

env
cr
Most
proteins

Single-stranded
HIV-1 RNA

p17^{gag}

p24^{gag}

p9^{gag}

STORIES OF PROGRESS:

HIV/AIDS

Overcoming one of the worst human pandemics

TRANSFORMING LIVES

PRESENT DAY...

ZAIN'S HIV/AIDS STORY

Zain was diagnosed, is able to manage his illness and can expect a near normal lifespan, thanks to starting combined antiretroviral (ARV) treatment early in the course of the infection. He now takes a one-a-day pill.

*THIRTY YEARS AGO...*

In 1988, Zain would have had a life expectancy of just one year from diagnosis and would not have had access to combined ARV treatment.

IN THE FUTURE...

Zain hopes a vaccine will prevent people like him being infected with HIV and halt the spread of AIDS.

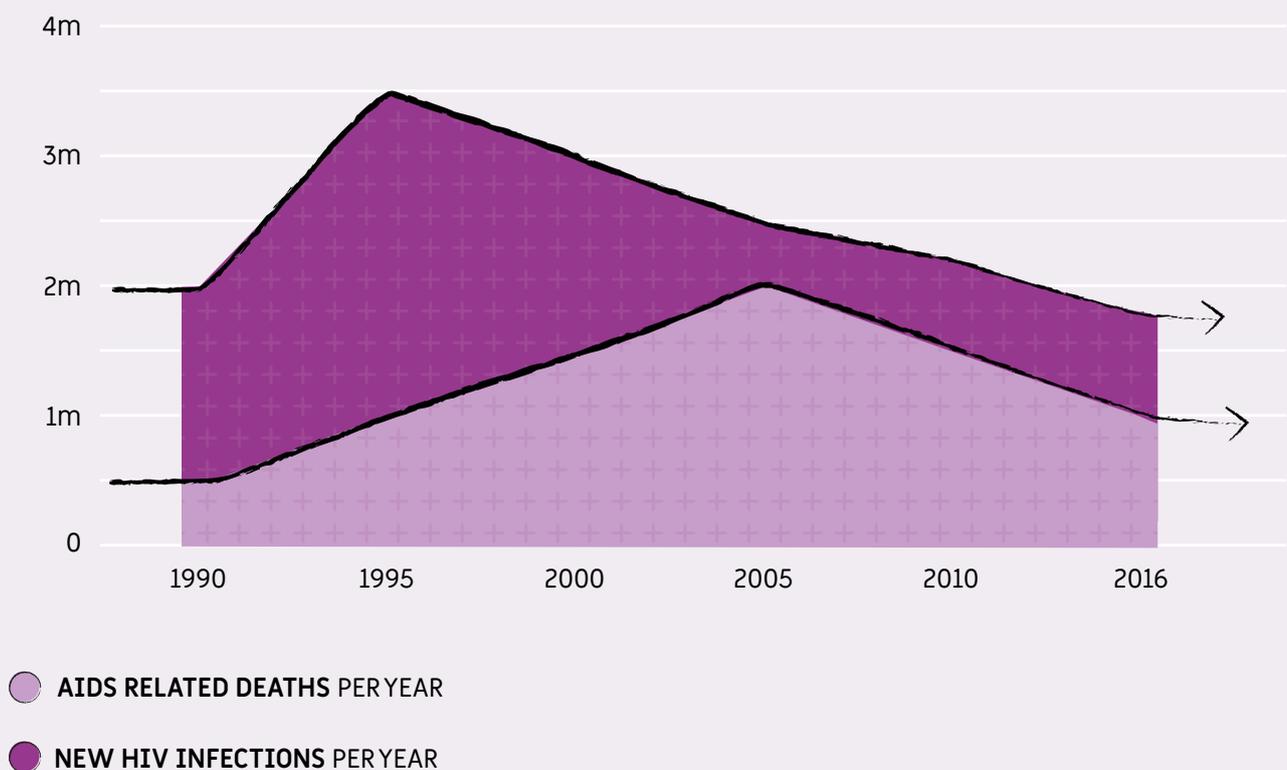
It has been 36 years since the world was first introduced to the term AIDS. With the first reported cases of HIV/AIDS (human Immunodeficiency virus / acquired immune deficiency syndrome) in the 1980s, the world faced a new and unknown virus.

