

Chapter 10

Sexually Transmitted Infections: Impact and Cost-Effectiveness of Prevention

Harrell W. Chesson, Philippe Mayaud, and Sevgi O. Aral



INTRODUCTION

Sexually transmitted infections (STIs) impose major health and economic burdens globally. More than 35 bacterial, viral, and parasitic pathogens have been identified as sexually transmissible. An estimated 498.9 million new cases of four of the curable STIs occurred among adults ages 15–49 years in 2008, an increase of 11.3 percent from the estimated 448.3 million new cases in 2005 (WHO 2012a). In 2008, these cases included 105.7 million new cases of chlamydia, 106.1 million new cases of gonorrhea, 10.6 million new cases of syphilis, and 276.4 million new cases of trichomoniasis (WHO 2012a). Males accounted for 266.1 million (53 percent) new cases. At any point in 2008, an estimated 100.4 million adults were infected with chlamydia, 36.4 million with gonorrhea, 36.4 million with syphilis, and 187.0 million with trichomoniasis (WHO 2012a).

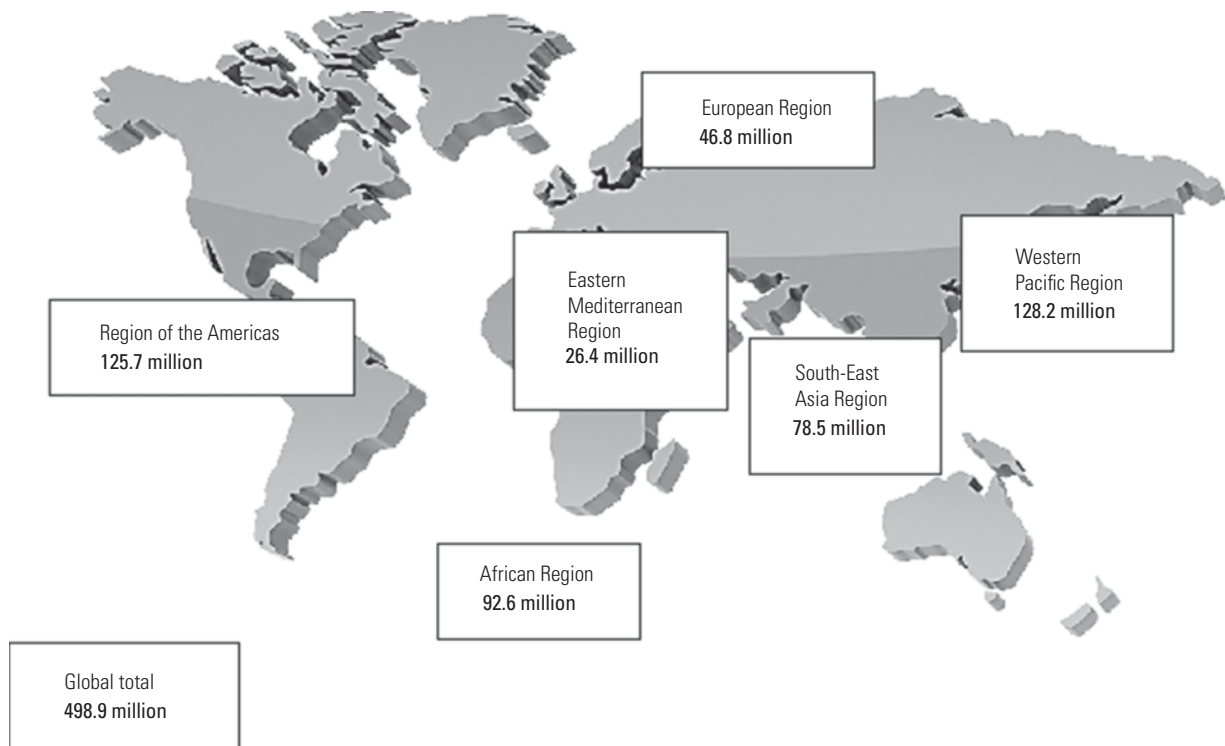
The incidence and prevalence of these curable STIs varies remarkably across World Health Organization (WHO) regions, as shown in map 10.1, figure 10.1, and table 10.1. In general, low- and middle-income countries (LMICs) have higher estimated burdens of STIs than do high-income countries (HICs) (WHO 2012a). However, comparing income and STI burden by region can be challenging because income can vary substantially across countries within a given region. For example, the Americas include two relatively wealthy countries—Canada and the United States—yet the overall prevalence of these four curable STIs is higher in this than in

any other region. The highest estimated prevalence and incidence rates of chlamydia and trichomoniasis occur in the Americas, while the highest rates of gonorrhea and syphilis are in Sub-Saharan Africa (figures 10.2 and 10.3). In general, trichomoniasis is the most prevalent STI across regions, with the exception of Europe and the Western Pacific, where chlamydia is more prevalent.

A great deal of uncertainty surrounds the global and regional estimates of the incidence and prevalence of these four STIs (WHO 2012a). Relative to the size of the population in each region, the Americas has the highest annual incidence rate of these four curable STIs (0.264), followed by Africa (0.241), Western Pacific (0.130), Europe (0.104), Eastern Mediterranean (0.085), and South-East Asia (0.083). However, given heterogeneity in the quality of STI surveillance across regions, it is difficult to make cross-regional comparisons.

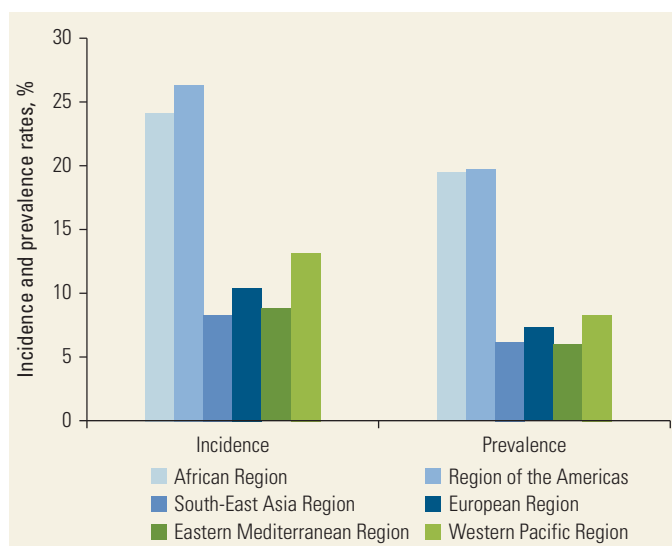
The incidence of STIs can vary substantially within, as well as across, regions according to the WHO's Global Health Observatory Data Repository. In 2010, the proportion of antenatal care attendees who were positive for syphilis was 0.2 percent in Côte d'Ivoire and 10.0 percent in the Central African Republic; the proportion of sex workers with active syphilis was 1.5 percent in Honduras and 17.5 percent in El Salvador; and the proportion with active syphilis among men who have sex with men (MSM) was 1.1 percent in Vietnam and 18.4 percent in Singapore. The incidence of STIs in a given country can vary substantially over time. For example, the percentage

Map 10.1 Estimated Incidence of Four Curable STIs in Adults



Source: WHO 2012a.
Note: STI = sexually transmitted infection.

Figure 10.1 Estimated Combined Incidence and Prevalence Rates of Four Curable STIs, Ages 15–49 Years, WHO Regions, 2008



Source: WHO 2012a.
Note: STI = sexually transmitted infection; WHO = World Health Organization. Calculated based on the estimated number of incidence cases and prevalence cases of four curable STIs (chlamydia, gonorrhea, syphilis, and trichomoniasis) and the estimated population ages 15–49 years as estimated by WHO (2012a). The combined rates were calculated by summing the number of estimated cases and dividing by the population size.

of MSM with active syphilis in Indonesia ranged from 4.0 percent in 2008 to 21.9 percent in 2012.¹ Differences in the burden of STIs across regions, and within regions over time, preclude the identification of feasible programs and policies that can successfully reduce the burden of STIs in a cost-effective manner in all settings.

HEALTH AND ECONOMIC BURDEN OF STIs

If left untreated, common STIs may cause complications, including pelvic inflammatory disease, ectopic pregnancy, postpartum endometriosis, infertility, and chronic abdominal pain in women; adverse pregnancy outcomes, including abortion, intrauterine death, and premature delivery; neonatal and infant infections and blindness; urethral strictures and epididymitis in men; genital malignancies; proctitis, colitis, and enteritis in MSM; arthritis secondary to gonorrhea and chlamydia; liver failure and liver cancer secondary to hepatitis B virus (HBV); myelopathy and lymphoma or leukemia due to human T-cell lymphotropic virus type 1; and central nervous system disease or meningoencephalitis secondary to syphilis or herpes simplex virus (HSV)

Table 10.1 Estimated Annual Incidence and Prevalence of Four Curable STIs, Ages 15–49 Years, by WHO Region, 2008

Indicator	WHO region (number of countries in region)						
	Africa (46)	Americas (35)	South-East Asia (11)	Europe (53)	Eastern Mediterranean (23)	Western Pacific (37)	All regions
Population (millions)	384.4	476.9	945.2	450.8	309.6	986.7	3,553.6
<i>Chlamydia</i>							
Incidence cases (millions)	8.3	26.4	7.2	20.6	3.2	40.0	105.7
Prevalence cases (millions)	9.1	25.2	8.0	17.3	3.0	37.8	100.4
Incidence (%)	2.2	5.5	0.8	4.6	1.0	4.1	3.0
Prevalence (%)	2.4	5.3	0.8	3.8	1.0	3.8	2.8
<i>Gonorrhoea</i>							
Incidence cases (millions)	21.1	11.0	25.4	3.4	3.1	42.0	106.1
Prevalence cases (millions)	8.2	3.6	9.3	1.0	1.0	13.3	36.4
Incidence (%)	5.5	2.3	2.7	0.8	1.0	4.3	3.0
Prevalence (%)	2.1	0.8	1.0	0.2	0.3	1.3	1.0
<i>Syphilis</i>							
Incidence cases (millions)	3.4	2.8	3.0	0.2	0.6	0.5	10.6
Prevalence cases (millions)	14.3	6.7	12.3	0.3	1.6	1.2	36.4
Incidence (%)	0.9	0.6	0.3	0.0	0.2	0.1	0.3
Prevalence (%)	3.7	1.4	1.3	0.1	0.5	0.1	1.0
<i>Trichomoniasis</i>							
Incidence cases (millions)	59.7	85.4	42.9	22.6	20.2	45.7	276.4
Prevalence cases (millions)	42.8	57.8	28.7	14.3	13.2	30.1	187.0
Incidence (%)	15.5	17.9	4.5	5.0	6.5	4.6	7.8
Prevalence (%)	11.1	12.1	3.0	3.2	4.3	3.1	5.3
<i>Four STIs combined</i>							
Incidence cases (millions)	92.6	125.7	78.5	46.8	26.4	128.2	498.9
Prevalence cases (millions)	74.4	93.3	58.3	32.9	18.8	82.4	360.2
Incidence (%)	24.1	26.4	8.3	10.4	8.5	13.0	14.0
Prevalence (%)	19.4	19.6	6.2	7.3	6.1	8.4	10.1

Source: WHO 2012a.

