

Global epidemiology of HIV

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Purpose of review

To provide an update on the epidemiology of HIV worldwide and by region, along with an overview of recent HIV epidemiological research.

Recent findings

The global prevalence of HIV-1 has stabilized at 0.8%, with 33 million people living with HIV/AIDS, 2.7 million new infections, and 2.0 million AIDS deaths in 2007. Heterosexual spread in the general population is the main mode of transmission in sub-Saharan Africa, which remains the most heavily affected region, with 67% of the global burden. Male–male sex, injection drug use, and sex work are the predominant risk factors in most other regions. Infection rates are declining in some regions, including some of the most heavily affected countries in Africa, but climbing elsewhere such as in eastern Europe and central Asia. Recent HIV epidemiologic research findings include new insights into the role of HIV viral load, co-infection with sexually transmitted infections, male circumcision, antiretroviral treatment, serosorting, and superinfection in HIV transmission and prevention.

Summary

The global prevalence of HIV has stabilized in this decade, but with important regional differences in trends and modes of transmission. Prevention and treatment programs have an expanding impact in preventing HIV infection and AIDS deaths.

Keywords

AIDS, global epidemiology, HIV, transmission

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Introduction

This overview summarizes the epidemiology of HIV-1 worldwide and by region in 2007, the latest available surveillance data from the Joint United Nations Program on HIV/AIDS (UNAIDS). An update is also provided on important new research findings in HIV epidemiology, with an emphasis on studies relevant to HIV prevention, systematic reviews, and meta-analyses. Other articles in this special issue and reviews published elsewhere provide more complete background information and discussions of the topics in this review article.

Global epidemiology of HIV/AIDS

In this decade, the global prevalence of HIV-1 infection stabilized at 0.8% (estimate range, 0.7–0.9%) (Table 1) [1••]. However, the overall number of people living with HIV increased as new infections continued to occur and AIDS deaths were prevented by increasingly available highly effective antiretroviral treatment (ART). Globally, there were an estimated 33.2 million (estimate range, 30.6–36.1 million) people living with HIV infection or

AIDS in 2007, an increase from 29.5 million in 2001 [1••]. The annual incidence of new HIV infections declined from an estimated 3.0 million in 2001 to an estimated 2.7 million (estimate range, 2.2–3.2 million) in 2007. There were an estimated 2.0 million (estimate range, 1.8–2.3 million) HIV-related deaths in 2007. This number represents an increase from 1.7 million deaths in 2001, but as access to treatment increased in this decade, the annual numbers of deaths peaked in 2005 and subsequently decreased. From 2002 to 2007, the number of people receiving ART in developing countries increased from 300 000 to 3.0 million, which was 31% of those who needed treatment [2••].

Globally, the percentage of people with HIV infection who are women has remained stable at 50% for several years [1••]. Adolescents and young adults aged 15–24 years account for 45% of new HIV infections worldwide. An estimated 370 000 (estimate range, 330 000–410 000) children aged 14 years or less were infected in 2007. This number has declined since 2002 as access to interventions to prevent mother–infant transmission have expanded. Availability of antiretroviral medicines to HIV-positive

Table 1 Global adult HIV/AIDS prevalence and adults and children living with HIV/AIDS, newly infected with HIV, and death due to AIDS, by region—2001 and 2007^a

