–24 [Review].
14. Gillison ML, Chaturvedi AK, Lowy DR. HPV prophylactic vaccines and the potential prevention of noncervical cancers in both men and women. Cancer. 2008;113(10 Suppl):3036–46 [Review].
15. Winer RL, Lee SK, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. Genital human papillomavirus infection: incidence and risk factors in a cohort of female university students. Am J Epidemiol. 2003;157(3):218–26 [Research Support, U.S. Gov't].
16. Partridge JM, Hughes JP, Feng Q, Winer RL, Weaver BA, Xi LF, et al. Genital human papillomavirus infection in men: incidence and risk factors in a cohort of university students. J Infect Dis. 2007;196(8):1128–36 [Research Support, N.I.H., Extramural].
17. Hariri S, Unger ER, Sternberg M, Dunne EF, Swan D, Patel S, et al. Prevalence of genital human papillomavirus among females in the United States, the National Health And Nutrition Examination Survey, 2003-2006. J Infect Dis. 2011;204(4):566–73 [Research Support, U.S. Gov't].
18. Molano M, Van den Brule A, Plummer M, Weiderpass E, Posso H, Arslan A, et al. Determinants of clearance of human papillomavirus infections in Colombian women with normal cytology: a population-based, 5-year follow-up study. Am J Epidemiol. 2003;158(5):486–94 [Research Support, Non-U.S. Gov't].
19. Moscicki AB, Shiboski S, Broering J, Powell K, Clayton L, Jay N, et al. The natural history of human papillomavirus infection as measured by repeated DNA testing in adolescent and young women. J Pediatr. 1998;132(2):277–84 [Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't].
20. Paavonen J. Human papillomavirus infection and the development of cervical cancer and related genital neoplasias. Int J Infect Dis. 2007;11 Suppl 2:S3–9 [Review].
21. Joseph DA, Miller JW, Wu X, Chen VW, Morris CR, Goodman MT, et al. Understanding the burden of human papillomavirus-associated anal cancers in the US. Cancer. 2008;113(10 Suppl):2892–900 [Research Support, U.S. Gov't].
22. Seaberg EC, Wiley D, Martinez-Maza O, Chmiel JS, Kingsley L, Tang Y, et al. Cancer incidence in the multicenter AIDS Cohort Study before and during the HAART era: 1984 to 2007. Cancer. 2010;116(23):5507–16 [Comparative Study Research Support, N.I.H., Extramural].
23. Centers for Disease Control and Prevention. Recommendations on the Use of quadrivalent human papillomavirus vaccine in males—Advisory Committee On Immunization Practices (ACIP), 2011. MMWR Morb Mortal Wkly Rep. 2011;60:1705–8.
24. Centers for Disease Control and Prevention. FDA licensure of bivalent human papillomavirus vaccine (HPV2, Cervarix) for use in females and updated HPV vaccination recommendations from the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep. 2010;59(20):626–9.
25. Centers for Disease Control and Prevention. Progress toward implementation of human papillomavirus vaccination—the Americas, 2006–2010. MMWR Morb Mortal Wkly Rep. 2011;60(40):1382–4.

26. Cohen MS. Classical sexually transmitted diseases drive the spread of HIV-1: back to the future. J Infect Dis. 2012;206(1):1–2 [Review].
27. Hayes R, Watson-Jones D, Celum C, van de Wijgert J, Wasserheit J. Treatment of sexually transmitted infections for HIV prevention: end of the road or new beginning? AIDS. 2010;24 Suppl 4:S15–26 [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't].
28. Workowski KA, Levine WC, Wasserheit JN, Centers for Disease Control and Prevention, Atlanta, Georgia. U.S. Centers for Disease Control and Prevention guidelines for the treatment of sexually transmitted diseases: an opportunity to unify clinical and public health practice. Ann Intern Med. 2002;137(4):255–62 [Review].
29. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases. Sex Transm Infect. 1999;75:3–17 [Review].
30. Rottingen JA, Cameron DW, Garnett GP. A systematic review of the epidemiologic interactions between classic sexually transmitted diseases and HIV: how much really is known? Sex Transm Dis. 2001;28:579–97 [Review].