Note: STI = sexually transmitted infection; WHO = World Health Organization.

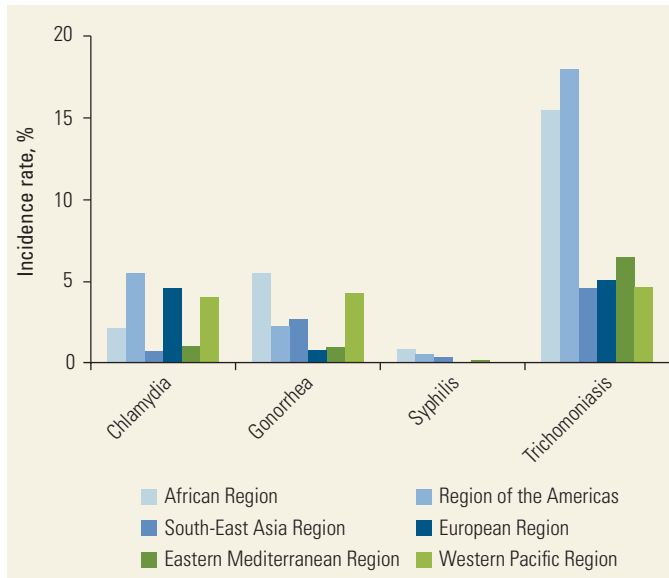
infection (Aral and others 2006; Holmes and Aral 1991; van Dam, Dallabetta, and Piot 1999).

STI sequelae disproportionately affect women and children. STIs are one of the leading causes of morbidity and mortality, as measured by disability-adjusted life years (DALYs) for reproductive-age women (Kamb and others 2007) in LMICs. Moreover, the health burden of STIs is often greatly underestimated. Although most cervical cancers are caused by human papillomaviruses (HPVs), the millions of DALYs caused by cervical cancer are not included in estimates of mortality and morbidity due to STIs; they

are typically listed in estimates of cancer (Low and others 2006).

The global burden of cervical and other cancers attributable to HPV is substantial. Of the estimated 610,000 HPV-attributable cancer cases worldwide in 2008, 490,000 occurred in LMICs, where 88 percent of cervical cancer deaths also occurred (Forman and others 2012). Similarly, HBV-related chronic hepatitis, liver failure, and liver cancer attributable to sexual, perinatal, or injection drug use transmission are seldom included in estimates of morbidity attributable to STIs.

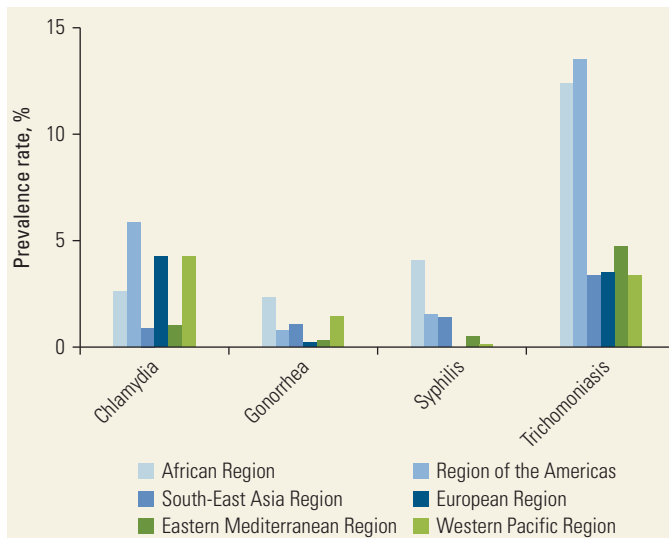
Figure 10.2 Estimated Incidence Rates of Four Curable STIs, Ages 15–49 Years, by WHO Region, 2008



Source: WHO 2012a.

Note: STI = sexually transmitted infection; WHO = World Health Organization. Calculated based on the estimated incidence of four curable STIs and the estimated population ages 15–49 years as estimated by WHO (2012a).

Figure 10.3 Estimated Prevalence Rates of Four Curable STIs, Ages 15–49 Years, by WHO Region, 2008



Source: WHO 2012a.

Note: STI = sexually transmitted infection; WHO = World Health Organization. Calculated based on the estimated prevalence of four curable STIs and the estimated population ages 15–49 years, as estimated by the WHO (2012a).

Delayed and Inadequate Diagnosis

Delayed or inadequate diagnosis and treatment of STIs in LMICs result in high rates of complications. To a large extent, inadequacies in health service provision and

health care seeking are responsible for the high levels of STIs and the high rates of complications and sequelae in LMICs (Aral, Hogben, and Wasserheit 2008). STI care is provided by a variety of health care providers, many of whom are poorly trained in STI case management, and the quality of care is often inadequate (Mayaud and Mabey 2004). Health care seeking for STIs is often delayed and inadequate, particularly among women, as a result of the asymptomatic nature of many STIs; low levels of awareness of sexual health; stigma associated with genital symptoms; and tendency to seek care through traditional healers, home remedies (Mayaud and Mabey 2004; Moses and others 1994; van Dam 1995), and pharmacies where drugs are dispensed by workers not trained in STI treatment.

Factors Affecting Duration and Burden in LMICs

In resource-poor settings, variables that affect the duration of infectiousness include adequacy of health worker training, attitudes of health workers toward marginalized groups, patient loads at health centers, availability of drugs and clinic supplies, and cost of care (Moses and others 2002). Improvements in these factors would greatly improve STI-related services, reduce the duration of infectiousness, and decrease the incidence of STIs (Aral 2002). However, in many LMICs, worsening economic conditions; increasing burden of human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS); and occasional health crises, such as natural disasters, refugee situations, or epidemics like the recent Ebola outbreak in West Africa, can adversely affect these variables (Nam and Blanchet 2014).

Sociocultural, economic, and political contexts also affect sexual behaviors that contribute to the STI burden in LMICs. Changes have included rising inequality in income and other factors within countries, growing inequality among countries, increased globalization, higher proportions of persons living outside of their cultures, increased numbers of unemployed people, and larger proportions of people living in postconflict societies (Aral 2002; Aral and others 2006). All of these changes are associated with increases in multipartner sexual activity. Furthermore, changes in technology, including the widespread use of cell phones and the Internet, can facilitate the formation of short-term sexual partnerships (Bull and McFarlane 2000). These technological changes, concurrent with changes in norms and attitudes, have led to the expansion of transactional and commercial sex that increases sexual exposure (Aral and Ward 2014).

Direct medical costs for eight major STIs have been estimated at US\$16.7 billion in the United States (Owusu-Eduese, Chesson, Gift, and others 2013). This estimate

includes costs in the United States in 2008 for gonorrhoea, chlamydia, syphilis, trichomoniasis, hepatitis B, diseases associated with sexually transmitted HPV, genital HSV-2 infections, and HIV infection. The total direct medical cost for each of these STIs in 2008 was computed as the estimated number of new cases in 2008 multiplied by the estimated discounted lifetime cost per case, adjusted to 2012 U.S. dollars. The estimated costs totaled US\$16.7 billion (range of US\$11.8 billion to US\$22.1 billion) when including HIV. Total costs excluding HIV infections were US\$3.2 billion. Although few estimates exist for LMICs, the direct medical costs of STIs are undoubtedly substantial given the high prevalence of these and other STIs in these settings. STIs also impose extensive productivity costs that can often exceed the direct medical costs (Owusu-Edusei, Chesson, Gift, and others 2013). Productivity costs are particularly burdensome in LMICs at both the individual and the community levels, especially for populations in which most people are under age 40 years (World Bank 2007). The youthful age composition in these countries contributes to the high prevalence and the direct costs of STIs. The economic burden of STIs in LMICs is so high that the treatment of curable STIs is considered one of the most cost-effective ways to improve health worldwide (World Bank 2007).

STIs can impose a considerable financial burden on those infected. For example, the cost of drugs is equivalent to several days' wages in most LMICs (Terris-Prestholt and others 2006). The direct costs associated with medical treatment of STI sequelae in LMICs have not been well defined, and the indirect costs associated with lost productivity due to STIs or STI sequelae are not known.

CHANGES IN SEXUAL BEHAVIORS AND PRACTICES, EPIDEMIOLOGY, AND PREVENTION

Significant changes have occurred in sexual behaviors and practices, epidemiology, and prevention. Technological advances, political conflicts, the economic downturn experienced in many HICs, and natural and health crises all have had important effects.

Sexual Behaviors and Practices

Most of the data on sexual behaviors and practices come from HICs. However, the increased volume of travel, sex tourism, transactional and commercial sex, and role of technology in establishing these connections have expanded sexual networks beyond national boundaries (Aral and Ward 2014; Ward and Aral 2006).

Moreover, population displacement in LMICs often affects sexual networks, for example, by allowing or forcing sexual mixing among groups that did not mix before the displacement (Hankins and others 2002).

Where available, systematically collected data on representative samples of the general population reflect increases in a number of risky behaviors, including the following: large numbers of sex partners, indiscriminate choice of sex partners, short periods between the time two people meet each other and the initiation of sexual activity, short time spent during the sexual encounter, lack or short duration of social links between sex partners, short duration of gaps between consecutive sex partners and sexual encounters, and a tendency for both partners to recruit each other for sex. These trends are observed particularly among younger cohorts. Moreover, sexual behaviors have been changing more rapidly for women than for men (Aral and Ward 2014; Mercer and others 2013).

Sexual practices have also been changing. Recent data from the United Kingdom and the United States suggest trends toward initiation of sex at a younger age, greater frequency of same-sex and bisexual behaviors, and greater frequency of oral and anal sex (Aral and Ward 2014). Although increases in oral sex began with the generation born between 1946 and 1964, increases in anal sex began with the generations born between 1965 and 2000 (Aral and Ward 2014).

These changes may result from temporal trends in demographic and social patterns. Marriage rates have declined, and divorce rates have risen in the Organisation for Economic Co-operation and Development countries and the United States (Aral and Ward 2014; International Futures Program 2011; Stevenson and Wolfers 2007). Globally, people who marry are doing so at older ages than before (Aral and Ward 2014). Because of these trends, many people spend a higher percentage of their adult lives outside of marriage (Aral and Ward 2014), which probably increases the number of sex partners.