The epidemic was defined by fear and death as HIV infection rates and AIDS-related deaths grew throughout the 1980s and 1990s. As the global response ramped up, thanks to scientific advances and programs targeting those in need, 2005 marked a turning point as the number of AIDS related deaths peaked. Although patients in developed countries have access to treatment and can expect near-normal lifespans, HIV/AIDS remains a particularly heavy burden in sub-Saharan Africa, where it is the leading cause of death for adults.

Breakthrough innovations, notably antiretroviral (ARV) therapy, have had significant impact on confronting the epidemic and enabling those infected with HIV to live long and healthy lives. Equally important have been partnerships to deliver access to treatment, care, and education to those most affected around the world.

Patients diagnosed with AIDS in 1990 could expect to live only months, during which time they would be likely to contract a number of other infections. Today, an HIV infected patient who receives ARV therapy may expect to live a normal lifespan. In fact, the HIV/AIDS death rate has dropped by 85% since 1991.

The global response delivering improved patient outcomes for those with HIV/AIDS has also strengthened healthcare systems and access more broadly, with knock-on effects of improving gender equality.



KEY MILESTONES

The HIV/AIDS epidemic is defined by scientific breakthroughs as well as transformative partnerships and initiatives that controlled the epidemic through generations:

- **1982:** The term AIDS is first used; tracking of disease begins in US.
- **1984:** The retrovirus that causes AIDS is identified.
- **1987:** The first antiretroviral (ARV) drug, zidovudine, is approved by the FDA as treatment for HIV.
- **1996:** 1996: Combined multi-drug ARV treatment is introduced, changing the course of the HIV epidemic.
- **1996:** The Joint UN Programme on HIV and AIDS (UNAIDS) is established, serving as the main advocate for accelerated global action on the epidemic.
- **2001:** UN Declaration of Commitment on HIV/AIDS calls for the respect of human rights of people living with HIV.
- **2002:** The Global Fund to fight AIDS, Tuberculosis and Malaria (The Global Fund) is set up, a public-private partnership to attract resources to fund prevention and treatment in resource limited settings.
- **2002:** FDA approval of the first rapid home-use HIV testing kit providing results in twenty minutes.
- **2003:** Launch of The President's Emergency Plan for AIDS Relief, a US government initiative to address the global HIV/AIDS epidemic.
- **2003:** Approval of new anti-HIV drug, enfuvirtide or T-20, the first in a new class of drugs designed to prevent entry of the virus into human cells.
- **2006:** The first one-a-day pill to treat HIV is approved in the US.
- **2010:** Medicines Patent Pool is founded, the first voluntary licensing and patent pooling mechanism in public health, aiming to improve access to affordable and appropriate HIV, hepatitis C and TB medicines.
- **2012:** The first medication to protect those who do not have HIV from infection, called pre-exposure prophylaxis, is approved.
- **2015:** UNAIDS announces that the MDG target of 15 million people on life-saving HIV treatment by 2015 has been met 9 months ahead of schedule.
- **2015:** Launch of the SDGs, which include a target to end the AIDS epidemic by 2030.

R&D AND INNOVATION: FROM DEATH SENTENCE TO LIFETIME TREATMENT FOR PATIENTS

THE HIV/AIDS CRISIS TRIGGERED A LEVEL OF GLOBAL SOLIDARITY THAT HAD NOT BEEN SEEN BEFORE. WE MUST GARNER THE SAME SUPPORT FOR NON-COMMUNICABLE DISEASES.