	Year	Adults and children living with HIV/AIDS	Adults and children newly infected with HIV ^b	Adult prevalence (age 15–49 years) (%)	Adult and child deaths due to AIDS
Sub-Saharan Africa	2007	22 000 000	1 900 000	5.0	1 500 000
	2001	20 400 000	2 200 000	5.7	1 300 000
North Africa and Middle East	2007	380 000	40 000	0.3	27 000
	2001	300 000	41 000	0.3	22 000
South and south-east Asia	2007	4 200 000	330 000	0.3	340 000
	2001	4 200 000	450 000	0.4	250 000
East Asia	2007	740 000	52 000	0.1	40 000
	2001	490 000	77 000	0.1	15 000
Latin America	2007	1 700 000	140 000	0.5	63 000
	2001	1 400 000	130 000	0.5	47 000
Caribbean	2007	230 000	20 000	1.1	14 000
	2001	210 000	20 000	1.1	15 000
Eastern Europe and central Asia	2007	1 500 000	110 000	0.8	58 000
	2001	650 000	230 000	0.4	6700
Western and central Europe	2007	730 000	27 000	0.3	8000
	2001	610 000	32 000	0.2	9600
North America	2007	1 200 000	54 000	0.6	23 000
	2001	1 100 000	44 000	0.6	18 000
Oceania	2007	74 000	13 000	0.4	1000
	2001	25 000	3800	0.2	–
Global total ^c	2007	33 000 000	2 700 000	0.8	2 000 000
	2001	29 500 000	3 000 000	0.8	1 700 000

^a Data from [2**].

^b 2001 data from [1**].

^c Estimate ranges for the 2007 global totals are in the text.

pregnant women for prevention of mother–child HIV transmission in developing countries increased from 9% in 2004 to 33% in 2007 [2**]. However, the number of children living with HIV has increased from 1.6 million in 2001 to 2.0 million (estimate range, 1.9–2.3 million) in 2007 [1**]. More than 96% of new infections are in low-income and middle-income countries [2**].

The global pandemic may be described in two broad patterns [2**]. In many countries, mostly in sub-Saharan Africa, particularly southern Africa, and some countries in the Caribbean, there are generalized epidemics with heterosexual transmission in the general population. Secondly, HIV disproportionately affects injection drug users (IDUs), men who have sex with men (MSM), and sex workers (both female and male) worldwide, including in most areas that also have generalized epidemics. The elevated risk to MSM in developing as well as developed countries was recently underscored in a meta-analysis comparing reported HIV prevalence data in MSM with the prevalence in reproductive-age adults. By region, the pooled odds ratio for MSM men was 33.3 in the Americas, 18.7 in Asia, and 3.8 in Africa [3*].

The global statistics mask important local and regional epidemiologic heterogeneity. There were encouraging reductions in prevalence in some countries, notably in sub-Saharan Africa, whereas infection rates increased in others, such as in eastern Europe and central Asia [2**]. It should also be noted that UNAIDS global and key regional estimates in 2007 were lower than those published

in 2006, owing largely to new data indicating that previous estimates had been too high [4]. Specifically, results from multiple population-based surveys generally indicated lower HIV prevalences than did those from sentinel site surveillance. Updated assumptions and methods based on that information were applied retrospectively to earlier data, thus the UNAIDS trend data reported here, including the global stabilization in prevalence and declines in some regions, are not simple the result of changing assumptions and methodology over time.

Overall, prevention program coverage remains incomplete. In 2005–2007, an estimated 60% of female sex workers (39 countries reporting) and 40% of MSM (from 27 countries) reported knowing where they can receive an HIV test and that they had been given condoms [2**]. For IDUs, an estimated 46% (from 15 countries) reported knowing where they could receive an HIV test and be provided with condoms and sterile injecting needles and syringes [2**].

Sub-Saharan Africa

This region is the most heavily affected by HIV, accounting for 67% of all people and 90% of children living with HIV worldwide and 75% of AIDS deaths in 2007 (Table 1) [1**]. There have been gains in availability of ART, but AIDS remains the leading cause of death in the region. In Malawi, for example, mortality in AIDS-affected age groups declined when access to free ART was scaled up in 2004–2006 [5]. Within sub-Saharan Africa, there is considerable heterogeneity in the severity

of the epidemic. Prevalence in most west African countries is less than 2%, whereas the prevalence is greater than 20% in three Southern African countries [2**]. A recent mathematical modeling study highlighted the importance of male circumcision in accounting for sub-regional differences because of the effect on transmission of HIV as well as other sexually transmitted infections which facilitate HIV transmission [6*].

