

HIV Epidemiology Update and Transmission Factors: Risks and Risk Contexts—16th International AIDS Conference Epidemiology Plenary

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The contexts in which the human immunodeficiency virus (HIV) pandemic is occurring are increasingly diverse. Individual-level risks for HIV infection are at the core of these epidemics and are powerfully impacted by social, structural, and population-level risks and protections. The emerging epidemics among injection drug users across Eurasia are largely the result of needle sharing, but the drivers of disease spread include increases in opiate availability, limited HIV infection prevention and programs for drug users, and undermining policy environments. An emerging epidemic of HIV infection among men who have sex with men in developing countries is primarily spread through unprotected anal intercourse but is also driven by limited HIV infection prevention services, social stigma, and the lack of human rights protection. The epidemic in southern Africa, which is spreading largely through heterosexual exposure, is driven by high rates of labor migration, concurrent sexual partnerships, gender inequalities, and the limited availability of male condoms. We need to do much more to control HIV infection, and social and structural risks are crucial intervention targets.

Despite recent reports of decreases in HIV infection prevalence in parts of Africa and Asia, the HIV infection and AIDS pandemic continued to spread in 2006. New epidemic foci arose in regions and populations that had been spared in the first decades of the AIDS pandemic, and ongoing spread was observed in the most heavily affected regions of southern Africa [1]. In 2005, an estimated 38.6 million people (range, 33–46 million people) worldwide were living with HIV infection, 4.1 million people (range 3.4–6.2 million people) became newly HIV infected, and ~2.8 million people died of AIDS [1]. The figure of 4.1 million persons who were newly infected in 2005 suggests that we cannot focus only on treating AIDS, but we must also reinvigorate HIV infection prevention and control efforts.

Individual-level risks for HIV acquisition and transmission

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remain at the core of diverse ongoing and emerging epidemics in 2006. However, individual-level risks for HIV infection are powerfully impacted by social, structural, and population-level risks and protections—what might be called “risk contexts” for epidemic HIV infection spread or control [2, 3]. These contexts are driven by the presence or absence of appropriate prevention tools and services, by enabling or undermining policy environments, by the protections or absence of human rights, by levels of social tolerance or stigma, and by civil strife and conflict [3–5]. Although more challenging to study than individual-level variables, contextual factors may be crucial to understanding why epidemic control has been achieved in some populations and not in others.

The third decade of the AIDS pandemic is marked by increasing contextual heterogeneity. Using a case studies approach, we investigated 3 epidemic contexts where HIV infection spread was ongoing or accelerating in 2006: the emerging injection drug user (IDU)–driven epidemics across Eastern Europe, central Asia, and the former Soviet Union; the emerging epidemic among men who have sex with men (MSM) in developing countries and among minority MSM in the United States; and the context of ongoing spread in southern Africa.

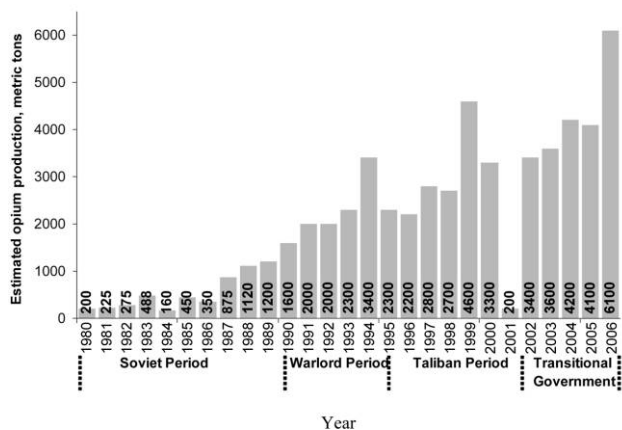


Figure 1. Afghanistan opium production, in metric tons, from 1980 to 2006. Adapted, with permission, from the United Nations' Office on Drugs and Crime (UNODC) World Drug Report for 2005 [18]. Data from 2006 are from the UNODC World Drug Report for 2006 [19] and Gall [20].

