HIV: from a devastating epidemic to a manageable chronic disease
In the decade since the United Nations declared HIV an unprecedented human catastrophe, the AIDS response has underscored the ethical imperative of fair access to medicine. WHO’s standard-setting work helped make prevention and treatment more accessible, safe, effective and efficient, and encouraged integrating HIV services into existing health systems. WHO has prequalified more than 250 products for HIV-related conditions. New targets aim to prevent 1.6 million new infections and 600,000 deaths per year, ending AIDS as a public health threat by 2030.

HIV, with its long incubation period, its multiple modes of often intimate transmission, and its defiance of monumental efforts to develop a vaccine and a definitive cure, is one of the most complex, the most challenging and arguably the most devastating of all infectious diseases that humanity has ever had to face.

In 2015, the global HIV epidemic claimed fewer lives than at any point in almost two decades, and fewer people became newly infected with HIV than in any year since 1991. The fact that the MDG target of halting and reversing the spread of HIV was met nine months ahead of schedule is a stunning achievement.

The HIV response changed the face of public health in profound ways, opening new options for dealing with multiple other health problems. Treatments can be found. Prices can plummet. Funds can be secured. High-impact services can be delivered in resource-constrained settings. Attitudes can change. Communities can be mobilized to take action. With sufficient will, commitment and resources, a bleak and depressing situation can be turned into one that offers hope.

Above all, the AIDS response underscored the ethical imperative – the life-and-death significance – of fair access to the best quality-assured medicines and diagnostics on offer, to all in need.

How this happened, including WHO’s specific role, deserves analysis. Recent achievements look all the more remarkable when viewed against the situation a decade ago. A look at these achievements also yields one of the best examples of how WHO’s standard-setting work and direct support to countries translates into lives saved and suffering averted.

By 2017, WHO estimated that more than 18 million poor people now had access to antiretroviral therapy.
An “unprecedented human catastrophe”

In 2002, WHO launched its “3 by 5” initiative with the goal of extending coverage with antiretroviral therapy to 3 million people in the developing world by the year 2005. The initiative, with “kick-start” funding from the Canadian government, stimulated a remarkable expansion of treatment programmes supported by generous funding in countries, most notably from the Global Fund and the United States President’s Emergency Plan for AIDS Relief. Despite this rapid expansion of treatment, international efforts were still running behind the epidemic. By 2005, more people were receiving treatment but many more were becoming newly infected. Efforts to get ahead of the epidemic needed to broaden the approach to include prevention and care as well as the delivery of treatments. The focus shifted from universal access to HIV treatment to universal access to HIV prevention, treatment and care.

The Political Declaration on HIV/AIDS, adopted by the United Nations General Assembly in 2006, described the epidemic as an “unprecedented human catastrophe” that posed “one of the most formidable challenges to the development, progress, and stability of our respective societies and the world at large”.

The list of concerns was long. The epidemic was still expanding. Women were particularly affected, accounting for the majority of people infected with HIV in sub-Saharan Africa. HIV was disproportionately affecting the young. Rates of infection in children and adults under the age of 25 years were rising, accounting for nearly half of all new infections. Previously agreed targets for improving access to prevention, treatment, care and support were not being met. Poverty was one factor fuelling the epidemic, but so were gender inequities, gender-based violence and the sexual exploitation of women and girls. In other regions, vulnerable and marginalized populations were those most affected, with epidemics among men who have sex with men, sex workers, transgender people, people who inject drugs, and prisoners.

In short, urgent and exceptional action was required at all levels to curb the devastating effects of the epidemic. The declaration stressed in particular the need to scale up significantly towards the goal of universal access to comprehensive prevention programmes, treatment, care and support by 2010. Universal access meant reaching everyone in need, including those living on the margins of society and beyond the reach of health services.