Data collected in LMICs over the past two decades have revealed the importance of sex work to the spread of STIs (Baral and others 2012) and the presence (and considerable prevalence) of MSM among sex workers (Baral and others 2007). These key populations have high prevalence of STIs, including HIV/AIDS, and play an important role in spreading STIs to the general population.

Epidemiology

The understanding of STI epidemiology in LMICs has been shaped by the reemergence and escalation of gonorrhoea and congenital syphilis; recognition of sexual

transmission as a key factor in the spread of other STIs; emergence of MSM as key populations in transmission; emergence and impact of HIV/AIDS mortality; and patterns of STI spread, such as clustering and globalization. Although these issues can be difficult problems globally, they are especially daunting to monitor, control, and prevent in LMICs.

Gonococcal Antimicrobial Resistance

Widespread, high-level gonococcal antimicrobial resistance has been observed in Africa, South-East Asia, and the Western Pacific (Bala and others 2013; Lahra, Lo, and Whiley 2013; Ndowa and others 2013). In addition to resistance to penicillin, tetracycline, and quinolones, decreased susceptibility to third-generation cephalosporins has been reported. Decreased susceptibility to treatment has been associated with increased gonorrhea incidence at the population level in the United States (Chesson and others 2014). These trends highlight the importance of sustaining and enhancing surveillance to monitor the spread and threat of antimicrobial resistance (Lahra, Lo, and Whiley 2013).

Congenital Syphilis and Other Complications of Syphilis in Pregnancy

Syphilis in pregnancy can lead to a wide range of adverse outcomes, including stillbirth, fetal loss, neonatal death, premature and low-birthweight infants, and infection or disease in newborns (John-Stewart and others 2017; Kahn and others 2014; Newman and others 2013; WHO 2012b). Even though these adverse outcomes could be prevented through antenatal screening programs, syphilis in pregnancy imposes a substantial global burden each year, resulting in 692,000–1,530,000 adverse outcomes annually (Kamb and others 2010). As measured by DALYs, the global burden of disease due to syphilis during pregnancy is comparable to that of mother-to-child transmission of HIV (Kahn and others 2014; Kamb and others 2010; WHO 2012b).

LMICs bear a disproportionate share of the global health and economic burden of syphilis in pregnancy (Kamb and others 2010). In the Mwanza Region of Tanzania, from 1998 to 2000, maternal syphilis accounted for more than 50 percent of all stillbirths and 17 percent of all adverse pregnancy outcomes among unscreened women (Watson-Jones and others 2002).

AIDS Mortality

The probable impact of AIDS mortality, before the advent of effective antiretroviral therapy (ART), on the declining incidence of bacterial STIs was substantial.

Empirical and model-based studies in HICs suggest that AIDS mortality contributed to declines in bacterial STIs through two main mechanisms:

- Behavioral responses to the HIV/AIDS epidemic, such as increased condom use and smaller number of partners
- AIDS mortality among those at highest risk of acquiring and transmitting STIs (Becker and Joseph 1988; Boily and Brunham 1993; Boily and others 2004; Chesson, Dee, and Aral 2003; Kault 1992).

However, a few years after effective ART became available in 1996, STI incidence increased in subpopulations most affected by HIV/AIDS. Syphilis outbreaks among MSM have been observed in metropolitan areas worldwide since the late 1990s, in large part because of decreased fear of HIV/AIDS and increased survival of persons with HIV/AIDS (Chesson and Gift 2008; Stolte and others 2004).

The availability of ART has increased greatly in LMICs. At the end of 2009, 5.25 million people in these settings were receiving ART, compared with 4 million at the end of 2008 (WHO 2010). Peterman and Furness (2015) report notable declines in syphilis in some parts of Africa and attribute these declines in part to syndromic treatment of genital ulcers and possibly the impact of AIDS mortality. Building on experience acquired during the syphilis resurgence among MSM in HICs, researchers have cautioned that an increase in STIs is possible in LMICs as a result of the increased availability of ART, particularly in areas with high coverage (Kenyon, Osbak, and Chico 2014; Kenyon and others 2014).

Key Populations

The role of key populations in the epidemiology of STIs in LMICs has become increasingly clear (Baral and others 2007; Baral and others 2012). In particular, MSM are understudied and underserved in these countries. Patterns of sexual networks linking MSM and the general population warrant future research so that appropriate responses can be developed.

Clustering, Social Determinants, and Globalization

Three additional patterns have influenced and enhanced understanding of STI epidemiology in LMICs:

- Geographic clustering and concentration of risk behaviors and infections
- Importance of context, social determinants, and structural drivers
- Globalization.

Nonuniform distribution and clustering of risk—both in behaviors and infections—have been reported for the epidemiologies of both HIV and other STIs (Chesson 2010a, 2010b; Leichliter and others 2010). More recent attention has been drawn to geographic concentration (Tanser and others 2009) and to the critical role of local context in the epidemiology of STIs. The Priorities for Local AIDS Control Efforts method can identify sites where people with high rates of partner change can receive STI prevention services (Weir and others 2003). Similarly, the Situational Analysis of Sexual Health method can identify specific locations where vulnerable and at-risk people can receive STI prevention services (Benzaken and others 2012). Insight into variations in STI epidemiology has important implications for prevention and control, including targeting of interventions and allocation of resources (Aral and Cates 2013).

In the past two decades, the importance of social determinants of sexual health and structural drivers for STI epidemiology have received increasing recognition. Examples of social determinants include low socioeconomic status and poor access to quality health care (Hogben and Leichliter 2008). Underlying social, economic, legal, and political structures have a notable influence on sexual behaviors (Hogben and Leichliter 2008; Parkhurst 2014). Moreover, these factors affect the formation, evolution, and persistence of STIs in key populations. Finally, globalization shapes and connects sexual behaviors, practices, and networks around the world (Aral, Bernstein, and Torrone 2015; Aral and Ward 2005, 2014; Ward and Aral 2006).

Current developments in methodological approaches promise to have an impact on the study and understanding of STI epidemiology in all settings. Two developments are particularly remarkable: (1) the increasing use of sophisticated geographic mapping methodologies (Tanser and others 2009) and (2) phylogenetic analyses combined with social epidemiology (Avila and others 2014), specifically, phylogenetic and network analyses. When combined, these approaches provide powerful explanations of transmission dynamics within and between groups; if used in conjunction with geospatial mapping, they may enhance the understanding of aspects of STI prevention science, such as subgroup targeting.

Prevention

Important changes in the approach to STI prevention have been influenced by the HIV epidemic. During the 1980s and 1990s, behavioral prevention dominated the HIV world and gained prominence in the STI domain. However, since the turn of the century, there has been

increasing recognition that behavioral interventions have not brought sustainable decreases in incidence (Aral 2011; Kippax and Stephenson 2012). Concurrently, remarkable progress has been made in biomedical approaches to preventing HIV/AIDS, including male circumcision, preexposure prophylaxis (PrEP), and ART (Baeten and others 2012; Dodd, Garnett, and Hallett 2010; Grant and others 2010; Katz and Wright 2008; Pretorius and others 2010; Thigpen and others 2012). Given the success of biomedical approaches to the prevention of HIV/AIDS, the field of STI prevention is drawing increasingly on biomedical interventions, reinforced by development of effective biomedical interventions for preventing STIs other than HIV. More specifically, the HPV and HBV vaccines, point-of-care diagnostic tests for syphilis and dual tests for syphilis and HIV, and an understanding of the preventive effects of circumcision for certain STIs are beginning to show promise in preventing specific STIs other than HIV.

STI prevention has also been influenced by other insights. Prevention activities have increasingly sought to achieve impact at the population level. In addition to protecting individuals, the focus has turned to decreasing population incidence. This shift has brought several other changes given that it requires system-level thinking, planning, and evaluation. It is important to take into account how interventions may have additive, synergistic, or antagonistic effects (Aral 2011; Aral and Douglas 2007; Parkhurst 2014). The social and epidemiological context and interactions between interventions and context have also emerged as important issues (Aral and Cates 2013; Parkhurst 2014).

More attention is being given to the elements of complex systems (mixing patterns, networks, clustering, and hot spots) and to social, economic, legal, and sexual structures (Blanchard and Aral 2010; Parkhurst 2014). The need for new approaches to designing prevention programs is now widely recognized (Aral and Blanchard 2012; Blanchard and Aral 2011; Parkhurst 2014).

With the reality of limited and declining resources, emphasis has been placed on accountability, resource allocation, efficiency, prioritization, and return on investment (Over and Aral 2006). These developments are changing the STI prevention field in important ways. The hope is that the next decade will bring significantly greater prevention for the money in LMICs, where health systems are often weak (Mills 2014). Reforming and strengthening of health care infrastructure may be needed before the recent advances in STI prevention science can be successfully implemented in these contexts.

EFFECTIVENESS OF STI PREVENTION INTERVENTIONS: LITERATURE REVIEW

Over the past 20 years, many STI prevention interventions have been rigorously evaluated for effectiveness. In a review of STI prevention interventions evaluated by randomized controlled trials (RCTs) in HICs and LMICs, Wetmore, Manhart, and Wasserheit (2010) found that 44 of 75 interventions (59 percent) significantly reduced the risk of acquiring at least one STI. Interventions were organized according to modality, including behavior change, vaginal microbicides, male circumcision, partner services, treatment, and vaccines. The percentage of trials in which a statistically significant reduction in the risk of a laboratory-confirmed STI was observed in the intervention arm (compared with the control arm) was highest for treatment, vaccines, and male circumcision, followed by behavioral interventions, partner services, and vaginal microbicides. These findings are consistent with those of Manhart and Holmes (2005), in which 54 percent of the trials led to a significant reduction in STI acquisition, transmission, or complications.

For this section, a literature search was conducted to identify studies of the impact of STI prevention interventions in LMICs. The search was conducted from January 2014 to April 2014, and the following databases were used: Cochrane Library, Database of Abstracts of Reviews of Effects, MEDLINE, and Embase. The MEDLINE search terms used to identify the relevant literature are listed in annexes 10A and 10B, and these search terms were amended as necessary to search the other databases. This search was supplemented with additional sources, such as the bibliographies of articles obtained in the search and previous reviews of the impact of STI prevention interventions (Manhart and Holmes 2005; Mayaud and Mabey 2004; Wetmore, Manhart, and Wasserheit 2010). Although this review and that of Wetmore, Manhart, and Wasserheit (2010) overlap, there are four key differences. First, this review was not systematic—no specific inclusion or exclusion criteria were applied. Instead, studies were selected to highlight key aspects of the evidence, focusing on studies that use biological outcomes rather than changes in attitudes or behaviors. Second, the search was not limited to RCTs, but also considered cohort and cross-sectional studies. Third, this review focused on interventions that were evaluated in LMICs. Finally, it included more recent articles, published from January 2000 to July 2014, than the earlier review, which included articles published through December 2009.