Most transmission in sub-Saharan Africa is through heterosexual transmission in the general population [2**]. Sex work is prevalent, but in a five-country study, sex work accounted for a relatively small proportion of new infections [7*]. Male–male sex is also an increasingly recognized mode of transmission [8]. A substantial proportion of heterosexual HIV transmission in Africa occurs among HIV-discordant stable couples, an estimated 55–93% in one study [9*]. A review of population-based surveys in west, central, and east Africa determined that at least two-thirds of the infected couples are discordant and, contrary to general perceptions that the male almost invariably introduces HIV into the dyad, the female is the infected partner in 30–40% of cases [10].

Infection rates appear to have reached a plateau in many countries, whereas there are significant declines in others [2**]. HIV prevalence in 15–24-year-olds may be used as a measure of recent trends in behavior change and HIV infection rates. The prevalence in pregnant women age 15–24 years has declined since 2000–2001 in 14 of 17 African countries with adequate data [2**]. Most striking, in Kenya HIV prevalence among young pregnant women declined by more than 25% in both urban and rural areas, whereas similar declines were observed in urban areas of Côte d'Ivoire, Malawi and Zimbabwe, and rural parts of Botswana. Reported trends in risk behavior show more mixed results and suffer from a significant variability in methods and quality from year to year and from country to country. The proportion of young people who reported having had sex with nonregular partners in the previous year decreased for both men and women in some countries, for women only in others, and increased for both sexes in others. There are more consistent reported increases in condom use by young people of both sexes during last sex with nonregular partners; however, that increased for women only in other countries and decreased for men in others. Although, in part, the regional reduction in HIV incidence likely reflects natural trends in the epidemic [11*], taken together, trends in decreasing risk behaviors with decreasing HIV prevalence suggest that prevention efforts are having an impact in some of the most-affected countries.

Which specific changes in sexual behavior may account for observed reductions in HIV transmission has been a controversial issue. A recent review of multiple data

sources on the behavior changes that resulted in the reduction in HIV prevalence in Uganda in the late 1980s and early 1990s concluded that Ugandans initially reduced the number of extra-marital sex partners and subsequently increased condom use with extra-marital partners [12**]. This finding suggests that prevention programs should not target a single risk behavior.

Asia

In Asia, there were about 5 million people with HIV infection in 2007, with an estimated 380 000 new infections and 380 000 AIDS deaths (Table 1) [1**]. As the epidemic matures in the region, there has been an overall decrease in the annual number of new infections and an increase in AIDS deaths since 2001. National trends in the region vary considerably. Prevalence is decreasing in Burma, Cambodia, and Thailand, whereas increasing rapidly in Pakistan, Vietnam, and some provinces of Indonesia [2**]. Rates of new infections are also increasing slowly in the very populous countries of Bangladesh and China. Injection drug use, sex work, male–male sex, and overlap in these behaviors continue to drive the spread of HIV in most Asian countries [2**]. Three cross-sectional surveys measuring the prevalence of HIV among MSM in Beijing in 2004, 2005, and 2006 documented an increasing HIV prevalence from 0.4% in 2004 to 4.6% in 2005 and 5.8% in 2006 [13].

Eastern Europe and central Asia

Since 2001, the number of people with HIV in eastern Europe and central Asia increased from 650 000 to 1.5 million in 2007 (Table 1) [1**]. The annual number of new infections has declined, largely due to a slowing of the epidemic in the Russian Federation, where new infections increased sharply in the late 1990s and peaked in 2001 [2**]. At 1.6% in 2007, prevalence in Ukraine is the highest in Europe or central Asia [14]. Incidence in Ukraine has more than doubled since 2001 and is increasing in central Asian countries also including Uzbekistan, which has the largest epidemic in central Asia. Together, the Russian Federation and Ukraine accounted for 90% of the new infections in the region in 2005 [1**]. Injection drug use and sex work largely fuel the epidemic, whereas male–male sex is likely an underreported factor [2**]. Of cases in the region reported in 2006 for which the mode of transmission was known, 62% were due to injection drug use and 37% were from heterosexual transmission. About 40% of reported new infections were in women, of them, an estimated 35% were infected through injection drug use, whereas another 50% acquired infection from drug-using partners [15].