In 2007, an estimated 33.2 million people were living with HIV, of whom 22.5 million were in sub-Saharan Africa, where AIDS was by far the leading cause of death. The year saw 2.5 million new HIV infections and 2.1 million deaths globally. Nearly 300 000 children under the age of 15 years were infected, and more than 12 million children in sub-Saharan Africa had lost one or both parents to AIDS.

At the end of 2007, nearly 3 million people in resource-constrained settings were receiving antiretroviral therapy, representing a jump of 1 million people compared with the previous year. Though the increase was encouraging, therapy was still reaching only 12% of those infected and only the sickest were considered eligible for treatment. A mere 20% of people with HIV were aware of their infection status, and prevention services were not reaching the majority of those at greatest risk. The world was still running behind a devastating epidemic.
The search for new preventive tools continued. In 2005, studies reported that male circumcision could lower the risk of HIV acquisition by men in sub-Saharan Africa. Subsequent research confirmed even better news: male circumcision could cut the risk of acquiring HIV by more than half. Acting on this evidence, WHO promoted voluntary medical male circumcision as a new preventive tool with good results. Between 2008 and 2015, nearly 12 million men underwent voluntary circumcision in 14 priority countries in eastern and southern Africa.

The power of reliable data

By 2007, the HIV response had significantly contributed to better health information systems, enabling some of the best global and country-level monitoring of any major health condition. WHO and UNAIDS produced detailed annual reports on changing HIV epidemics, their social determinants, and the responses in individual countries and globally. Evidence was emerging about what worked best to reduce HIV risks, to shrink the gaps in service coverage, to step up access to life-prolonging therapy, and to reduce the number of new infections and deaths. Evidence further revealed the vibrant role that community networks and civil society initiatives played in getting services closer to people, providing home-based care, and calling loudly for better coverage with more affordable drugs.

Better data revealed additional statistics with significant programmatic implications. Preventive interventions were not reaching girls and young women. Newer data showed that, in sub-Saharan Africa, girls and young women accounted for more than 70% of all young people infected with HIV. In terms of awareness of their HIV status, more women were being tested, but men were being missed.

At the 17th International AIDS Conference held in Mexico City in 2008, WHO launched a package of priority interventions designed to help low- and middle-income countries move towards universal access to HIV prevention, treatment, care, and support. The package captured what the global AIDS response needed to deliver to reach this goal.

Using mathematical modelling, WHO scientists estimated that universal and annual voluntary testing, followed by immediate antiretroviral therapy – regardless of the clinical stage or CD4 count – could reduce new HIV infections by 95% within ten years. But that was an aspirational calculation in the realm of “ifs”. Such a dramatic shift in the approach to control would need better and cheaper drugs plus the persuasive power of a breakthrough. That, too, would come.

While some asked whether the world could treat its way out of the epidemic, others argued that renewed and intensified efforts in HIV prevention would be needed to push the epidemic into an irreversible decline. As history would prove, an epidemic as widespread, entrenched, and difficult as HIV needed both.
Dramatic leaps in treatment access

Significant court rulings in Brazil and India, aided by vocal civil society groups, opened the market for low-cost generic antiretroviral medicines. The WHO prequalification programme rigorously assessed their safety and efficacy compared with originator products, adding an important layer of quality control. The programme also kept close watch over quality standards, removed products from its list when standards slipped and updated the list, in line with WHO treatment guidelines, as safer and more effective medicines came on the market. Confidence in the quality of low-cost generics, prequalified by WHO, increased.

As the volume of low-priced generics grew, funding initiatives, like the Global Fund, PEPFAR and the Clinton Health Access Initiative, could reach significantly more people with available funds. UNITAID kicked in, first as a drug-purchasing facility and later to support innovations such as fixed-dose combination drugs, which improve patient adherence, and badly needed paediatric formulations. This support also shaped market dynamics to increase access to more affordable medicines and diagnostics. That role accelerated in 2010 when UNITAID established the Medicines Patent Pool. Together, all these initiatives contributed to a 100-fold drop in the price of antiretroviral therapy and vastly increased supplies, triggering the fastest scale up of a life-saving intervention in history.