EPIDEMICS AND RISK CONTEXTS

The IDU-driven epidemics of Eurasia. IDUs accounted for ~10% of all new cases of HIV infection in 2005 but accounted for one-third of all cases of HIV infection outside sub-Saharan Africa [1]. Aceijas et al. [6] estimated that, in 2004, 4 of 5 IDUs globally lived in a developing country. The countries in which the majority of HIV infections were attributed to injection drug use in 2005 include Russia, Ukraine, the central Asian republics, Iran, China, Indonesia, Nepal, and Vietnam [1, 6, 7].

Individual-level associations of HIV infection. Risks for HIV infection among IDUs at the individual level include correlates of needle sharing and equipment lending and borrowing; consistent findings for these risks have been reported from Iran, Thailand, Russia, China, and Tajikistan [6, 8–10]. Other consistent findings include frequency of injection, daily or more-frequent injection, and a history of incarceration [11, 12]. A number of studies have found that sexual risks for HIV infection may play important roles in disease acquisition, in addition to the risks related to injection drug use [13, 14]. These “dual-risk” sexual and injection profiles may be particularly important among adult female IDUs and MSM IDUs [13, 14]. Opiate substitution therapy has been protective against HIV infection, as has been access to comprehensive prevention services, including needle and syringe exchange programs [15].

Beyond the individual level, the Eurasian HIV epidemics share at least 3 structural drivers: (1) marked increases in narcotics production and trafficking, primarily from Afghanistan; (2) widespread lack of evidence-based HIV infection prevention and drug treatment services [16]—that is, interventions for which there is scientific evidence of efficacy for HIV infection prevention, either from controlled trials or multiple observational studies (e.g., methadone maintenance therapy)—and in-

stead, the implementation of prevention efforts that are based on moral or value-oriented approaches, for which empirical studies have not demonstrated efficacy; and (3) restrictive policy environments marked by police harassment, high rates of incarceration, human rights violations, and social stigma.

The first structural driver of the spread of HIV infection in the Eurasian region is markedly increasing heroin availability, particularly along heroin trafficking routes [17]. Afghanistan, Burma (Myanmar), and Laos together accounted for >90% of all illicit opium production in 2005 [19]. Licit opiate production, primarily contained to Australia, India, and Turkey, has not been associated with the spread of HIV infection [16]. Figure 1 shows opiate production in Afghanistan from 1980 to 2006. Opiate production rose to an all-time high of >6100 metric tons of opium in 2006 [20]. The central Asian countries near Afghanistan experienced a 17-fold increase in opiate use during 1990–2002 [19]. Iran, which borders Afghanistan, seized more opiates than any other country in 2005 and has an estimated IDU population of 200,000 persons [7, 19].

The second structural driver of the HIV infection epidemic in the region has been the lack of evidence-based prevention services in heroin trafficking zones. Opiate analog substitution therapy remains illegal in Russia and in much of the former Soviet Union [4]. Harm-reduction programs, although not illegal in most of the region, are strongly opposed by the United States and generally remain limited to pilot projects or small-scale community-based efforts [4]. The United States continues its ban on federal funding for needle and syringe exchanges, both domestically and globally. However, the President's Emergency Plan for AIDS Relief provides methadone for HIV-infected IDUs. This is likely to impact HIV infection prevention most significantly in Vietnam, the only country participating in the plan that has a predominantly IDU-driven epidemic. Access to prevention services sharply lags for IDUs across Eurasia. The Global Prevention Working Group estimates that <10% of IDUs in this region have access to comprehensive prevention services [21, 22]. UNAIDS estimates that a 60%

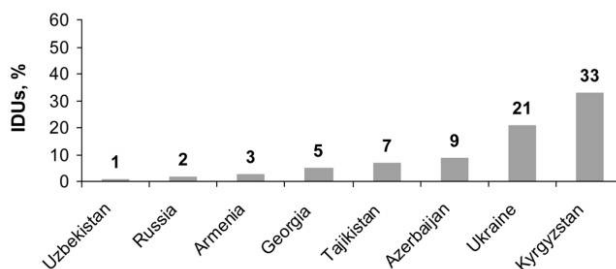


Figure 2. Percentage of injection drug users (IDUs) reached by needle and syringe exchange programs in selected countries of the former Soviet Union, 2005. Adapted, with permission, from the UNAIDS 2006 report on the global AIDS epidemic [1] and from the Open Society Institute [23].

coverage for needle and syringe exchange program access among IDUs is needed to achieve epidemic control [1]. Figure 2 shows the levels of coverage in selected countries of the former Soviet Union; none approach the 60% level.