Mariângela Simão,
WHO

Advances in R&D have transformed HIV from an untreatable and almost uniformly fatal virus into a manageable, chronic condition. These innovations have extended the lives of millions of people living with HIV. In the 30-plus years since the discovery of the HIV virus, more than 30 medicines have been approved to treat the HIV infection. Over time, medicines have improved in tolerability, efficacy, and convenience for patients.

A major breakthrough was the development of ARV therapy, which works by preventing HIV from multiplying, reducing the viral load in the body and allowing the immune system to keep it in check. The first generation of these therapies was developed in the mid 1980s by Burroughs-Wellcome (now GSK) in collaboration with the National Cancer Institute. Azidothymidine was the first ARV drug to be approved by the US FDA as treatment for HIV.

Since then, research has improved both understanding of the disease and its evolution, simplifying the medication mechanism for patients.

As understanding of the disease and the effects of ARV on patients grew, a 'combination therapy' approach emerged as far more effective than any single drug treatment. So-called 'cocktail' approaches work by combining drugs in different sequences. The adoption of HAART (highly active antiretroviral therapy) in 1996 inaugurated a new era in HIV treatment. The combination approach was quickly incorporated into clinical practice and has since become the default therapeutic approach.

Preventing transmission from mother to child also has huge implications for halting the spread of HIV/AIDS and is another key focus area for R&D. Increased understanding of ARV therapies allowed the use of treatment on pregnant mothers. Through increased understanding of ARV therapies it was found that HIV positive mothers adhering to ARV for several weeks or months before birth could eliminate the risk of transmission to the baby through pregnancy, birth, and breastfeeding.

A key challenge has been enhancing access to, and funding for treatment in resource-scarce communities, including many of the geographies worst affected by the virus. The development of less costly care regimens has allowed the extension of effective treatment. For example, NNRTIs (non-nucleoside reverse transcriptase inhibitors) now provide a lower cost option for LMICs and facilitated treatment expansion efforts.

Newer classes of drugs include integrase inhibitors, today a recommended first-line treatment in many cases, which work by preventing the virus from incorporating its DNA into the host genome.

PARTNERSHIPS ADDRESS THE FULL LIFECYCLE OF HIV/AIDS, DELIVERING CARE TO THOSE WHO NEED IT MOST

RESEARCH COLLABORATION

Partnerships have played a crucial role in supporting R&D advances for the treatment of HIV/AIDS, bringing together academia, governments, and industry. The National Cooperative Drug Discovery Group Programme for the Treatment of AIDS (NCDDG-AIDS) is a collaboration platform established early in the epidemic. The AIDS Clinical Trial Group (ACTG) supports clinical trials and laboratory studies in order to set standards of care for HIV infection.

TREATMENT FOR VULNERABLE GROUPS

A key challenge has been the development of pediatric ARV formulations. Initiatives like the Pediatric HIV treatment Initiative (PHTI), The Global Accelerator for Pediatric formulations (GAP-f) and the Collaborative Initiative for Pediatric HIV Education and Research (Cipher) aim to close the treatment gap between adults and children.

In 2011, the Global Plan to eliminate new HIV infections among children by 2015 was launched by organizations convened by the President's Emergency Plan for AIDS Relief and The Joint UN Programme on HIV and AIDS (UNAIDS). As part of this, companies pledged funding for programs to ensure access to treatment for pregnant women and maternal and family planning health services. Pledges included Johnson & Johnson at USD 15 million, and more recently AstraZeneca with USD 10 million over five years to cover HIV/AIDS. The number of children acquiring HIV infection declined from 360,000 in 2009 to 160,000 in 2016.

Mother to child transmission is preventable and has been virtually eliminated in the developed world. Saving Mothers Giving Life - a public-private partnership between USAID, MSD, and others - makes strategic investments to reduce deaths of mothers with HIV. The International Partnerships for Microbicides, a partnership between civil society, research-based pharmaceutical manufacturers, and research centers develops HIV prevention products and other sexual and reproductive health technologies for women with a focus on microbicides. Other public-private partnerships include between ViiV Healthcare and the Pediatric European Network for the Treatment of AIDS, which develops treatment strategies for children living with HIV including project EPIICAL, a predictive in vitro platform to treat HIV-infected children, as well as those to support research and build research and healthcare capacity in pediatrics HIV with the Clinton Health Access Initiative, Amfar TREAT Asia and the International AIDS Society.