The public health approach pushed by WHO fuelled the drive to constantly streamline and simplify recommended strategic options and technical advice. WHO also worked to ensure that the quality of services and programmes, even in very poor countries, was not compromised by cost constraints and achieved outcomes comparable to those in well-off countries. WHO took a leading role in monitoring the effectiveness and safety of recommended drugs. When evidence emerged that certain drugs showed unacceptable adverse effects, WHO moved rapidly to change treatment recommendations and call for their withdrawal.

In a most encouraging trend, evidence was emerging that adults with HIV on long-term combination therapy could reach a life expectancy comparable with that in the general population. In poor communities, what had once been a death sentence was transformed into a disease that could be managed like other chronic conditions. To capitalize on these encouraging trends, countries asked WHO to provide more detailed policy advice and operational guidance.

The threat of HIV epidemics stimulated major investments in HIV research, ranging from basic and clinical research through to implementation research and findings from the social sciences. Never before had public health benefitted from such a rapid evolution of medical science and its practical application, from better understanding of the immune system, to the development of new drugs and diagnostics, to the identification of the health behaviours and social determinants that were driving the epidemics. WHO was well-positioned to tap the best scientific data, clinical evidence and experiences from country programmes, and then translate these data into practical technical guidance adapted to resource-constrained settings. When breakthroughs occurred, which were many and frequent, WHO convened expert consultations to interpret the results and gather advice on how to reflect their significance in revised guidelines for countries.
Universal access: edging closer

As prospects for a massive scale up of treatment brightened, AIDS began to lose its status as an “exceptional” disease requiring a unique strategic approach that set it apart from other diseases. HIV could now be managed within the existing health system. The move towards a more normalized approach was formally recognized by a World Health Assembly resolution, adopted in May 2010, that called for the integration of HIV services with existing health services, including those for maternal, neonatal, and child health, reproductive and sexual health, tuberculosis, and harm reduction programmes for people who inject drugs. That resolution was followed by WHO’s global health sector strategy on HIV 2011-2016, approved in 2011.

In June 2010, WHO introduced a new treatment framework – a five-pronged programmatic approach aimed at making antiretroviral therapy more accessible, safe, effective and efficient. As a contribution to efficiency gains, the framework introduced concepts of radical simplification, standardization and cost reduction while also acknowledging the gains that come from community engagement in providing testing and treatment.

The treatment framework relied on simplified, less toxic drug regimens which could maintain therapeutic efficacy with minimal clinical monitoring. The recommended drug regimens also carried high barriers to the development of drug resistance. Asking patients to take only one pill a day – a combination of three different drugs – was a further simplification designed to improve patient adherence. WHO scientists estimated that implementation of the treatment framework could prevent 15.5 million new infections over the coming five years.

Estimated numbers of people receiving antiretroviral therapy globally and by WHO Region and percentage coverage globally, 2000-2015

Source: WHO
Breakthrough: the true power of antiretroviral therapy

In 2011, three decades after the first reports of AIDS were published, a groundbreaking trial, conducted by the US National Institutes of Health, showed that antiretroviral therapy also contributes to HIV prevention. In discordant couples, where one partner had HIV and the other did not, treatment of the person with HIV resulted in a 96% reduction in transmission to the partner. Those results were hailed as a true game-changer that would drive a revolution in the approach to prevention. At that time, sexual transmission accounted for about 80% of new infections. That breakthrough also changed the vocabulary, from references to the devastating AIDS epidemic to talk about HIV as a preventable and treatable infection.

The fact that treatment could double as prevention had two additional positive effects. First, it provided a powerful incentive for people to be tested and immediately started on therapy. Second, it changed the public face of the disease. The stigma of contagion associated with an HIV positive status lost much of its sting.