In this summary of the literature, interventions were organized according to intervention modality using a structure adapted from Mayaud and Mabey (2004).

Specifically, interventions were organized as primary prevention (behavioral interventions, male circumcision, vaccines, and microbicides), STI case management, partner notification and management, targeted interventions and periodic presumptive treatment (PPT), mass treatment, and community-level and structural interventions.

Primary Prevention

Table 10.2 summarizes selected studies of the impact of primary prevention interventions, categorized as behavior change interventions, male circumcision, vaccines, and microbicides.

Behavior Change Interventions

Promotion of condom use, STI and HIV education, and knowledge and skill building are common behavior change interventions. Interventions to increase condom use are generally effective in reducing STI incidence in high-risk populations (Celentano and others 2000; Feldblum and others 2005; Patterson and others 2008), although promotion of male and female condoms is likely of modest benefit in populations already exposed to interventions promoting male condoms (Hoke and others 2007). However, Fontanet and others (1998) found that female sex workers in Thailand who had the option of using female condoms in situations where male condoms were not used had STI incidence rates that were 24 percent lower than those using male condoms only.

Male Circumcision

Male circumcision has a protective effect against HSV-2, HPV, and *Mycoplasma genitalium* in circumcised men (Auvert and others 2009; Mehta and others 2012; Tobian and others 2009) and against trichomoniasis and bacterial vaginosis in their female partners (Gray and others 2009). Effects of male circumcision on trichomoniasis were mixed (Mehta and others 2009; Sobngwi-Tambekou and others 2009); no protective effect was observed against gonorrhea, chlamydia, or syphilis (Mehta and others 2009; Sobngwi-Tambekou and others 2009; Tobian and others 2009). Although the trials of male circumcision found no significant impact on chlamydia, Castellsague and others (2002) and Castellsague and others (2005) present evidence that women with uncircumcised partners have a higher prevalence of chlamydia than women with circumcised partners.

HPV Vaccines: HSV, HPV, and HBV

An HSV-2 glycoprotein-D–adjuvant vaccine administered to persons with no serological evidence of previous

Table 10.2 Selected Evaluations of the Effectiveness of Primary STI Prevention Interventions, with a Focus on Interventions in Low- and Middle-Income Countries

Type of intervention and study	Description of intervention	Setting	Key results
<i>Behavior change interventions</i>			
Ford and others 2000	Peer education program addressing topics such as STIs and HIV, condom use, and condom negotiation	Female sex workers in Bali, Indonesia	Gonorrhea prevalence was lower in clusters with a peer educator versus clusters without.
Celentano and others 2000	Institution-based, 15-month intervention to promote consistent and proper condom use, reduce alcohol consumption, and reduce brothel patronage	Men in Royal Thai Army	Relative risk of STI infection (gonorrhea, syphilis, chancroid, nongonococcal urethritis) was 0.15 for those in intervention group versus those in control group.
Feldblum and others 2005	Male condom promotion intervention, comparing clinic-based counseling and peer promotion to peer promotion only	Female sex workers in Madagascar	Odds ratios for aggregate STI prevalence (chlamydia, gonorrhea, trichomoniasis) were significantly lower for group with clinic plus peer versus peer alone.
Hoke and others 2007	Male and female condom promotion intervention, comparing clinic-based counseling and peer promotion to peer promotion only among those already exposed to intensive male condom promotion	Female sex workers in Madagascar	STI prevalence (chlamydia, gonorrhea, trichomoniasis) did not differ significantly by study arm.
Jewkes and others 2008	A 50-hour program to build knowledge and skills	Men and women ages 15–26 years in Eastern Cape Province, South Africa	A 33 percent reduction in incidence of HSV-2 occurred in the intervention group.
Patterson and others 2008	Brief condom promotion intervention	Female sex workers in Mexico	A 40 percent decline in cumulative STI incidence (HIV, syphilis, gonorrhea, chlamydia) occurred in the intervention group.
Chong and others 2013	Online education program addressing topics such as sexual rights, contraception, condom use and STIs and HIV, empowerment, and violence prevention	Adolescents attending Colombian public schools	Among those sexually active at baseline, the intervention group had a 5 percent reduction in self-reported STIs (including chlamydia, gonorrhea, trichomoniasis, and syphilis).
<i>Male circumcision</i>			
Mehta and others 2009	Randomized trial of circumcision to prevent HIV and other STIs	Men ages 18–24 years in Kisumu, Kenya	No significant impact of circumcision on incidence of gonorrhea, chlamydia, or trichomoniasis was noted.
Sobngwi-Tambekou and others 2009	Randomized trial of circumcision to prevent HIV and other STIs	Men ages 15–29 years in Orange Farm, South Africa	Male circumcision reduced trichomoniasis, but no effect on gonorrhea and chlamydia was noted.
Auvert and others 2009	Randomized trial of circumcision to prevent HIV and other STIs	Men ages 15–29 years in Orange Farm, South Africa	Male circumcision reduced prevalence of high-risk HPV types in men.
Tobian and others 2009	Randomized trial of circumcision to prevent HIV and other STIs	Men ages 15–29 years in Rakai, Uganda	Statistically significant lower rates of HSV-2 seroconversion and HPV prevalence were noted among circumcised males; no significant impact on syphilis incidence was noted.

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Table 10.2 Selected Evaluations of the Effectiveness of Primary STI Prevention Interventions, with a Focus on Interventions in Low- and Middle-Income Countries (continued)

Type of intervention and study	Description of intervention	Setting	Key results
Gray and others 2009	Randomized trial of circumcision to prevent HIV and other STIs	Men ages 15–29 years in Rakai, Uganda, and their wives or long-term consensual partners	Male circumcision reduced the risk of genital ulceration, trichomoniasis, and bacterial vaginosis in female partners.
Mehta and others 2012	Randomized trial of circumcision to prevent HIV and other STIs	Men ages 18–24 years in Kisumu, Kenya	Circumcision nearly halved the odds of urogenital <i>Mycoplasma genitalium</i> .
Vaccines			
Stanberry and others 2002	Randomized trial of safety and efficacy of genital herpes vaccine	Men and women ages 18 years and older in Australia, Canada, Italy, and the United States	Among women with no serological evidence of previous HSV-1 infection, vaccine offered partial protection; no efficacy was noted for women seropositive for HSV-1 at baseline or for men regardless of their HSV serological status.
Harper and others 2004	Randomized trial of safety, immunogenicity, and efficacy of bivalent HPV vaccine	Women ages 15–25 years at enrollment in Brazil, Canada, and the United States	Vaccine protected against HPV 16 and 18 infection and associated cervical lesions, with evidence of cross-protection against other HPV types.
Villa and others 2006	Randomized trial of safety, immunogenicity, and efficacy of quadrivalent HPV vaccine	Women ages 16–23 years in Brazil, Nordic countries, and the United States	Vaccine protected against HPV 6, 11, 16, and 18 infection and associated cervical lesions and genital warts.
Garland and others 2007	Randomized trial of safety, immunogenicity, and efficacy of quadrivalent HPV vaccine	Women ages 16–24 years in Asia-Pacific, Europe, Latin America, and North America	Vaccine protected against external anogenital, vaginal, and cervical lesions associated with HPV 6, 11, 16, and 18.
Future II Study Group 2007	Randomized trial of safety, immunogenicity, and efficacy of quadrivalent HPV vaccine	Women ages 15–26 years in Asia-Pacific, Europe, Latin America, and North America	Vaccine protected against HPV 16– and 18–associated cervical intraepithelial neoplasia grade 2 or worse.
Muñoz and others 2009	Randomized trial of safety, immunogenicity, and efficacy of quadrivalent HPV vaccine	Women ages 24–45 years in Colombia, France, Germany, the Philippines, Spain, Thailand, and the United States	Vaccine protected against HPV 6, 11, 16, and 18 infection and associated disease.
Paavonen and others 2009	Randomized trial of safety, immunogenicity, and efficacy of bivalent HPV vaccine	Women ages 15–25 years from 14 countries in Asia-Pacific, Europe, Latin America, and North America	Vaccine protected against HPV 16– and 18–associated cervical intraepithelial neoplasia grade 2 or worse, with some protection against HPV 31, 33, and 45.
Giuliano and others 2011	Randomized trial of safety, immunogenicity, and efficacy of quadrivalent HPV vaccine	Men ages 16–26 years in Africa, Asia-Pacific, Europe, Latin America, and North America	Vaccine protected against HPV 6, 11, 16, and 18 infection and associated external genital lesions.
Palefsky and others 2011	Randomized trial of safety, immunogenicity, and efficacy of quadrivalent HPV vaccine	MSM ages 16–26 years in Australia, Brazil, Canada, Croatia, Germany, Spain, and the United States	Vaccine protected against anal intraepithelial neoplasia in MSM.
Joura and others 2015	Randomized trial of immunogenicity and efficacy of nonavalent HPV vaccine	Women ages 16–26 years in 18 countries	Vaccine protected against high-grade cervical, vulvar, and vaginal disease and persistent infection related to HPV 31, 33, 45, 52, and 58 and generated antibody response to HPV 6, 11, 16, and 18 that was noninferior to that of the quadrivalent HPV vaccine.

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Table 10.2 Selected Evaluations of the Effectiveness of Primary STI Prevention Interventions, with a Focus on Interventions in Low- and Middle-Income Countries (continued)

Type of intervention and study	Description of intervention	Setting	Key results
<i>Microbicides, suppressive therapy, and barrier methods</i>			
Richardson and others 2001	Randomized trial of nonoxynol-9 gel for STI prevention	Female sex workers in Mombasa, Kenya	Intervention group had higher gonorrhea incidence than control group; no differences for other STIs.
Roddy and others 2002	Randomized trial of nonoxynol-9 gel for STI prevention	Women in Cameroon	Gel provided no protective effect against urogenital gonococcal or chlamydial infection.
Corey and others 2004	Suppressive therapy (once-daily valacyclovir) to reduce HSV transmission	HSV-2–discordant couples in Australia, Canada, Europe, Latin America, and the United States	Suppressive therapy reduced HSV transmission to the susceptible partner by about 75 percent.
Ramjee and others 2008	Randomized trial of diaphragm, lubricant gel, and condoms versus condoms alone to prevent STIs	Women in southern Africa	STI incidence (chlamydia, gonorrhea) did not differ significantly by study arm. Among consistent users, persons in the diaphragm arm had a lower risk of acquiring gonorrhea.
Karim and others 2010	Randomized trial of 1 percent vaginal gel formulation of tenofovir for HIV prevention	Women in KwaZulu-Natal, South Africa	There was a 39 percent reduction in HIV acquisition (54 percent among those with high adherence) and a 51 percent reduction in HSV-2 acquisition.
Bukusi and others 2011	Randomized trial of topical penile microbicide (62 percent alcohol in gel) to prevent bacterial vaginosis in sex partners	Heterosexual couples in Kenya	The hazard ratio of diagnosis of bacterial vaginosis was 1.44 in intervention arm versus control arm.
Guffey and others 2014	Randomized trial of microbicides BufferGel and 0.5 percent PRO 2000 for prevention of nonulcerative STIs	Women in Malawi, South Africa, Zambia, Zimbabwe, and the United States	Candidate microbicides did not protect against gonorrhea, chlamydia, or trichomoniasis.