People practicing intravenous drug use (IDU) remain disproportionately affected by HIV, accounting for one in 10 new HIV infections worldwide. Harm reduction strategies target IDU by focusing on explicit and peer-based education about the risk of HIV from sharing injecting equipment, needle syringe programs, drug treatment (especially opiate substitution treatment), and community development.

PARTNERING FOR DELIVERY

Diagnosis is as important to effective HIV/AIDS treatment as medicines. Currently, only 60% of people with HIV know their status. AmpliCare, a public-private partnership



between Roche, the Clinton Foundation, USAID, and UNICEF aims to address barriers that prevent early diagnosis of infants with a focus on sub-Saharan Africa. Roche has redesigned its tests, developed a novel methodology for gathering and transporting blood samples, as well as introducing SMS technology for test results. This has resulted in expanded access to diagnosis in the remotest areas, where over six million infants have been tested for HIV.

Despite the breakthroughs in treatment, by 2000, less than one million of the 34 million people living with HIV/AIDS were accessing ARV therapy. In particular, many in developing countries were left behind as treatments were not accessible.

In 2000, UNAIDS, WHO, Boehringer Ingelheim, BMS, Roche, GSK and MSD announced a plan to improve access to treatment – the Accelerating Access Initiative (AAI). The program, which concluded in 2012, applied preferential pricing to ARVs, opening the door to a new future of access to ARV medicines in developing countries and laying the foundation for future access to medicine initiatives.

Many companies have made commitments reflecting the need for affordable treatment options for the most affected countries. One mechanism to improve access to ARVs is voluntary licensing agreements whereby the patent holder grants a voluntary license over product patents in certain countries to generic manufacturers, which enables them to develop, manufacture and sell generic versions of the licensed product(s) in resource-limited settings. GSK gave the first voluntary license in 2001 for Retrovir, Epivir and Combivir in South Africa. Within a year there was a significant increase in supply and reductions in ARV prices in the developing world. The scope and approach to voluntary licensing agreements has continued to evolve – both directly between patent-holding companies and generic manufacturers, and through the UN-

backed Medicines Patent Pool – and remains a key approach in improving access to ARVs. ViiV Healthcare’s voluntary licensing approach, for example, enables accelerated access to the innovative new HIV treatment, dolutegravir, across all LMICs, least developed and Sub-Saharan African countries.

Access to treatment grew in the 2000s. By 2006, 28% of those in need in sub-Saharan Africa received treatment, compared to just 2% in 2003; 2007 saw a 54% increase in the number of people in LMICs receiving ARV therapy. There is a need for continued progress in access for LMICs, alongside interventions in prevention, diagnosis and broader health system strengthening.

STRENGTHENING HEALTH SYSTEMS

Caring for those living with HIV/AIDS extends beyond provision of treatment. Since 1999, the ‘Secure the Future’ initiative run by the Bristol Myers Squibb Foundation has supported those living with HIV/AIDS in sub-Saharan Africa, with particular focus on women and children and the links between cervical cancer and HIV. The Foundation has invested USD 181 million to date, partnering with governments and NGOs to build comprehensive care models through investments at a community level to support outreach, home based care, and psycho-social support.

UNAIDS highlights the connection between HIV/AIDS responses and human rights. Education plays a crucial role in the fight against HIV and AIDS and stigma against those living with it. It also promotes awareness of how to protect from AIDS, encourages people to get tested and reduces discrimination against HIV-positive people. GSK and ViiV Healthcare’s Positive Action programs tackle societal barriers to addressing the global HIV epidemic such as stigma and discrimination, gaps in education and sexual health services. The programs support community-based organizations and NGOs to focus on populations worst affected by HIV such as women and girls, adolescents, men who have sex with men, transgender people, incarcerated individuals, sex-workers, and intravenous drug users.