By 2012, the situation looked even more encouraging. An estimated 9.4 million people had access to antiretroviral therapy. Funding was stable, with a large share coming from domestic sources. The HIV response had pushed life-saving health services to reach formerly excluded communities, advancing efforts to achieve universal health coverage. In 2013, WHO took the next big step towards simplification by issuing its first consolidated guidelines on the strategic use of antiretroviral therapy for both prevention and treatment. The consolidated guidelines contained recommendations on what drugs to give, but also on how to deliver services to reach a maximum number of people.

At the same time, studies demonstrated people who are not infected yet face an exposure risk could block acquisition of HIV by taking antiretroviral drugs prior to exposure. In 2012, WHO made its first recommendation on using such pre-exposure prophylaxis of HIV infection as an effective additional approach to HIV prevention.

A tipping point is reached

In 2013, the epidemic reached its tipping point. For the first time in the decades-long history of this disease, the number of people newly started on antiretroviral therapy in 2013 surpassed the number of new infections. That epidemiological breakthrough was facilitated by advances on multiple fronts.

WHO recommended diversifying HIV testing approaches, including provider-initiated and community-based testing services, as a way to increase the number of people aware of their HIV status and thus able to reap the benefits of early antiretroviral therapy. More evidence emerged on the effectiveness of pre-exposure prophylaxis in different populations. Studies conducted by WHO and supported by UNITAID produced compelling evidence that pre-exposure prophylaxis...
was both effective and acceptable in key populations. In 2015, WHO recommended its use in all population at a substantial risk of HIV infection.

**The decision to integrate HIV services with maternal, child health, reproductive and sexual health services was reaping additional benefits.** In 2016, Armenia, Belarus, the Republic of Moldova, and Thailand joined Cuba as countries where the elimination of mother-to-child transmission of HIV had been validated by WHO. Belarus, the Republic of Moldova and Thailand were also validated as having eliminated mother-to-child transmission of syphilis. Cuba was the first country to achieve both milestones in 2015. In the African region, several countries with very high levels of maternal testing and treatment are currently approaching the elimination targets. Their prospects of success have been boosted by earlier diagnosis of HIV in pregnant and breast-feeding women.

Data also improved. WHO provided capacity-building support to 80 countries to enhance the collection and analysis of surveillance and programme data to measure programme performance and impact along the continuum of HIV services. That work benefitted from close collaboration with the US President’s Emergency Plan for AIDS Relief, the US Centers for Disease Control and Prevention, and the Bill and Melinda Gates Foundation.

In May 2016, the World Health Assembly adopted the Global Health Sector Strategy on HIV for 2016–2017, together with global strategies on viral hepatitis and sexually transmitted infections. These three strategies used a common framework of universal health coverage. The HIV strategy, driven by the goal of eventually eliminating the infection as a public health problem, aimed to steer the HIV response in a new direction. It emphasized the importance of embedding the HIV response in the broader public health agenda as a contribution to the target set out in the 2030 Agenda for Sustainable Development. The strategy underscored the need for countries to define an essential set of HIV interventions and services to be included in national health benefit packages, funded through national health budgets. The strategy also highlighted the need to adapt HIV services and ensure sustainable financing so that all people can access the HIV services they need without experiencing financial hardship.

**“Treat all”: ultimate simplification, ultimate fairness**

The Global Health Sector Strategy adopted the UNAIDS "90-90-90" targets for 2020 – 90% of people with HIV knowing their HIV status, 90% of those diagnosed with HIV receiving antiretroviral therapy, and 90% of people on antiretroviral therapy achieving viral suppression. In June 2016, WHO launched its "treat all" consolidated guidelines on the use of antiretroviral therapy for treating and preventing HIV infection. The guidelines hit the ground running. Close to 80 low- and middle-income countries had already adopted "treat all" policies or planned to do so within the year – a critical step towards achieving the 90-90-90 targets. WHO worked closely with ministries of health to ensure the rapid translation of the new recommendations into national policy and implementation plans.