Note: HIV = human immunodeficiency virus; HPV = human papillomavirus; HSV = herpes simplex virus; MSM = men who have sex with men; STI = sexually transmitted infection.

HSV-1 infection partially protected women, but not men, from acquiring genital herpes disease, with efficacy of about 75 percent across two trials (Stanberry and others 2002). In contrast, the bivalent, quadrivalent, and nonavalent HPV vaccines have shown remarkably high efficacy in preventing infection and disease, and the bivalent and quadrivalent vaccines may also offer some cross-protection against other types of HPV (Malagon and others 2012). These safe and effective vaccines could reduce the burden of cervical cancer and potentially other cancers, such as vulvar, vaginal, penile, anal, and oropharyngeal cancers (Markowitz and others 2014). In HICs with routine HPV vaccination programs, reductions in the prevalence of HPV and incidence of HPV-associated health outcomes, such as genital warts and cervical precancers, have been observed at the population level (Drolet and others 2015; Fairley and others 2009; Flagg, Schwartz, and Weinstock 2013; Hariri and others 2013; Markowitz and others 2013; Tabrizi and others 2012).

The HBV vaccine has been available for many years and is increasingly used in infants in many countries; vaccine programs are also now available in some countries for adolescents and young adults who did not receive the vaccine as infants. However, many adults at risk today have never received the HBV vaccine. For example, in an Internet survey conducted in the United States in 2010, 42.4 percent of HIV-negative MSM older than age 31 years reported never having received the HBV vaccine (Matthews, Stephenson, and Sullivan 2012). A cross-sectional survey of MSM in Beijing, China, in 2012 found that only 38.9 percent had received the HBV vaccination (Wang and others 2012).

Microbicides

Randomized trials have found that PrEP with antiretrovirals can reduce HIV acquisition among heterosexual men and women in serodiscordant couples (Baeten and others 2012; Thigpen and others 2012) and in MSM

(Grant and others 2010). A randomized trial of couples serodiscordant for HSV-2 in Australia, Canada, Europe, Latin America, and the United States found that once-daily valacyclovir for suppressive therapy reduced transmission of HSV-2 to the seronegative partner by about 75 percent (Corey and others 2004). However, an RCT in HIV-discordant couples in which the partner with HIV was also infected with HSV-2 found that daily acyclovir did not reduce the risk of HIV transmission to the HIV-negative partner (Celum and others 2010).

Karim and others (2010) and Karim and Baxter (2013) report that a 1 percent vaginal gel formulation of tenofovir reduced the risk of HIV and HSV-2 acquisition in a randomized trial involving women in KwaZulu-Natal, South Africa. Specifically, it reduced HIV acquisition by 39 percent (54 percent among those with high adherence) and HSV-2 acquisition by 51 percent. However, in a randomized, placebo-control trial of tenofovir-based PrEP in women in South Africa, Uganda, and Zimbabwe (the VOICE study), none of the drug regimens reduced HIV-1 acquisition rates in the intent-to-treat analysis (Marrazzo and others 2015). Similarly, the FACTS 001 trial in more than 2,000 women in nine sites in South Africa found that pericoital vaginal application of tenofovir 1 percent gel was not effective in preventing HIV acquisition (Rees and others 2015). In both the VOICE and the FACTS 001 studies, low rates of adherence to the drug regimen were considered a primary reason for this result.

An RCT involving sexually active women in southern Africa at risk for STIs found that providing condoms alone (control) was as effective as providing a diaphragm and lubricant gel in addition to condoms (intervention) in preventing chlamydia and gonorrhea (Ramjee and others 2008). However, consistent use of a diaphragm could be protective given that the incidence of gonorrhea among women in the intervention arm was significantly lower among those who reported always using a diaphragm.

STI Case Management

Pettifor and others (2000) review the literature on the effectiveness of syndromic management of STIs. Their review includes 5 studies of WHO algorithms for management of urethral discharge, 5 for genital ulcers, and 13 for vaginal discharge. Overall, the literature suggests that algorithms for urethral discharge, vaginal discharge, and genital ulcer disease can be effective. For example, La Ruche, Lorougnon, and Digbeu (1995) reported therapeutic success rates of 92 percent for male urethritis, 87 percent for vaginal discharge, and 100 percent for genital ulcer disease. The studies reviewed in Pettifor and others (2000) also show that

the algorithms to detect cervical infection can be improved by incorporating risk scores based on factors such as sexual history. Other studies also provide evidence that risk scores can improve the efficiency of syndromic management algorithms (Cornier and others 2010). Pettifor and others (2000) conclude that, although syndromic management can be effective for managing STIs, affordable, rapid, and effective diagnostic techniques to improve detection are urgently needed in resource-poor settings.

Although evidence is limited, widespread implementation of syndromic management as an approach to STI case management likely has reduced the burden of STIs, particularly in resource-poor settings (Aral and others 2006). A community randomized trial in Mwanza, Tanzania, found that syndromic treatment of STIs resulted in a 40 percent reduction in HIV incidence and a reduction in symptomatic urethritis in men and prevalence of syphilis seroreactivity (Grosskurth and others 1995; Mayaud and others 1997). Prevalence rates of other STIs were lower in the intervention communities as well, although the differences were not statistically significant for all indicators. A community randomized trial in Masaka, Uganda, offers evidence that the syndromic management of STIs reduced the incidence of curable STIs but not HIV (Kamali and others 2003). In a cluster randomized trial in Eastern Zimbabwe, an intervention that included syndromic management of STI had no impact over time on the incidence of STI symptoms, although male patients in the intervention communities were significantly more likely than those in the control communities to report cessation of symptoms (Gregson and others 2007). An RCT comparing enhanced syndromic management and PPT among hotel-based sex workers in Bangladesh found that both strategies were effective for STI control (McCormick and others 2013). A randomized trial involving men in Malawi with urethritis found that the addition of metronidazole to the syndromic management of male urethritis can reduce trichomoniasis infection in men (Price and others 2003).

Partner Notification and Management

Alam and others (2010) conducted a systematic literature review of the feasibility and acceptability of partner notification for STIs in low-resource settings and summarized the evidence that partner notification interventions can yield positive outcomes. An RCT in Harare, Zimbabwe, involving men and women with a syndromically diagnosed STI found that a partner referral intervention (client-centered, private session with a trained counselor) significantly increased the

likelihood that at least one partner would be reported, compared with standard care in which the treating clinician discussed partner referral (Moyo and others 2002). A randomized trial in Kampala, Uganda, involving men and women with a syndromically diagnosed STI found that a significantly higher percentage of partners were treated using patient-delivered partner medication compared with patient-based partner referral (Nuwaha and others 2001).

Although no published evaluations are available of the impact of partner services on STI incidence in LMICs, evidence is available from trials conducted in HICs. Studies from the United States, for example, have shown that the administration of suppressive therapy to partners infected with HSV-2 in serodiscordant couples can reduce the incidence of HSV-2 seroconversion in uninfected partners (Corey and others 2004) and that expedited partner treatment (including patient-delivered therapy to a partner) can reduce the risk of persistence or reoccurrence of gonococcal or chlamydial infection in the index patient (Golden and others 2005). Golden and others (2015) conducted a community-level stepped-wedge RCT of a public health intervention to increase the uptake of expedited partner therapy. The intervention increased the percentage of persons receiving patient-delivered partner therapy and those receiving partner services. The investigators estimated that the intervention was associated with reductions of about 10 percent in chlamydia positivity and gonorrhea incidence, although these reductions were not statistically significant, perhaps as a result of inadequate statistical power and of state-financed uptake of parts of the intervention in control communities. Further trials are needed to assess the impact on STIs and cost-effectiveness of partner notification interventions in LMICs (Alam and others 2010; Ferreira and others 2013).

The potential benefits of partner notification strategies for STIs in LMICs are supported by encouraging results for HIV in LMICs. For example, Henley and others (2013) found that only 3.2 index cases needed to be interviewed, on average, to identify one additional person with HIV in Cameroon. Similarly, an RCT in Malawi found that 51 percent of partners returned for counseling and testing in the provider referral group in which health care providers notified partners, compared with 24 percent in the passive referral group in which patients were responsible for notifying their partners (Brown and others 2011). The health impact and cost-effectiveness of partner notification could be improved substantially by integrating HIV testing into STI clinics and providing HIV testing to partners of STI clinic patients. Furthermore, this integration could

improve the diagnostics part of the HIV treatment continuum.

Targeted Interventions and Periodic Presumptive Treatment

Interventions commonly target groups at high risk of STI acquisition and transmission. These interventions can include the provision of PPT, which is the systematic treatment of people at high risk with a combination of drugs targeting the prevalent curable STIs. As shown by four rigorous evaluations, PPT interventions can be highly effective in reducing the STI burden within targeted groups. In an RCT among female sex workers in Kenya, the provision of monthly prophylaxis substantially reduced the incidence of gonorrhea, chlamydia, and trichomoniasis, but not of HIV (Kaul and others 2004). Reductions of about 45 percent in the prevalence of cervical infection with gonorrhea and chlamydia were observed among commercial sex workers in the Lao People's Democratic Republic after monthly PPT over a three-month period (O'Farrell and others 2006). Substantial reductions in STIs were also observed among hotel-based sex workers in Bangladesh following the provision of monthly PPT over a nine-month period (McCormick and others 2013). PPT with vaginal suppositories containing metronidazole and miconazole among HIV-negative women with one or more vaginal infections in Kenya and in Birmingham, Alabama, significantly reduced the prevalence of bacterial vaginosis among women during 12 months of follow-up, compared with women receiving a placebo (McClelland and others 2015). Steen, Chersich, and de Vlas (2012) noted that reductions in gonorrhea and chlamydia on the order of 50 percent were common across the 15 studies included in their review of PPT of curable STIs among sex workers.