31. Centers for Disease Control and Prevention. Seroprevalence of herpes simplex virus type 2 among persons aged 14–49 years—United States, 2005–2008. MMWR Morb Mortal Wkly Rep. 2010;59(15):456–9.
32. Sutton M, Sternberg M, Koumans EH, McQuillan G, Berman S, Markowitz L. The prevalence of Trichomonas vaginalis infection among reproductive-age women in the United States, 2001-2004. Clin Infect Dis. 2007;45(10):1319–26 [Research Support, U.S. Gov't].
33. Gray RH, Kigozi G, Serwadda D, Makumbi F, Watya S, Nalugoda F, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet. 2007;369(9562):657–66 [Randomized Controlled Trial].
34. Smith DK, Grohskopf LA, Black RJ, Auerbach JD, Veronese F, Struble KA, et al. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. MMWR Recomm Rep. 2005;54(RR-2):1–20 [Practice Guideline].
35. Centers for Disease Control and Prevention. Interim guidance: preexposure prophylaxis for the prevention of HIV infection in men who have sex with men. MMWR Morb Mortal Wkly Rep. 2011;60(3):65–8.
36. Abdool Karim Q, Abdool Karim SS, Frohlich JA, Grobler AC, Baxter C, Mansoor LE, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. Science. 2010;329(5996):1168–74 [Randomized Controlled Trial; Research Support, N.I.H.; Research Support, Non-U.S. Gov't].
37. Marrazzo JM, Cates W. Interventions to prevent sexually transmitted infections, including HIV infection. Clin Infect Dis. 2011;53 Suppl 3:S64–78 [Review].
38. Phillips DM, Sudol KM, Taylor CL, Guichard L, Elsen R, Maguire RA. Lubricants containing N-9 may enhance rectal transmission of HIV and other STIs. Contraception. 2004;70(2):107–10 [Research Support, U.S. Gov't].
39. Oakeshott P, Kerry S, Aghaizu A, Atherton H, Hay S, Taylor-Robinson D, et al. Randomised controlled trial of screening for Chlamydia trachomatis to prevent pelvic inflammatory disease: the POPI (prevention of pelvic infection) trial. BMJ. 2010;340:c1642 [Multicenter Study; Randomized Controlled Trial; Research Support, Non-U.S. Gov't].
40. Brown ZA, Selke S, Zeh J, Kopelman J, Maslow A, Ashley RL, et al. The acquisition of herpes simplex virus during pregnancy. N Engl J Med. 1997;337(8):509–15.
41. Handel S, Klingler EJ, Washburn K, Blank S, Schillinger JA. Population-based surveillance for neonatal herpes in New York City, April 2006-September 2010. Sex Transm Dis. 2011;38(8):705–11.
42. Flagg EW, Weinstock H. Incidence of neonatal herpes simplex virus infections in the United States, 2006. Pediatrics. 2006;127(1):e1–8 [Research Support, U.S. Gov't].
43. ACOG Committee on Practice Bulletins. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. No. 82 June 2007. Management of herpes in pregnancy. Obstet Gynecol. 2007;109(6):1489–98.

44. Corey L, Wald A. Maternal and neonatal herpes simplex virus infections. N Engl J Med. 2009;361(14):1376–85.
45. Kimberlin DW, Whitley RJ, Wan W, Powell DA, Storch G, Ahmed A, et al. Oral acyclovir suppression and neurodevelopment after neonatal herpes. N Engl J Med. 2011;365(14):1284–92.
46. Shah SS, Aronson PL, Mohamad Z, Lorch SA. Delayed acyclovir therapy and death among neonates with herpes simplex virus infection. Pediatrics. 2011;128(6):1153–60.
47. 2012 Case definitions: nationally notifiable conditions infectious and non-infectious case. Atlanta, GA: Centers for Disease Control and Prevention; 2012 [cited July 11, 2012]. http://www.cdc.gov/osels/ph_surveillance/nndss/phs/infdis2011.htm