Caribbean

The epidemic has remained relatively stable in the Caribbean (Table 1) [1**], with some declines in incidence in urban areas in Haiti and the Dominican Republic;

the two countries account for about three quarters of people with HIV living in the region [2**]. Heterosexual transmission is the predominant mode of transmission in the region, whereas male–male sex is an important factor in some countries [2**].

Latin America

HIV trends in Latin America have also been relatively unchanged in the past decade (Table 1) [1**], with most transmission attributed to male–male sex and sex work [2**]. In a recent study in five central American countries, HIV seroprevalence in MSM ranged from 7.6 to 15.3%, and estimated incidence ranged from 2.7 to 14.4 per 100 person-years [16]. For female sex workers, HIV seroprevalence ranged from 0.2% to a high of 9.6% in Honduras, where estimated HIV seroincidence was 3.2 per 100 person-years [16].

North America

Incidence has been fairly stable in North America (Table 1) [1**], although recent estimates indicate that incidence was higher than previously thought in the USA [17*]. With life-saving ART widely available, the numbers of people living with HIV has increased. Male–male sex remains the most important mode of transmission, followed by heterosexual transmission, whereas transmission attributed to injection drug use has declined [2**]. Recent reports in the USA highlight racial and ethnic disparities in the burden of disease. The estimated incidence of HIV per 100 000 population in 2006 was 115.7 in black men, 43.1 per 100 000 in Hispanic men, and 19.6 in white men [18]. For women, the rates were 83.8, 29.4, and 11.5, respectively. Another recent insight into HIV epidemiology has been gained through an analysis of the rate of HIV transmission from infected individuals [19]. The estimated rate has declined from 92 per 100 persons living with HIV/AIDS in 1980 when infection was rapidly spreading before the epidemic was detected to 44 per 100 in 1984. In the last decade, transmission has further decreased from eight per 100 in 1997 to five per 100 in 2006, the most recently available data.

Western and central Europe

Overall trends are relatively stable in western and central Europe (Table 1) [1**] with considerable diversity among countries. Heterosexual transmission accounts for the largest share of transmission, with a substantial proportion in western Europe among persons born in sub-Saharan Africa and the Caribbean [2**]. Incidence in men who have sex with men has increased in recent years in western Europe, along with reports of increases in unprotected sex [20**]. Transmission among IDUs has decreased, although it remains the main mode of transmission in Estonia, Latvia, Lithuania, and Poland [2**].

Middle East and North Africa

The limited information from the Middle East and North Africa indicate a relatively low prevalence of 0.3% and relatively stable trends with an estimated 40 000 persons newly infected in 2007 (Table 1) [1**]. Injection drug use and sex work are the main transmission risk factors. Sudan has the highest number of persons infected, with heterosexual intercourse as the main mode of transmission [2**].

Oceania

Although relatively concentrated in Papua New Guinea, the HIV epidemic is increasing in Oceania with 13 000 new infections in 2007 (Table 1) [1**]. The number of new cases doubled in that country from 2002 to 2006. The main mode of transmission is heterosexual sex, with significant proportions of men reporting patronage of female sex workers. Transmission attributed to male–male sex is the main mode in Australia and has increased in recent years [2**].

HIV transmission

Several recently published studies, systematic reviews, and meta-analyses of HIV transmission topics are especially relevant to HIV prevention. A systematic review and meta-analysis shed new light on the risk of HIV-1 transmission per heterosexual contact in high-income versus low-income countries. In high-income countries in the absence of ART, overall female-to-male (0.04% per act) and male-to-female (0.08% per act) transmission rate was relatively low compared with low-income countries where, outside the commercial sex context, the female-to-male per-act estimate was 0.38% and the male-to-female rate was 0.30%. The per-act transmission risk estimate for receptive anal intercourse was much higher (1.7%). Rates were also higher in the early and late phases of HIV infection than for the asymptomatic latent phase, with genital ulcers in either couple member, and in uncircumcised versus circumcised men [21**].