The WHO (2008) reviewed the effectiveness of presumptive treatment, finding that PPT can lead to rapid, short-term reductions in STI prevalence among high-risk groups and that ongoing STI services help sustain these reductions. However, research is needed regarding the use of PPT in high-risk populations and the impact of PPT on the emergence of antimicrobial resistance in sexually transmitted and other pathogens.

Reducing STI prevalence among core groups (for example, sex workers) through PPT can have notable public health effects (such as prevention of STIs in the clients of sex workers), although the evidence is limited. An intervention of PPT plus STI prevention education targeted to high-risk women in a South African mining community was found to reduce the prevalence of gonorrhea and chlamydia not only in the women in the intervention but also in the miner population (Steen and

others 2000). In contrast, a cluster randomized trial of PPT conducted among female sex workers in Benin and Ghana found substantial reductions in gonorrhea but not in chlamydia among sex workers themselves after nine months, and no impact on the prevalence of gonorrhea or chlamydia among their clients (Labbe and others 2012).

Although PPT can be effective, interventions targeting high-risk groups do not have to include PPT to be effective. For example, Avahan, the India AIDS Initiative, offers combination interventions for high-risk groups that include activities such as peer-based education, clinical services for STIs, condom promotion and distribution, and community mobilization. Among female sex workers in Maharashtra, India, Avahan led to significant declines in the prevalence of syphilis, chlamydia, and gonorrhea (Mainkar and others 2011). It also led to reductions in syphilis among high-risk MSM and male-to-female transgender persons (Subramanian and others 2013). Peer-mediated interventions have also shown promise among female sex workers in Mombasa, Kenya, where peer-based STI and HIV education and condom promotion among female sex workers increased consistent condom use with clients, but these interventions did not have a statistically significant impact on STI acquisition (Luchters and others 2008).

Mass Treatment

A community RCT in Rakai, Uganda, evaluated the efficacy of repeated mass treatment of STIs. The prevalence of syphilis seropositivity and trichomoniasis infection in women was significantly lower in intervention communities than in control communities, but there was no significant reduction in the prevalence of other STIs. However, in a subanalysis of pregnant women, the prevalence of trichomoniasis, bacterial vaginosis, gonorrhea, and chlamydia was significantly lower in communities that received mass treatment.

Although rigorous evaluations of the population-level impact of mass treatment strategies in LMICs are rare, mathematical modeling exercises suggest that mass treatment combined with sustained syndromic management could be an effective STI control strategy and substantially reduce STI-attributable HIV incidence (Korenromp and others 2000). This model suggests that the impact of a single round of mass treatment on STI incidence would be temporary without continued rounds of mass treatment or a sustained complementary intervention, such as syndromic management.

In general, however, mass treatment is discouraged because of its cost, adverse effects, promotion of resistance, and other factors (Mayaud and Mabey 2004). For example, a targeted mass treatment program to provide azithromycin to more than 4,000 at-risk persons in British Columbia

resulted in a temporary decrease in syphilis rates, but rates rebounded rapidly and soon exceeded previous levels (Pourbohloul, Rekart, and Brunham 2003; Rekart and others 2003). The intervention might have contributed to the rebound by increasing the number of people susceptible to infection (Pourbohloul, Rekart, and Brunham 2003). Emergence of azithromycin-resistant *Treponema pallidum* occurred during the intervention (Mabey 2009). The impact on azithromycin resistance of other bacteria was not studied. For these and other reasons, researchers have cautioned that mass treatment interventions should not be undertaken routinely (Pourbohloul, Rekart, and Brunham 2003; Rekart and others 2003).

Community and Structural Interventions

STI prevention interventions can be implemented at the individual, risk group, or community level. Although this literature review is stratified by intervention modality and not by level of implementation, most of the interventions reviewed thus far were targeted to individuals or high-risk groups.

The MEMA kwa Vijana (“good things for young people”) intervention, a random community intervention in the Mwanza Region of Tanzania, examined the impact of a multipronged intervention that included school-based sexual and reproductive health education, youth-friendly health services, peer condom promotion, and community activities. Although the intervention increased knowledge and decreased reported risk behaviors, it had no apparent effect on HIV or HSV-2 seroprevalence, incidence of other STIs, or pregnancy outcomes at the end of the trial (Hayes and others 2005), and no effect on HIV after about 10 years (Doyle and others 2010).

Community-based interventions have also been used to improve the quality of syndromic management of STIs. A district RCT in Lima, Peru, examined an intervention to improve the recognition and management of STI syndromes by pharmacy workers (Garcia and others 2003). The intervention was found to improve STI recognition and management, as well as STI and HIV risk-reduction counseling. A subsequent trial that chose 20 cities throughout Peru to receive or not receive this intervention resulted in substantial and significant improvements in STI syndromic management at pharmacies in the intervention cities but not in the control cities. The community trial in Peru (Peru PREVEN Study) combined four intervention modalities:

- Provision of training, workshops, and educational materials to pharmacy workers and clinicians
- STI screening and treatment for female sex workers by mobile outreach teams

- Provision of PPT using metronidazole to female sex workers with bacterial vaginosis
- Condom promotion among female sex workers by mobile outreach teams and among the general population by social marketing of low-cost condoms (Garcia and others 2012).

Adjusted for baseline prevalence, among 12,930 young adults ages 18–29 years there was a nonsignificant reduction in chlamydia, trichomoniasis, and gonorrhea infection and in syphilis seroreactivity. However, significant reductions were noted in certain subgroups, specifically young adult women and female sex workers in intervention cities.

Randomized trials at the clinic level offer comparable findings in Pakistan (Shah and others 2007) and South Africa (Harrison and others 2000). A cluster randomized trial in rural Vietnam showed that educational programs with interactive training can increase STI-related knowledge and practices of health care providers such as pharmacists, doctors, and nurses (Lan and others 2014).

Structural (or environmental) interventions to prevent STIs, including HIV, seek to change the physical and social environments in which risky sexual behavior takes place, with a focus on making healthy options the default choice (Frieden 2010; Kerrigan and others 2006). Government policies and regulations are a common example of structural interventions. A government policy in Puerto Plata, the Dominican Republic, requiring condom use between sex workers and clients (with penalties for violations incurred by owners of sex establishments), combined with a community-solidarity intervention, was associated with a 50 percent reduction in STI prevalence among female sex workers (Kerrigan and others 2006). This reduction was more substantial than that observed in Santo Domingo, the Dominican Republic, which received the community-solidarity intervention alone.

Although not evaluated through an RCT or comparative effectiveness design, the Thai government's response to prevention of HIV in the late 1980s and early 1990s provides compelling evidence of the potential impact of structural interventions. The response included three main components: the provision of condoms to commercial sex venues, the imposition of sanctions on commercial sex venues not adhering to the 100 percent condom use policy, and a mass advertising campaign advising men to use condoms with commercial sex workers (Hananberg and others 1994). Within four years, condom use in commercial sex acts increased to 94 percent from 14 percent; STIs in males declined about 80 percent, with notable reductions in HIV incidence as well (Hananberg and others 1994; Punpanich, Ungchusak, and Detels 2004).

Charania and others (2011) concluded that structural interventions to increase the availability of condoms do increase condom use, based on their review of 21 published studies. However, a Cochrane Review of nine RCTs of structural and community-level interventions to increase condom use found no evidence that these interventions reduced HIV or STIs (Moreno and others 2014). These findings are not necessarily contradictory, given key differences in their approaches. For example, unlike the review by Moreno and others (2014), the review by Charania and others (2011) focused exclusively on structural interventions, was not limited to RCTs, and examined behavioral outcomes (condom use) rather than health outcomes (STI or HIV incidence).

A cash transfer program was tested in a trial of never-married women ages 13–22 years in Zomba District of Malawi (Baird and others 2012). The provision of cash was intended to increase household income and sustain school enrollment in an attempt to offset two possible risk factors for HIV and STIs: poverty and lack of education. The cash transfer program was shown to reduce HIV and HSV-2 incidence, indicating high effectiveness in a low-income setting (Baird and others 2012).

Alcohol control policies (alcohol taxation and restrictions on advertising) have been proposed to reduce STIs and HIV/AIDS in Sub-Saharan Africa (Chersich and others 2009), given research linking alcohol consumption to risky sexual behaviors. In HICs, alcohol control policies have been associated with substantial declines in alcohol-related health outcomes, such as motor vehicle fatalities and homicides (Cook and Durrance 2013). They have also been shown to reduce risky sexual behaviors and STI incidence and to improve sexual health (Chesson, Harrison, and Kassler 2000; Cohen and others 2006; Dee 2001; Grossman, Kaestner, and Markowitz 2005; Sen and Luong 2008; Staras and others 2014). Grossman, Kaestner, and Markowitz (2005) found that a 10 percent increase in the state excise taxes on beer was associated with lower gonorrhea rates among males ages 15–24 years in the United States. Dee (2001) estimated that establishing a minimum legal drinking age of 21 years in the United States reduced childbearing by about 6 percent among black teenagers.

COST-EFFECTIVENESS OF STI PREVENTION INTERVENTIONS: LITERATURE REVIEW

The cost-effectiveness of STI prevention interventions depends in part on the degree to which reductions in STIs other than HIV might influence the HIV epidemic. In general, the estimated cost-effectiveness of STI prevention interventions is much higher if the potential

benefits of preventing STI-attributable HIV transmission or acquisition are included. Modeling exercises have suggested that syndromic management of STIs can have a substantial influence on HIV incidence in LMICs and be cost saving in many scenarios (White and others 2008). However, given the scientific debate regarding the effects on HIV of STI treatment and prevention, some experts have advised assessing the cost-effectiveness of STI prevention interventions without considering the potential impacts on HIV (Galarraga and others 2009). This section focuses on studies that assess the cost-effectiveness of STI prevention in its own right, without regard to the potential effects on HIV.

A literature search was conducted to identify studies of the cost-effectiveness of STI prevention

interventions in LMICs. The search was conducted through July 2014 using the same databases as those listed for the literature search on effective STI prevention interventions. Search terms used to identify the relevant literature are provided in annexes 10A and 10B. This search was supplemented with additional sources, such as the bibliographies of articles obtained in the search. Costs and cost-effectiveness ratios have been updated to 2012 U.S. dollars. The cost-effectiveness of programs to prevent syphilis during pregnancy and HIV/AIDS are not included in this review because this topic is addressed in chapter 6 of this volume (John-Stewart and others 2017). Table 10.3 summarizes selected studies of the cost-effectiveness of prevention interventions.