A third driver has been climates of stigma, hostility, and human rights violations against injection drug users [22–25]. Several mechanisms for these structural factors as drivers of the spread of HIV infection have been reported. There is evidence of increases in syringe sharing among IDUs during police crackdowns [26]. Decreases in attendance at voluntary drug treatment and needle and syringe exchange programs have been reported following increased police surveillance [4]. A 2006 report from Russia identified fear of registration as a drug user as a primary barrier to seeking drug treatment [27].

The most extreme examples of punitive risk contexts are related to incarceration. Recent studies from Thailand, Iran, and Afghanistan reveal that IDUs who use drugs while incarcerated are >6 times as likely to become HIV infected as IDUs who do not use drugs while incarcerated [8, 9, 28].

Taken together, these structural and contextual factors have made Eurasia the region with the fastest growing IDU-related HIV infection epidemics. However, some important structural reforms have occurred. In 2005, the World Health Organization added methadone and buprenorphine to its essential drugs list. In addition, several countries, including Iran and China, have launched methadone maintenance and harm-reduction programs.

HIV infection among MSM in developing countries.

Since the first recognition of HIV infection and AIDS in the United States, HIV infection has disproportionately affected MSM. In 2003, the Centers for Disease Control and Prevention estimated that 63% of new HIV infections in the United States were among MSM [29]. HIV infection rates among minority MSM in the United States, particularly among black MSM, were high and increasing in 2006, despite little evidence of greater individual-level risks, compared with individual-level risks for white MSM in the United States [30, 31]. The Centers for Disease Control and Prevention's 5-city study of MSM conducted in 2004–2005 found that the prevalence of HIV infection was 46% among black MSM—more than double the 21% prevalence among white MSM [31].

In 2005–2006, a new epidemic trend has emerged: high rates of HIV infection among MSM in developing countries that are often not linked to heterosexual prevalence. Figure 3 shows the reported prevalence of HIV infection among MSM, compared with national HIV infection prevalence among adults of reproductive age, from the 2006 UNAIDS global estimate for Senegal, Thailand, Cambodia, and other countries. All reports show substantial rates of HIV infection among MSM, whereas HIV infection rates among the general population are low and even decreasing [1, 32–37]. Senegal, Thailand, and Cambodia

have achieved control of the spread of HIV infection among heterosexual populations; however, none of these countries included MSM in their national HIV infection surveillance, and all are experiencing substantial MSM-related epidemics of HIV infection. In Senegal, Wade et al. [33] found that 99 (21.5%; 95% CI, 17.8%–25.6%) of 463 MSM were HIV-positive in 2004. In a recent assessment using venue day-time sampling with repeat measures in 2003 and 2005, Van Griensven et al. [39] found high HIV infection prevalence and incidence among a population of MSM in Bangkok, Thailand. Overall, the prevalence of HIV infection among these men increased from 17.3% in 2003 to 28.3% in 2005 ($P < .05$); among the youngest men (those aged ≤ 22 years), this prevalence increased from 12.9% to 22.3% ($P < .05$).

Individual-level risks for HIV infection among MSM.

Individual-level risks for HIV infection among MSM are similar in high- and low-income countries. Acquisition risks are focused on the highest probability exposure—that is, unprotected anal intercourse—but also include frequency and number of sexual partners, IDU-related risks, and use of noninjection drugs [32–39]. Use of methamphetamines has been identified with heightened sexual exposure among MSM in several settings [40, 41]. As with heterosexually exposed men, HIV infection in MSM is associated with herpes simplex virus–2 infection, other sexually transmitted infection, and (in at least 1 US study [41]) with being uncircumcised.