Further highlighting the disproportionate role of the acute infection period in HIV transmission, a study using phylogenetic analysis to characterize the short-term dynamics of the epidemic among MSM in London estimated that 25% of transmission events occurred within 6 months after infection [22]. A similar study in Canada estimated that up to half of subsequent transmission was in the acute infection period [23*]. However, a mathematical modeling study indicated that in Africa no stage of infection is dominant in driving the epidemic, with the early, latent, and late stages contributing 17, 51, and 32%, respectively, to transmission in Kisumu, Kenya, whereas the estimate was 25, 44, and 31%, respectively, in Yaoundé, Cameroon [24*].

A case–control study of MSM being evaluated for primary HIV infection and their recent male sex partners underscored the importance of viral load in HIV transmission [25^{••}]. Fifteen HIV-transmitting men had a higher median seminal plasma viral load (SVL) and median blood plasma viral load (BVL) than did 32 men who did not transmit. BVL and SVL are not necessarily highly correlated; a review of 19 studies on the association found a mean correlation coefficient of 0.45 (range = 0.07–0.64) [26]. BVL was usually higher than SVL, but varied depending on the presence of other STD and ART use.

Another systematic review and modeling study suggested that prevention and treatment of co-infections such as tuberculosis and herpes simplex virus type 2 (HSV-2) infections may result in modest reduction in BVL even without ART and thereby both slow disease progression and reduce infectiousness [27].

Sexually transmitted infections

A recent systematic review and meta-analysis confirmed that genital tract infections increase both the detection and the concentration of HIV-1 in the genital tract, particularly when the infection is symptomatic [28]. In the above-mentioned MSM case–control study, positive HSV-2 serostatus was associated with the risk of transmission but not acquisition of HIV [25^{••}]. This finding is consistent with the negative result from studies of HSV-2 treatment to reduce HIV acquisition risk [29] and supports the premise of an ongoing trial of HSV-2 suppression in dually HIV-1/HSV-2-infected persons to reduce HIV infectiousness [30]. Furthermore, a mathematical model of HSV-2 and HIV-1 transmission in sub-Saharan Africa suggested a more substantial role for HSV-2 in facilitating HIV spread than other sexually transmitted infections. In contrast, according to the authors, HIV had only a modest impact on HSV-2 prevalence [31].

As the most common nonviral STD worldwide, *Trichomonas vaginalis* infection could have a significantly population-level impact on HIV transmission. In a case–control study of female HIV-1 seroconverters, the prevalence of trichomoniasis before HIV infection was 11.3% in seroconverters and 4.5% in controls [32]. In multivariate analysis, the adjusted odds ratio for HIV acquisition in women with *T. vaginalis* was 2.7.

Male circumcision

Male circumcision has been shown to significantly reduce female-to-male HIV transmission, but it had not been well studied in MSM. In MSM, there is disproportionate infection risk from receptive anal sex for which circumcision would not be expected to be protective. A recent meta-analysis of 15 studies that quantitatively examined

the association between circumcision and HIV in MSM found no significant overall effect, with a weighted overall odds ratio of 0.95 (95% confidence interval 0.81–1.11) among a total of 52 726 MSM participants, 52% of whom were circumcised [33[•]].

Although most data on male circumcision and HIV transmission are from sub-Saharan Africa, in an analysis of clinic records for African–American men attending STD clinics in Baltimore, circumcision was not associated with HIV infection status overall, but among men with known HIV exposure to an HIV-infected female partner, circumcision was associated with a statistically significant 51% reduction in risk for HIV infection [34[•]].