Table 10.3 Selected Cost-Effectiveness Analyses of Primary STI Prevention Interventions in Low- and Middle-Income Countries

Type of intervention and study	Description of intervention evaluated	Setting of intervention	Key cost-effectiveness results (2012 U.S. dollars unless noted otherwise)
<i>Behavior change interventions</i>			
Chong and others 2013	Online education program addressing topics such as sexual rights, contraception, condom use and STIs and HIV, empowerment, and violence prevention.	Adolescents attending Colombian public schools	Cost per STI averted ranged from \$95 to \$824, depending on assumptions regarding duration of intervention's effect.
<i>HPV vaccination</i>			
Goldie and others 2008; Levin and others 2015; Natunen and others 2013	HPV vaccination of females, either alone or in combination with cervical cancer screening.	LMICs eligible for support from Gavi, the Vaccine Alliance	HPV vaccination of females can be highly cost-effective even in the poorest countries.
<i>STI case management</i>			
Sahin-Hodoglugil and others 2003	Three protocols for diagnosing and treating gonorrhea and chlamydia: "gold-standard" care, syndromic management, and mass treatment.	Women in Africa	Cost-effectiveness of each protocol varied by locale. Syndromic management had two key advantages: low program costs and relative ease of implementation.
Adams and others 2003	Training pharmacists in syndromic management of urethral discharge and genital ulcer disease in males and vaginal discharge and pelvic inflammatory disease in females.	Peru	Intervention was cost saving from the societal perspective.
Colvin and others 2006	Provided syndromic management packets (including an information leaflet and appropriate antibiotics) to primary care clinics.	Durban, South Africa	A savings of US\$2.39 occurred per additional patient appropriately managed for urethral discharge in males and vaginal discharge and lower abdominal pain in females.
Vickerman, Ndowa, and Mayaud 2008	Modification in STI treatment guidelines for syndromic management of genital ulcer disease that incorporated antiviral treatment for HSV-2 in certain situations.	LMICs	Although the incorporation of HSV-2 treatment could increase program costs, it could potentially increase the proportion of herpetic ulcers treated, while reducing the cost per ulcer appropriately treated.

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Table 10.3 Selected Cost-Effectiveness Analyses of Primary STI Prevention Interventions in Low- and Middle-Income Countries (continued)

Type of intervention and study	Description of intervention evaluated	Setting of intervention	Key cost-effectiveness results (2012 U.S. dollars unless noted otherwise)
<i>Targeted interventions and periodic presumptive treatment</i>			
Borgi and others 2005	Voucher scheme to increase STI services for high-risk groups, including sex workers and their clients.	Managua, Nicaragua	Average cost per STI cured was US\$140.17.
Carrara and others 2005	Providing STI clinical services and outreach to female sex workers and their male clients through nongovernmental organizations, with a focus on the management of genital discharge syndrome and genital ulcer syndrome.	Cambodia	Average cost per syndrome cured or improved was about US\$84.35–US\$154.34 for men and US\$89.73–US\$154.34 for women.
Marseille and others 2001	Distribution of 6,000 female condoms to female sex workers and to women with at least one casual partner per year.	Rural South Africa	The intervention was estimated to have averted 6 HIV infections, 33 gonorrhea infections, and 38 syphilis infections and to pay for itself in averted HIV and STI treatment costs.
Lafort and others 2010	Establishing a dedicated clinic specifically for high-risk populations (female sex workers and long-distance truck drivers).	Northern Mozambique	Cost per clinic visit was US\$4.76.
<i>Mass treatment</i>			
Sahin-Hodoglugil and others 2003	Mass treatment compared with syndromic management.	Women in Africa	Mass treatment offered relative advantages in number and percentage of cases cured, but relative disadvantages in overall program costs and costs associated with overtreatment.
<i>Community and structural interventions</i>			
Sweat and others 2004	Structural intervention was a system of sanctions levied on sex establishment owners for failing to follow government policies requiring condom use during sex work; administered in conjunction with an environmental intervention that included community mobilization, peer education, and distribution of educational materials and promotional items.	Dominican Republic	The cost per DALY averted was US\$1,468.94 with the environmental intervention alone. When the structural intervention was included along with the environmental intervention, the estimated number of HIV infections averted more than doubled and the cost per DALY averted was US\$566.02.

Note: DALY = disability-adjusted life year; HIV = human immunodeficiency virus; HPV = human papillomavirus; HSV = herpes simplex virus; LMICs = low- and middle-income countries; STI = sexually transmitted infection.

Primary Prevention

Behavior Change Interventions

Although several studies have examined the cost-effectiveness of behavioral interventions to prevent HIV in LMICs (McCoy, Kangwende, and Padian 2010; Townsend, Mathews, and Zembe 2013), the literature search yielded only one study of the cost-effectiveness of behavioral interventions to prevent other STIs. The study assessed the cost-effectiveness of an online education program for adolescents attending public schools in

Colombia (Chong and others 2013). The intervention addressed topics such as sexual rights, contraception, condom use and STIs and HIV, empowerment, and violence prevention. The findings suggested a cost per STI averted of US\$95–US\$824, depending on assumptions about the duration of the intervention's effect (table 10.3).

Male Circumcision

Adult male circumcision is a cost-effective and potentially cost-saving intervention for preventing heterosexual

acquisition of HIV in men, according to a review of published studies (Uthman and others 2010). The cost-effectiveness of male circumcision to prevent STIs (other than HIV) has not been analyzed and is not of vital importance given that preventing HIV is the main goal of adult male circumcision.

HPV Vaccination

Although HPV vaccination is a relatively new intervention, a substantial body of research examines its cost-effectiveness in LMICs. Levin and others (2015) and Natunen and others (2013) reviewed the cost-effectiveness of HPV vaccination in LMICs with high rates of cervical cancer. Goldie and others (2008) assessed the cost-effectiveness of HPV vaccination in 72 countries eligible for support from Gavi, the Vaccine Alliance. Two key themes emerge from this literature. First, HPV vaccination of females (either alone or in combination with cervical cancer screening) can be highly cost-effective even in the poorest countries. Second, despite favorable cost-effectiveness, HPV vaccine programs will likely not be affordable in many countries. Gavi has helped address the affordability issue, making HPV vaccine available at less than US\$5 per dose to Gavi-eligible countries as of 2014, compared with more than US\$100 per dose in HICs.²

Microbicides

A modeling study suggested that a hypothetical microbicide with 55 percent efficacy in preventing male-to-female HIV transmission would be highly cost-effective in LMICs with generalized epidemics, but it likely would be less cost-effective in HICs (Verguet and Walsh 2010). In another modeling study, Terris-Prestholt and others (2014) calculated per act efficacy against HIV and HSV-2 consistent with the overall efficacy of the 1 percent vaginal gel formulation of tenofovir, as reported in the CAPRISA trial (Karim and others 2010). Results indicate that the gel could be cost-effective or cost saving in LMICs, depending on its price. However, subsequent trials have not confirmed that the gel reduces HIV/AIDS acquisition. The literature search yielded no cost-effectiveness analyses of using microbicides strictly to prevent STIs other than HIV/AIDS.

STI Case Management

Sahin-Hodoglugil and others (2003) used a decision tree model to examine the cost-effectiveness of three protocols for diagnosing and treating gonorrhea and chlamydia in women in Sub-Saharan Africa: gold-standard care (use of the best available yet expensive diagnostic tests), syndromic management, and mass treatment. They found that the cost-effectiveness of each strategy varied

by locale, depending on STI prevalence, program coverage, and health-seeking behavior. Syndromic management had two key advantages—low program costs and relative ease of implementation—which likely explains why it is often used in resource-poor settings. This finding is consistent with a systematic review of the costs of treating curable STIs in LMICs (Terris-Prestholt and others 2006), which found that syndromic management had lower costs than other management strategies. However, syndromic management had a lower estimated impact on the percentage of chlamydia and gonorrhea cases cured than the gold-standard or mass treatment options (Sahin-Hodoglugil and others 2003).

Three studies examined the cost-effectiveness of strategies to improve the quality of syndromic management:

- An intervention in Peru that trained pharmacists in syndromic management of urethral discharge and genital ulcer disease in males and vaginal discharge and pelvic inflammatory disease in females was found to be cost saving from the societal perspective (Adams and others 2003).
- An intervention in Durban, South Africa, that provided syndromic management packets (including an information leaflet and appropriate antibiotics) to primary care clinics was found to cost US\$2.39 per additional patient appropriately managed for urethral discharge in males and vaginal discharge and lower abdominal pain in females (Colvin and others 2006).
- Vickerman, Ndowa, and Mayaud (2008) examined the cost-effectiveness of a modification in the 2003 WHO guidelines for syndromic management of genital ulcer disease that incorporated antiviral treatment for HSV-2 in certain situations, such as in populations with HSV-2 prevalence of 30 percent or more. Although the incorporation of HSV-2 treatment could increase program costs, it could potentially increase the proportion of herpetic ulcers treated while reducing the cost per ulcer appropriately treated.

Incorporating HSV-2 treatment could be an affordable and cost-effective strategy in certain situations, depending on factors such as the cost of HSV-2 therapy. Perhaps more important, the implementation of syndromic management for genital ulcers that includes treatment for chancroid, in accordance with the WHO guidelines (WHO 2003), has been credited with major reductions in or even elimination of chancroid in many parts of the world (Ryan, Kamb, and Holmes 2008; Spinola 2008; Steen 2001). To the extent that chancroid is an important risk factor for HIV transmission, syndromic management to reduce its incidence may be exceptionally cost-effective (Makasa, Buve, and Sandøy 2012).

Partner Notification and Management

The literature search yielded no cost-effectiveness analyses of partner notification and partner management strategies for STIs other than HIV in LMICs. However, partner management strategies for HIV illustrate the potential for such strategies to be cost-effective for STIs. For example, Rutstein and others (2014) found that, in Sub-Saharan Africa, the incremental cost per HIV transmission averted was US\$3,014.93 for “contract” notification, in which there is an agreement that the provider will attempt to notify partners if the index patient fails to do so within one week, compared with passive referral in which the index patient is encouraged to notify partners. Furthermore, partner notification is regarded as an efficient approach to identifying HIV-positive individuals in need of therapy and also identifies HIV-negative partners who may benefit from PrEP.

Targeted Interventions and Periodic Presumptive Treatment

Borghini and others (2005) examined the cost-effectiveness of a voucher scheme implemented in Managua, Nicaragua, to increase STI services for high-risk groups, including sex workers and their clients. The vouchers covered free STI services from a range of providers. The analysis focused on the cost of treating four STIs, and the incremental cost per STI cured by the voucher intervention was US\$140.17.

Carrara and others (2005) examined the cost-effectiveness of providing STI clinical services and outreach to female sex workers and their male clients in Cambodia through nongovernmental organizations. The analysis focused on the management of genital discharge syndrome and genital ulcer syndrome; the average cost per syndrome cured or improved was about US\$84.35 to US\$154.34 for men and US\$89.73 to US\$154.34 for women.