What have been the structural drivers of HIV infection in these diverse MSM contexts? In much of the developing world, homosexuality is both illegal and highly stigmatized. Wade et al. [33], the authors of the Senegal study, noted that the sexual practices of MSM remain illegal in more than one-half of Africa's countries. Cáceres et al. [42] reviewed the global literature on MSM and found that virtually no African epidemiologic

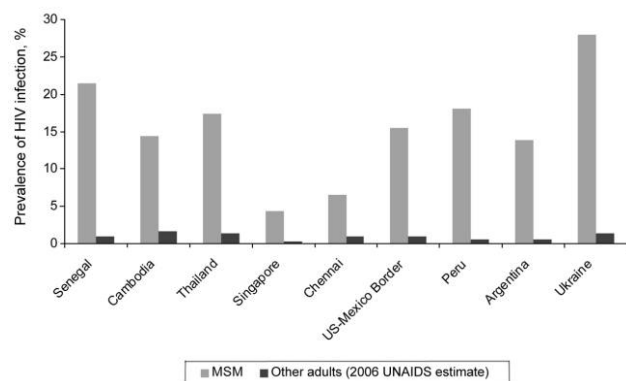


Figure 3. Prevalence of HIV infection among men who sex with men (MSM) and other adults of reproductive age. Adapted from Tabet et al. [32], Wade et al. [33], van Griensven et al. [34], Dandona et al. [35], Girault et al. [36], the Action for AIDS [37], Diess et al. [38], and the Centers for Disease Control and Prevention [39].

Table 1. Prevalence of HIV infection among adults aged 15–49 years in sub-Saharan Africa in 2003 and 2005.

Region, country	Population-based survey prevalence, % (year)	Adjusted 2003 prevalence, %	2005 prevalence, %	Trend in prevalence
Southern				
Botswana	25.2 (2004)	24.0	24.1	Stable
Lesotho	23.5 (2004)	23.7	23.2	Stable
South Africa	16.2 (2005)	18.6	18.8	Increasing
Eastern				
Burundi	3.6 (2002)	3.3	3.3	Decreasing in capital city
Rwanda	3.0 (2005)	3.8	3.1	Decreasing in urban areas
Tanzania	7.0 (2004)	6.6	6.5	Stable
Uganda	7.1 (2004–2005)	6.8	6.7	Stable
Western				
Burkina Faso	1.8 (2003)	2.1	2.0	Decreasing in urban areas
Cameroon	5.5 (2004)	5.5	5.4	Stable
Ghana	2.2 (2003)	2.3	2.3	Stable
Guinea	1.5 (2005)	1.6	1.5	Stable
Senegal	0.7 (2005)	0.9	0.9	Stable
Sierra Leone	1.5 (2005)	1.6	1.6	Stable
Horn				
Ethiopia	1.6 (2005)	1.0–3.5	0.9–3.5	Decreasing in urban areas

NOTE. Adapted, with permission, from the UNAIDS 2006 report on the global AIDS epidemic [1].

HIV studies included questions on the behaviors of MSM, and they found no reports on population prevalence of MSM behaviors. HIV epidemics among MSM in Asia, Eastern Europe, and the Americas are also occurring in cultural environments marked by homophobia, stigma, and discrimination [1, 33–37, 40–42]. UNAIDS has stated that vulnerability to HIV infection is dramatically increased where sex between men is criminalized [1]. In an example of positive structural change, officials of India's National AIDS Control Organization have called for the repeal of India's law that makes sex between men a crime, as an HIV infection prevention strategy [43]. They noted that the law, although little enforced, legitimized police harassment of MSM and of MSM peer and outreach workers and was actively inhibiting HIV infection prevention efforts.

Finally, the lack of targeted HIV infection prevention services remains a key structural epidemic driver. UNAIDS estimates that >1 in 20 MSM globally had access to appropriate HIV infection prevention and care services in 2005 [1].

The generalized epidemic in southern Africa. In the generalized epidemic and high-prevalence zone of southern sub-Saharan Africa, there is little evidence of epidemic control. Nearly one-third of persons infected with HIV worldwide live in this small region, as do slightly over one-half of all HIV-seropositive women aged ≥ 15 years [1]. This regional epidemic contrasts with the lower prevalence and stable or decreasing rates of HIV infection observed across the eastern, western, and

Horn regions of Africa (table 1). How might these disparities be explained?