Botswana is an example where public-private partnerships have improved health system capacity for treatment and prevention in a country with one of the highest adult prevalence rates in the world. In 2000, MSD joined with BMGF and the government of Botswana to form the African Comprehensive HIV/AIDS Partnerships (ACHAP). ACHAP developed a comprehensive approach to increase prevention and treatment of HIV/AIDS and care for those infected in support of the government of Botswana’s response to the epidemic. The MSD Foundation and BMGF committed to support ACHAP with USD 106.5 million. In addition, MSD donated its antiretroviral medicines to Botswana’s national ARV treatment program for the duration of the partnership. Botswana was among the first countries in sub-Saharan Africa to reach universal access to treatment for HIV.

Building on this progress, in 2016, ViiV announced an agreement to supply its latest HIV medicine to support the government of Botswana’s national Treat All program, which aims to ensure people living with HIV in the country get tested and receive treatment.

2030: THE END OF THE AIDS EPIDEMIC?

Ending the AIDS epidemic by 2030, as set out in SDG target 3.3, will only be achieved with innovation and multi-sector partnerships.

Despite the array of effective HIV prevention tools such as male and female condoms, pre-exposure prophylaxis, voluntary male circumcision, and behavior change interventions (e.g. the use of clean needles), 1.8 million people became newly infected with HIV in 2016.

UNAIDS outlines the priority challenges for the next decade in their ambitious 90-90-90 targets for 2020:

90%

of all people living with HIV know their HIV status

90%

of all people diagnosed with HIV infection receive sustained ARV therapy

90%

of all people receiving ARV therapy will have viral suppression

To get there, many look to industry and partners for additional pre-exposure options, a cure or vaccine, and support closing the gap in treatment.

THE SEARCH FOR A CURE

While current treatments enable patients to live longer lives, the search for a cure continues. Researchers have successfully lowered levels of the virus to undetectable levels in certain children for a period of time, though there has not yet been a confirmed case of an infant totally cured. AIDS researchers continue to improve our understanding of how interventions can best impact infant immune system responses to HIV. Many R&D eradication efforts focus on 'flushing' the HIV virus out of latently infected cells, which are often seen as the major barrier to cure. This so called 'shock and kill' technique works by 'waking up' inactive cells, forcing them to produce new virus particles that are susceptible to current antiretroviral drugs. Several techniques for this are in development with research ongoing into cytokine therapy, valproic acid, and histone deacetylase inhibitors.

VACCINE DEVELOPMENT

The development of a vaccine holds promise but has proven elusive due to the genetic diversity of the virus and its ability to rapidly mutate. The International AIDS Vaccine Initiative brings together public and private actors to research, design and develop vaccine candidates. Researchers are optimistic that a vaccine will be found in our lifetime. For example, Johnson & Johnson is working to develop a mosaic-based vaccine is yielding encouraging results from clinical studies and is progressing to the next phase of clinical development.

CLOSING THE FUNDING GAP

Of the 37 million people globally living with HIV, 21 million have access to ARV therapy – and more year-on-year. Yet, millions still lack access to therapy, many in LMICs. It is estimated that just 12 million of the 25 million living with HIV/AIDS in Africa receive ARV therapy. UNAIDS estimates the funding gap for HIV in LMICs over the 2015 to 2020 period stands at USD 26 billion, and it looks to public and private partners to ensure the gains in R&D innovation do not exclude those in need of existing or older treatments. Individual R&D-based pharmaceutical manufacturers – through licensing, pricing initiatives and various partnerships – continue to seek to improve access for LMICs, alongside critically needed interventions in prevention, diagnosis and broader health system strengthening. Only a holistic approach will ensure critical treatments are available to all people in need.