Antiretroviral treatment and prevention

There has been increasing interest in the extent to which ART reduces infectiousness and HIV transmission. A mathematical model of universal HIV testing and immediate ART regardless of CD4 cell count in South Africa predicted that both HIV incidence and mortality would be reduced to less than one case per 1000 people per year within 10 years of full implementation of the strategy, and reduce the prevalence of HIV to less than 1% within 50 years [35[•]]. In an observational study of HIV-discordant couples in Rwanda and Zambia, ART use was associated with a 79% reduction in HIV incidence in the initially HIV-uninfected partner [36[•]]. Definitive randomized, controlled data are being generated in the HPTN 052 trial that compares the HIV infection rates of two groups of HIV-serodiscordant couples. The index case of the first group starts taking ART as soon as the couple is enrolled in the study, whereas the index case of the second group starts taking ART when the CD4⁺ cell count is below 250 cells/ μ l [37].

Despite enthusiasm for this approach, it must be noted that ART use does not eliminate transmission risk. Among 145 HIV-infected men enrolled in an assisted reproductive technology program, 5% had detectable HIV-1 RNA in semen, although they had no other STD and their blood viral load was undetectable for at least 6 months on ART [38]. Also, there are concerns that ART use may increase libido and risky sex practices because of perceived reduction in infectiousness. However, in a study in South Africa, unprotected sex at last sex among patients on ART decreased significantly from a baseline after 1 year [39], and there was a decrease in risk behavior with ART use in the observational discordant couples study [36[•]].

Serosorting

‘Serosorting’, that involves some variation of being exposed only to sexual partners who are of the same

HIV status, has been adopted by some as a risk reduction strategy, although the effectiveness of this approach is unknown. A study assessing whether MSM who serosort differed in their HIV infection risk was conducted at a large gay pride festival in 2006 [40]. About one-third of HIV-uninfected men engaged in serosorting. Men who serosorted were more likely to believe that it offered protection, perceived themselves as being at no relatively higher risk, and had more unprotected anal intercourse partners. However, over half reported their frequency of HIV testing as yearly or less frequently and therefore were potentially unknowingly recently infected. The effectiveness of serosorting for HIV prevention depends on the accuracy of infection status disclosures. A mathematical model of the risks of HIV transmission under various circumstances differed by the type of disclosures made [41^{*}]. Accounting for rates of unrecognized HIV infection, treatment status, and differences in infectivity by stage of infection, in some circumstances serosorting can increase rather than decrease HIV transmission risk.

Superinfection

The risk and clinical significance of superinfection with another infecting HIV strain after primary infection is established are not fully understood and are especially relevant to serosorting by HIV-infected individuals and to vaccine development. Previous studies indicated that superinfection did have important clinical consequences but was generally limited to the initial infection period [42,43]. However, in a cohort of 36 high-risk Kenyan women screened for HIV-1 superinfection over a 5-year period beginning at primary infection, seven cases of superinfection were detected. In this study, superinfection occurred throughout the course of the first infection: during acute infection in two cases, between 1 and 2 years after infection in three cases, and as late as 5 years after infection in two cases [44^{*}]. On the contrary, in a study of 49 HIV-infected MSM on ART having unprotected sex in stable, seroconcordant relationships, there were no cases of superinfection [45^{*}], suggesting that it is not common in this specific setting.

Conclusion

In conclusion, although the global prevalence of HIV has stabilized, the burden of disease and number of new infections remains high, with significant regional differences in epidemiologic trends and transmission risk groups. The global scaling up of programmes to prevent infection and provide care and treatment to infected individuals is inconsistent and incomplete, but is having an impact where there is substantial coverage. With ongoing commitment of resources, new epidemiologic insights, such as the relationship between treatment with antiretroviral drugs, HIV viral load, and infectiousness,

hold the promise of heightened effectiveness of and synergies in HIV/AIDS programs worldwide.

Acknowledgement

Disclaimer: The findings and conclusions in this article are those of the author and do not necessarily represent the views of the CDC.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 334–335).

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