Individual-level risks for heterosexual HIV acquisition and transmission. Risk factors for the acquisition and transmission of HIV through a heterosexual exposure route are well characterized, but their relative importance varies by location, and the relationships between biological, behavioral, and social risks are incompletely understood. An increasing body of evidence suggests that herpes simplex virus–2 infection is a critical factor for infection [44]. Male circumcision has emerged as a relative protective factor against HIV acquisition. Ecologic data regarding male circumcision have been supported by 1 prospective randomized trial and are currently under investigation in 2 others [45]. High herpes simplex virus–2 infection prevalence and a low frequency of male circumcision were identified in the 4-city study of HIV infection in Africa [46] as key factors that indicated high disease prevalence. Detectable HIV-1 load in blood samples has been associated with sexual transmission in several discordant couples studies [47]. Male condom use is powerfully protective against HIV acquisition and transmission and other sexually transmitted infections. Younger age of initial sexual activity has emerged as a risk for HIV infection among adolescents for both boys and girls [48, 49]. Marriage has been promoted as being protective against HIV infection, although in many recent studies in southern Africa and beyond, it has been implicated as a risk factor for HIV infection in young

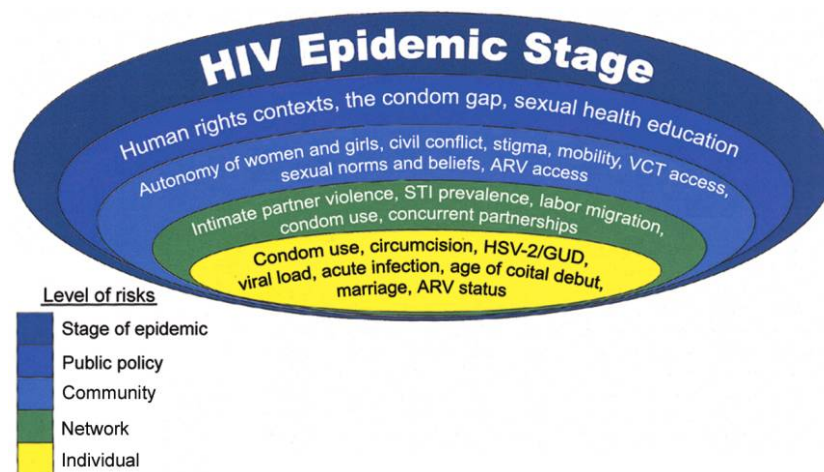


Figure 4. Modified ecological model for HIV risks and risk contexts in southern Africa. Adapted from Rhodes and Simic [2]. ARV, antiretroviral therapy; GUD, genital ulcer disease; HSV-2, herpes simplex virus 2; STI, sexually transmitted infection; VCT, voluntary counseling and testing.

women [50–52]. Risks for HIV infection associated with marriage include low rates of condom use by husbands with their wives and high rates of extramarital sex by men [53, 54].

What are the drivers beyond the individual level in this epidemic context? Gender inequalities have been suggested by many as playing a central role, and they may be exacerbated in environments of conflict and civil strife [1, 55]. Several groups have identified the marked disparity in HIV acquisition risk among adolescent girls versus boys in the African south: age-specific HIV infection prevalence rates among girls begin to increase earlier and faster than rates among boys [49]. In the 2005 national study of HIV infection [54], the divergence of HIV infection prevalence rates in South Africa begins in early adolescence: there is a 9.4% rate of infection among girls aged 15–19 years, but only a 3.2% rate of infection among boys in that age group. The difference is most pronounced between the ages of 25 and 29 years, when women have an infection prevalence of 33.3%, compared with 12.1% among men. Several factors may help explain these gender differences in infection risk, including gender-based violence and sexual coercion. Dunkle et al. [56] observed that intimate-partner violence against women in South Africa has led to an increased risk of HIV infection (adjusted OR, 1.5; 95% CI, 1.2–1.9). Sexual coercion rates are also substantial for girls and boys in South Africa, with 8.6% of 269,705 secondary school students reporting at least 1 episode of coerced sex in the previous 12 months [57]. Rape or nonintimate-partner violence may also be important—if difficult to study—risks for HIV infection.

