Rethinking Global Pharmaceutical Policy

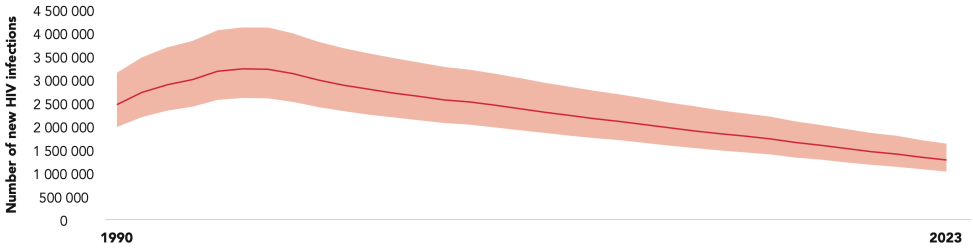
William Fisher and Talha Syed

Appendix 3: HIV/AIDS

(version 1, December 2024)

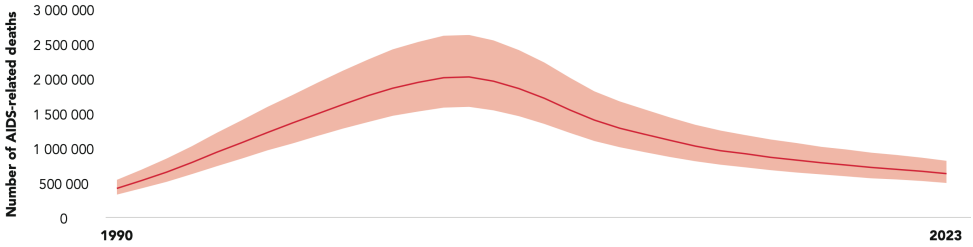
HIV/AIDS is a contagious disease, caused by a virus.[1] It may have been transmitted from chimpanzees to humans in the early 20th century in what is now the Democratic Republic of Congo, but first had a major impact on human populations in the early 1980s. Today, it infects roughly 40 million people in the world.[2] In 2023, 630,000 of them died. This is significantly fewer than the 2.4 million who died during 2005, the peak year of the HIV epidemic.[3] Since 2001, the number of people who are newly infected with HIV each year has been declining, but it is still roughly 1.3 million.[4] The result is that the total number of people living with HIV in the world continues to climb. More detail concerning these trends are provided by the following excerpts from the most recent report from UN AIDS. [5]

Figure 0.1 Number of new HIV infections, global, 1990–2023, and 2025 target



Source: UNAIDS epidemiological estimates, 2024 (https://aidsinfo.unaids.org/).

Figure 0.2 Number of AIDS-related deaths, global, 1990–2023, and 2025 target



---

[1] HIV is a retrovirus, which (unlike most viruses) stores its genetic information in the form of single-stranded RNA, rather than DNA. After it has invaded a host cell, the HIV virus uses an enzyme to generate DNA from the RNA – a process known as "reverse transcription" because ordinarily RNA is "transcribed" from DNA. This modified DNA is then incorporated into the genome of the host cell, after which the virus is perpetuated by the replication of the host-cell DNA. The principal host cells targeted by HIV are CD4+ T lymphocytes and related components of the immune system.

[2] World Health Organization, *HIV/AIDS, Data and Statistics*, https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/j0482-who-ias-hiv-statistics_aw-1_final_ys.pdf?sfvrsn=61d39578_3.

[3] See WHO, "Key Facts HIV," https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/key-facts-hiv-2020.pdf?sfvrsn=582c3f6e_13.

[4] Source: UN AIDS, "The Urgency of Now: AIDS at a Crossroads" (2024)

[5] Source: UN AIDS, "The Urgency of Now: AIDS at a Crossroads" (2024)

HIV is transmitted from one person to another in three main ways: through unprotected sexual relations; through sharing of needles or syringes (typically by intravenous drug users); and from mother to child during pregnancy, birth, or breastfeeding. In the 1980s and '90s, it was also sometimes transmitted through blood transfusions or organ transplants, but those methods are now rare. In many developed countries, the primary form of sexual transmission has been through male-to-male relations, but in developing countries, the primary form has been through heterosexual relations.

The disease caused by HIV typically proceeds through three main phases. Roughly three weeks after transmission, the infected person begins to suffer from symptoms that resemble those associated with influenza: fever, tender lymph nodes, rashes, sores, diarrhea, and so forth. The underlying cause of these symptoms is a sharp drop in the concentration of CD4 lymphocytes in the person's blood and intestinal mucosa and a resultant degradation of her immune system. Roughly nine weeks after transmission, this acute phase of the disease subsides. It is succeeded by a long period of clinical latency, during which the person's CD4 count initially rebounds (in the blood, although not in the mucosa), then very slowly declines. The average duration of the latency period is 8 years, but it can be as long as 20 years. Some infected persons never move beyond this phase. In most, however, latency gradually gives way to the set of debilitating and life-threatening symptoms known as AIDS. As the person's CD4 count drops and her immune system deteriorates, she is beset by a growing set of opportunistic infections and viral induced cancers. If untreated, she typically dies within two years.