The consolidated guidelines removed all limitations on eligibility for therapy among people living with HIV. The recommendations made all populations and groups with HIV, including pregnant
women and children, eligible for treatment. Prospects for reaching universal access improved considerably. As another contribution to simplified treatment programmes, WHO recommended the same once-per-day combination pill for all adults living with HIV, including those with tuberculosis, hepatitis and other co-infections. The recommendations were ambitious in their expected impact, yet simplified in their approach, firmly rooted in evidence, and driven by an ethical imperative.

The recommendations aimed to improve the quality of HIV treatment and to bring the world closer to the universal health coverage ideals of integrated services, community-centred and community-led health care approaches, and shared responsibility for effective programme delivery.

The treat-all recommendations marked major improvements for programmes but most especially for people, including pregnant women. Previous recommendations in 2013 called for lifelong antiretroviral therapy for all pregnant and breastfeeding women with HIV to prevent HIV transmission to babies but also to take care of women’s health. The 2016 guidelines reinforced these recommendations and promoted a life-course approach to HIV prevention and treatment, consistent with the ‘Born Free, Stay Free and AIDS Free’ framework. That framework aimed to strengthen efforts to eliminate mother-to-child transmission of HIV, scale-up paediatric treatment, prevent new HIV infections among adolescent girls, and provide treatment to adolescent girls and women.

Compared with the extraordinary increase in access to treatment, uptake of HIV testing was disappointingly sluggish. In 2015, around 40% of people infected with HIV globally were still not aware of their status and were still missing out on the enormous benefits of treatment. In guidelines issued near the end of 2016, WHO promoted the simplified new diagnostic tests that enabled people to test themselves for HIV, with results available in 20 minutes or less. Doing so was a way to both get more people started on treatment and further normalize the epidemic by reducing stigma and discrimination.

The phenomenal expansion of HIV programmes poses its own set of challenges. The large number of people now being treated makes it essential to maintain the quality of services, to ensure the most efficient use of resources, to achieve the best treatment outcomes, and to prevent the emergence of HIV drug resistance. In July 2017, WHO will launch the first Global Action Plan on HIV Drug Resistance. The plan sets out guidance that can help countries prevent and, if necessary, manage the emergence of HIV drug resistance, a risk that could threaten the remarkable gains made over the past 15 years. The plan aims to position HIV drug resistance within the broader WHO framework of tackling antimicrobial resistance.

Unstoppable momentum

The momentum is set to continue. By the end of 2016, WHO had prequalified more than 250 finished pharmaceutical products for treating HIV-related conditions, 29 active pharmaceutical ingredients, and two male circumcision devices. Since 2013, more than 100 countries have drawn on WHO technical support to develop concept notes for their Global Fund grant applications. The quality of funding applications improved, resulting in grants totalling $2 billion for country HIV programmes.
By 2017, WHO estimated that more than 18 million poor people now had access to antiretroviral therapy. In a remarkable achievement for a global health initiative, treatment coverage in eastern and southern Africa surpassed the global average.

Further expanding access to treatment is now at the heart of new “fast track” treatment targets for 2020, with the aim of ending the AIDS epidemic as a public health threat by 2030. WHO estimates that meeting the fast-track targets could prevent 1.6 million new infections and 600,000 deaths per year.

Inspired by past achievements, optimism is great that sufficient momentum can be built to push the HIV epidemic into an irreversible decline, though the road ahead is not an easy one. The encouraging global outlook conceals the many countries with a major HIV burden yet low treatment coverage. Stark inequalities mar the landscape of service access. Stigma stifles the health-seeking behaviour of marginalized groups. The yearly number of new infections, stuck at more than 2 million, is way too high for a disease that can be prevented as well as treated. In some places, the number of new cases shows a stubborn upward trend.

The fact that HIV claimed more than a million lives in 2015 is a sobering reminder of the struggle ahead. The availability of affordable and highly effective medicines makes that figure stand out even more as an ethically compelling reason to do more.
This report is available on WHO’s website
www.who.int/publications/10-year-review/en/