Social mobility, largely as a result of labor migration patterns, is another marked feature. In 2003, there were ~2.5 million legal migrants working in South Africa, of whom the majority were migrants from rural regions of South Africa and neigh-

boring Lesotho, Botswana, and Mozambique [58]. The return of refugees and the increased social and labor mobility in post-conflict Mozambique have been implicated in that country's rising rates of HIV infection [1]. In a series of studies from KwaZulu Natal, South Africa, Lurie et al. [58] identified a post-apartheid pattern of recurrent circular migration that was strongly associated with HIV infection among both male migrants and their nonmigrating female partners. Migrant men were 26 times more likely to have been infected by an outside partner rather than by their spouse ($P < .01$).

Halperin et al. [59] have recently proposed that, although African men and women do not report a higher number of lifetime sexual partners, the level of concurrent partnerships is much higher than in other regions of the world. Concurrent partnerships may have the potential to create more complex sexual networks, within which HIV infection can spread. Furthermore, a recent report from the Rakai district of Uganda by Wawer et al. [60] enumerates differential per-coital transmission rates of HIV infection as a factor of stage of infection. The highest rates of transmission were found among those with acute infections, with an adjusted relative risk of 7.25 (95% CI, 3.05–17.25), compared with prevalent infections. The increased prevalence of concurrent relationships in conjunction with a higher likelihood of HIV transmission among those least likely to be aware of their changed serostatus may help explain these dynamics. There is at least 1 additional structural factor of relevance: the inadequate supply of condoms. The Global HIV Prevention Working Group [21] calculated that current funding supports only 3 condoms per man per year in sub-Saharan Africa, resulting in an estimated shortage of 1.9 billion condoms per year in this region.

An ecological model for HIV infection risk in southern Africa. We have developed an ecological model to describe the multiple levels of risk in southern Africa (figure 4). At the core are such individual risks for infection acquisition and transmission as frequency of condom use, male circumcision status, herpes simplex virus-2 infection status, HIV load, and antiretroviral treatment status. At the relationship level, intimate partner violence, labor migration, and concurrent partnerships increase the risk of infection. At the community level, the associations widen. These likely include the level of autonomy for women and girls, stigma, social mobility, and community sexual norms and beliefs. At the national and political levels, there are human rights contexts, civil strife, the condom gap, and access to sexual health education. Each of these operate in the context of advanced epidemic stage.

DISCUSSION

We have described 3 epidemic contexts for HIV infection in 2006: IDUs in Eurasia, MSM in the global south, and the concentrated epidemic zone in southern Africa. In each, individual-level factors play primary roles and remain key prevention targets. However, structural realities are powerful drivers of spread and may substantially determine individual-level risks for HIV infection. Where needle and syringe exchange are unavailable to IDUs, we observe more needle sharing and more HIV infection. While the amount of heroin produced continues to increase and new markets continue to open, we observe epidemics of heroin use—particularly where there is little drug treatment. When MSM remain hidden and their behavior remains illegal, we expect epidemics of HIV infection among MSM to continue.

What can be done to respond to these realities? A great deal. We must take harm-reduction programs to scale everywhere that heroin is trafficked and break the logjam on substitution therapy. Targeted interventions for those at risk for HIV infection must be driven by the needs of those who are served and must be informed by sound epidemiological data. For the generalized epidemics of southern Africa, social and national mobilization surrounding gender inequality, sexual rights, and risk reduction are urgent priorities.

A number of challenges remain for the epidemiologic investigation of the AIDS pandemic. Too many studies are cross-sectional and are individual-level analyses of selected populations, thereby limiting our ability to assess causality. We do not have a globally accepted assay for cross-sectional estimates of incidence—thus, surveillance systems are limited to assessments of trends in prevalence. Furthermore, contextual analyses addressing issues such as the impact of human rights limitations on HIV acquisition, are still limited by our ability to assess attributable risks at community and population levels. In the

third decade of the pandemic, we are still not doing enough to control the spread of HIV infection.

Acknowledgments

Potential conflicts of interest. C.B.: no conflicts.

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