Various schemas have been developed to mark the progress of the disease. With respect to developing countries, the most influential is the set of four "clinical stages" defined by the World Health Organization. Stage 1 is "asymptomatic" – corresponding roughly to the latency period described above. Stage 2 (CD4 count under 500) is characterized by "mild symptoms" (e.g., recurrent respiratory infections, herpes zoster, fungal nail infections); stage 3 (CD4 count under 350) by "advanced symptoms" (e.g., weight loss, chronic diarrhea, pulmonary tuberculosis, pneumonia); and stage 4 (CD4 count under 200) by "severe symptoms" (e.g., "wasting syndrome," extrapulmonary tuberculosis, Karposi's sarcoma, disorders of the central nervous system).[6]

No cure for HIV/AIDS currently exists. However, since the early 1990s, medicines have become available that can slow or halt the progress of the disease. These medicines are commonly known as "anti-retroviral" drugs (ARVs), less commonly as "anti-retroviral therapies" (ARTs) or "highly active antiretroviral therapies" (HAARTs). The most effective are reverse transcriptase inhibitors, which impede the process by which modified DNA is generated from HIV RNA.[7] Inhibitors of this sort include zidovudine (AZT), tenofovir (TDF), lamivudine (3TC), staduvine

---

[6] For lists of the other symptoms that characterize each stage, see http://www.who.int/hiv/pub/guidelines/HIVstaging150307.pdf, pp. 15-16 (adults) and 17-18 (children).

[7] See note ___, above.

(d4T), and emtricitabine (FTC).[8] Combinations ("cocktails") of these drugs have proven to be more effective than single drugs; typically, they are administered in combinations of three.[9]

If a course of these drugs is administered soon enough, it usually slows dramatically the progress of the disease. In some cases, however, the patient either develops resistance to the drugs or suffers increasingly severe side effects. At that point, he or she is usually given so-called "second-line" ARVs. These typically combine previously unused reverse transcriptase inhibitors with protease inhibitors (PIs), which impede the replication of the virus and the release of viral particles from the host cell into the bloodstream.[10] If the second-line drugs lose effectiveness, they are replaced by "third-line" ARVs – sometimes called "salvage regimens."[11]

Because HIV plagues developed countries as well as developing countries, it has received more attention from researchers, foundations, pharmaceutical firms, and governments than have TB, malaria, or dengue. Much of that attention has focused on vaccine development. Unfortunately, progress has been slow. Researchers face several hurdles: the fact that, in the overwhelming majority of cases, HIV infection does not result in protective immunity, which deprives us of the naturally generated antibodies that are ordinarily employed to design vaccines;[12] the genetic diversity among HIV strains and the speed with which the virus evolves in vivo;[13] and the difficulty of inducing immune protection in the mucosa, where the virus commonly enters the body.[14]

Despite these impediments, some progress has been made. Since 2003, five HIV vaccines have shown sufficient promise to warrant clinical trials. The first three candidates failed to show significant efficacy, and the trials were halted. The other two, however, continue to be evaluated. HVTN 705 (Imbokodo), a broad-spectrum candidate, is currently being tested on 2,600 women in five African countries, and HVTN 706 (Mosaico) is being tested on gay men and transgender women in the United States, Latin America and Europe. Results of these trials are expected in

---

[8] For a comprehensive catalogue of the ARVs used in developing countries, see MSF, Untangling the Web of Antiretroviral Price Reductions — 18th Ed., (2016), https://msfaccess.org/sites/default/files/HIV_report_Untangling-the-web-18thed_ENG_2016.pdf., pp. 16-46.

[9] For a catalogue of the principal combinations of ARVs, see ibid., pp. 47-69; Clinton Health Access Initiative, "Hiv Market Report: The State of Hiv Treatment, Testing, and Prevention in Low- and Middle-Income Countries," (2019).

[10] PIs that target HIV include saquinavir (developed by Roche), ritonavir (developed by Abbott [renamed AbbVie]), indinavir (developed by Merck), nelfinavir (developed by Agouron Pharmaceiuticals and Eli Lilly), and fosamprenavir (a variant of amprenavir, developed by GlaxoSmithKline).

[11] See, e.g., Khan et al., Second-line Failure and First Experience with Third-Line Antiretroiviral Therapy in Mumbai, India, 7 Global Health Action 24861 (2014), available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4119292/pdf/GHA-7-24861.pdf .