Marseille and others (2001) examined the cost-effectiveness of an intervention to distribute female condoms to female sex workers and to women with at least one casual partner per year. The distribution of 6,000 female condoms was expected to avert 6 HIV infections, 33 gonorrhea infections, and 38 syphilis infections and to pay for itself in averted HIV and STI treatment costs.

Increasing access to STI prevention services by establishing a dedicated clinic specifically for high-risk populations could be a cost-effective strategy in LMICs. A study of the costs and use of a nighttime clinic in northern Mozambique for high-risk populations (female sex workers and long-distance truck drivers) found a cost per clinic visit of about US\$4.76, based on a monthly

clinic cost of US\$2,233.02 and treatment of 475 clients per month (Lafort and others 2010). Expanding the hours of operation, widening the geographic coverage of the clinic, and targeting additional risk groups could reduce the cost per client served.

Mass Treatment

Only one cost-effectiveness analysis of mass treatment strategies in LMICs was found (Sahin-Hodoglugil and others 2003). Their decision tree analysis suggested that mass treatment offered relative advantages over gold-standard care and syndromic management in number and percentage of cases cured, but relative disadvantages in overall program costs and costs associated with overtreatment. The decision trees used in the analysis did not account for the potential for mass treatment to promote antimicrobial resistance or for the potential adverse effects on persons treated unnecessarily.

Community and Structural Interventions

Sweat and others (2006) examined the cost-effectiveness of environmental and structural interventions to prevent HIV among female sex workers in the Dominican Republic. The environmental intervention consisted of activities such as community mobilization, peer education, and distribution of educational materials and promotional items. The structural intervention was a system of sanctions levied on sex establishment owners for failing to follow government policies requiring condom use during sex work. Accordingly, the structural intervention consisted of holding the establishment owners—not the commercial sex workers—responsible for ensuring that condoms were used consistently in all commercial sex transactions in the establishment. The cost per DALY averted was US\$1,468.94 with the environmental intervention alone. When the structural intervention was included along with the environmental intervention, the estimated number of HIV infections averted more than doubled and the cost per DALY averted was reduced to US\$566.02. Although the cost-effectiveness ratios were sensitive to various assumptions, the inclusion of the structural intervention consistently resulted in more favorable cost-effectiveness estimates (Sweat and others 2006).

Studies of the cost-effectiveness of structural interventions to prevent STIs in LMICs are rare, but structural interventions could yield substantial and lasting impacts at relatively low cost. For example, in a review of HIV prevention interventions in the United States,

alcohol taxation ranked as one of the most cost-effective of all available interventions (Cohen, Wu, and Farley 2004).

KEY ISSUES REGARDING IMPACT AND COST-EFFECTIVENESS

HIV-Related Benefits of Preventing STIs Other than HIV

Few published studies examine the cost-effectiveness of interventions to control and prevent STIs other than HIV in LMICs. The review focused primarily on studies of the cost-effectiveness of prevention programs for specific STIs other than HIV that did not include costs averted and health benefits gained by preventing STI-attributable HIV infections. The inclusion of potential HIV prevention benefits could substantially alter the estimated cost-effectiveness of STI control and prevention programs (Chesson and Pinkerton 2000), particularly those targeted to high-risk populations. To the extent that prevention or control of STIs reduces the incidence of HIV, any effective STI intervention would be expected to be cost-effective, provided that the intervention itself is not excessively costly and that its effect on HIV is not too small. Furthermore, STI-related interventions can sometimes be cost-effective by reducing the progression of HIV in people infected with both HIV and another STI. For example, Vickerman and others (2011) found that suppressive therapy for HSV-2 in women with HSV-2 and HIV could be a cost-effective public health intervention based on the benefits of reducing the progression of HIV and improving the retention of women in care, a potential benefit of HSV-2 therapy suggested by Baggaley and others (2009).

To the extent that a variety of interventions targeting curable STIs might also reduce the risk of potentially fatal, incurable, and chronic STIs other than HIV such as sexually transmitted HPV, HBV, and HSV, the cost-effectiveness of such interventions would be more favorable when these additional benefits are included.

Conversely, certain HIV prevention interventions might also reduce other STIs. However, their cost-effectiveness is generally not as sensitive to the inclusion of other STI-related benefits as the reverse. For example, circumcision is a highly cost-effective (and potentially cost-saving) intervention for the prevention of HIV acquisition in men (Uthman and others 2010). Because it is cost-effective when considering HIV-related benefits alone, there is little need to include the potential benefits of preventing other STIs, at least in settings where prevention of other STIs is not the primary goal of circumcision.

Screening and Treatment for Syphilis in Pregnancy

The prevention of mother-to-child transmission of HIV and syphilis is addressed in chapter 6 of this volume (John-Stewart and others 2017). However, screening and treatment for syphilis in pregnancy warrants special mention here for several key reasons. First, the global burden of disease due to syphilis during pregnancy is comparable to that of mother-to-child transmission of HIV (WHO 2012b). Second, screening and treatment for syphilis in pregnancy is an inexpensive and highly cost-effective intervention (Blandford and others 2007; Hawkes and others 2011; Kahn and others 2014; Owusu-Edusei, Gift, and Ballard 2011; Rydzak and Goldie 2008; Schmid 2004; Terris-Prestholt and others 2003). However, despite their low cost and favorable cost-effectiveness, screening for and treatment of syphilis in pregnancy are vastly underutilized in LMICs today (WHO 2012b).

HPV and HBV Vaccination

Given the scarcity of published studies on the cost-effectiveness of interventions to prevent STIs in LMICs, the exceptionalism of HPV and HBV vaccination warrants mention. HPV vaccination is unique among STI prevention interventions in that its effectiveness has been demonstrated in RCTs, and its cost-effectiveness in LMICs has been analyzed extensively, as reviewed by Natunen and others (2013) and Levin and others (2015). Similar data exist for HBV vaccination (Kane 1995). However, young girls have limited access to HPV vaccine in poorer settings because of the high cost of the vaccine and other challenges associated with vaccinating (de Sanjosé and others 2012; Kane 2010). Nonetheless, Gavi's support for HPV vaccines is expected to increase access in LMICs and eventually reduce the disproportionate burden of HPV-associated cancers in these settings.

Income and Income Inequality

Aral and others (2006) examined the association between two economic measures—income and income inequality and STI burden—at the country level. For each country setting, income was measured using gross national income, and income inequality was measured using the Gini coefficient, which can range from 0 (complete equality) to 1 (complete inequality). The burden of STIs was negatively associated with income and positively associated with income inequality. Their analysis suggested that these two economic measures could explain almost half of the variation across countries in STI prevalence among low-risk groups (16 percent of the variation among high-risk groups).

These findings are consistent with other analyses in HICs. Bingham and others (2014) used the Gini coefficient to examine income inequality and gonorrhea incidence rates across 11 countries. Their analysis showed significant positive associations between income inequality and gonorrhea rates in women. Owusu-Edusei, Chesson, Leichliter, and others (2013) examined county-level data in the United States and found that racial disparities in income were associated with racial disparities in STI burden. One possible explanation is that racial income disparity contributes to residential segregation by race, which has been identified as a social determinant of STI risk (Hogben and Leichliter 2008; Owusu-Edusei, Chesson, Leichliter, and others 2013; Thomas and Gaffield 2003).

Research and Development Agenda

Aral and others (2006) provided the following list of priorities for global STI research, and they remain priorities today:

- Development, evaluation, and implementation of STI prevention and control interventions, including therapeutic interventions such as drug treatment and therapeutic vaccines, and primary prevention interventions such as prophylactic vaccines, structural interventions, and behavioral interventions
- Enhanced efforts to control the spread of drug-resistant strains of gonorrhea
- Development and evaluation of tools and methods for assessing the burden of STIs and STI-related sequelae and for allocating STI prevention resources efficiently to reduce this burden
- Development and evaluation of tools to promote early detection and treatment of STIs, particularly inexpensive and practical rapid diagnostic tests for gonorrhea and chlamydia
- Development and evaluation of strategies to identify persons at highest risk for STIs and to offer prevention services to reduce their risk of acquisition and transmission, especially to highly stigmatized populations (MSM, transgender persons, and sex workers)
- Promotion of health services research to inform the integration of practical and cost-effective prevention strategies or systems into the public health infrastructure
- Implementation of studies in support of global elimination programs, such as for syphilis and possibly cervical cancer
- Continued research on the importance of social determinants of STIs, with the goal of reducing racial and geographic disparities in sexual health.

CONCLUSIONS

STIs impose a considerable health and economic burden globally. Primary prevention and control of STIs in LMICs can be an efficient use of resources, although the impact and cost-effectiveness of interventions can vary substantially across settings. Furthermore, estimates of the cost-effectiveness of STI control in LMICs can be subject to considerable uncertainty and might not be generalizable across settings. The findings of this literature review should be considered in light of the limitations inherent in cost-effectiveness studies of STI control in LMICs, such as incomplete cost data and imprecise estimates of program impact.

Behavioral interventions can often lead to reductions in the risk of acquiring STIs, at least in the short term. In contrast, interventions with long-lasting effects—such as adult male circumcision and HPV and HBV vaccination—can have a more pronounced impact on disease burden at the individual and population levels. Given the challenges of providing STI prevention and treatment services in LMICs, structural interventions are needed to make it easier and more realistic for people to choose safer behaviors. Unfortunately, establishing that a given intervention is effective and cost-effective is not enough to ensure its delivery. Screening for syphilis in pregnancy remains vastly underutilized, even though it is relatively inexpensive, effective, and cost-effective. The underutilization of effective and cost-effective interventions highlights the need for more health services research and stronger health systems—not only to improve the delivery of STI prevention interventions in LMICs, but also to expand access to STI prevention services, especially among the most vulnerable populations.

ANNEXES

The annexes to this chapter are as follows. They are available at <http://www.dcp-3.org/infectiousdiseases>.

- Annex 10A. Search Terms Used to Identify Literature on the Impact of STI Prevention Interventions
- Annex 10B. Search Terms Used to Identify Literature on the Cost-Effectiveness of STI Prevention Interventions

NOTES

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US\$1,045 or less

- Middle-income countries (MICs) are subdivided:
 - (a) lower-middle-income = US\$1,046–US\$4,125
 - (b) upper-middle-income (UMICs) = US\$4,126–US\$12,745
 - High-income countries (HICs) = US\$12,746 or more.
1. These numbers represent the WHO's best estimates, using indicators that aim for comparability across countries and time; they are updated as more recent or revised data become available or when changes occur in the methodology used. Visit the Global Health Observatory at <http://apps.who.int/gho/data/?theme=main>.
 2. Visit the Gavi website at <http://www.gavi.org>.

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