[12] *See* David A. Garber et al., *Prospects for an AIDS Vaccine: three big questions, no easy answers*, THE LANCET INFECTIOUS DISEASES Vol. 4 at 397 (July 2004). The significance of this circumstance is suggested by the fact that live-attenuated varicella zoster virus vaccine is the only vaccine ever to be developed for "pathogens that reproducibly establish lifelong infection in their hosts." *Id.* at 399.

[13] Several factors have been identified as particularly problematic to the antibody approach to vaccine development: (1) virus particles are difficult to neutralize, (2) the rapid evolution of the virus in vivo, (3) extraordinarily high levels of viral genetic diversity and (4) the down-regulation of MHC-1 molecules on the surface of infected cells. *See id.* at 399.

[14] WHO, "Global Update on the Health Sector Response to Hiv, 2014," (2014)., p. 23.

2022 and 2024, respectively. Even if (as is likely) neither candidate proves to be the Holy Grail, the trials should help in the development of additional candidates.[15]

Until an effective vaccine emerges, efforts to halt the AIDS pandemic will continue to focus on reducing the frequency of transmissions of the HIV virus from one person to another. Strategies of these sorts include:

- encouraging use of condoms during sexual relations (which sharply reduces transmissions of the virus) through education or through gender-empowerment campaigns;[16]
- male circumcision (which significantly reduces sexual transmissions from females to males, though not necessarily transmissions from males to females or males to males);[17]
- sexual-abstinence programs (the efficacy of which is as yet unproven);
- providing testing and medical services to sex workers and to intravenous drug users, who are much more likely to be HIV-positive than the general population;[18]
- providing sterile or disposable syringes to intravenous drug users;[19]
- prophylactic administration of ARVs, especially to the infected partners in serodiscordant couples and to infected pregnant women (which, if begun early enough, nearly eliminates transmission of the virus to their children);[20]
- testing blood supplies, to prevent transmission through infusions;[21] and
- the use of various precautions by health-care workers, to reduce transmissions from their patients.

---

[15] The long and discouraging story of efforts to develop an effective vaccine is chronicled in Maggie L. Shaw, "The Search for an Hiv Vaccine Continues," *AJMC* (2021), https://www.ajmc.com/view/the-search-for-an-hiv-vaccine-continues; NIH, "Experimental Hiv Vaccine Regimen Ineffective in Preventing Hiv," (2020), https://www.niaid.nih.gov/news-events/experimental-hiv-vaccine-regimen-ineffective-preventing-hiv; AIDS Vaccine Advocacy Coalition, "Hiv Vaccines: An Introductory Factsheet," (2019).; Miles P. Davenport et al., Predicting the Impact of a Nonsterilizing Vaccine against Human Immunodeficiency Virus, JOURNAL OF VIROLOGY Vol. 78, No. 20 (Oct 2004); Khabir Ahmad, New HIV/AIDS vaccine enters phase II trials, THE LANCET Vol. 5, at 138 (Mar. 2005).; Edward Nwanegbo et al., Prevalence of Neutralizing Antibodies to Adenoviral Serotypes 5 and 35 in the Adult Populations of The Gambia, South Africa, and the United States, CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, Vol. 11, No.2 at 351 (Mar. 2004); Richard D. Klausner et al., *The Need for a Global HIV Vaccine Enterprise*, SCIENCE, Vol. 300 at 2036 (June 27, 2003).

[16] See Johnson et al., "The Effect of Changes in Condom Usage and Antiretroviral Treatment Coverage on Human Immunodeficiency Virus Incidence in South Africa," 9 J R. Soc. Interface 1544 (2012). The current rates of condom use in the countries where HIV is most prevalent are reviewed in WHO, "Global Update on the Health Sector Response to Hiv, 2014.", pp. 11-12.

[17] See Auvert, Randomized Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk," 2 PLoS Med. E298 (2005); Gray, "Male Circumcision for HIV Prevention in Rakai, Uganda," 369 Lancet 657 (2007); Bailey, "Male Circumcision for HIV Prevention in Young Men in Kisumu, Kenya," 369 Lancet 643 (2007).

[18] See WHO, "Global Update on the Health Sector Response to Hiv, 2014.", Table 2.2.

[19] See WHO, "EFFECTIVENESS OF STERILE NEEDLE AND SYRINGE PROGRAMMING IN REDUCING HIV/AIDS AMONG INJECTING DRUG USERS" (2004), http://www.who.int/hiv/pub/prev_care/effectivenesssterileneedle.pdf?ua=1; WHO, "Best Practices for Injections and Related Procedures ToolKit" (2010), http://www.who.int/injection_safety/toolbox/9789241599252/en/.

[20] WHO, "Global Update on the Health Sector Response to Hiv, 2014.", Chpt. 3.

[21] WHO, Notes 58, 60.