How does antiretroviral treatment work?

Drugs used to treat HIV, known as antiretrovirals or antiretroviral therapy (ART), prevent HIV from replicating and infecting new immune system cells in the body. ART therefore reduces the levels of HIV in an individual’s body to extremely low levels as well as preventing damage to his or her immune system. In contrast, when HIV is left untreated, it is the depletion of immune function that leaves the body vulnerable to a wide range of infections and which eventually leads to serious illness and death.

Individuals who are diagnosed soon after HIV infection and begin ART without delay are able to remain in good health for decades, with a life expectancy similar to that of people who don’t have HIV. However, for many people without good enough access to high quality health services, this potential has yet to be realised.

Global uptake of treatment

In 2017, it was estimated that 79% of adults who knew their status were receiving treatment. This is a dramatic increase from 2014 when only 41% of adults and 32% of children living with HIV were receiving ART. The number of people on treatment has increased from 7.5 million people in 2010 to 21.7 million people in 2017.

Men are less likely than women to receive treatment; children and adolescents are also underserved. In 2017 it was estimated that less than half of those under 15 were receiving antiretroviral treatment. Although the availability of treatment has improved in all parts of the world, the proportion of people living with HIV receiving ART varies considerably between regions. There are particular gaps in low- and middle-income countries, especially those in Eastern Europe and the Middle East.

However, as the burden of HIV is concentrated in a few key countries, improvements in the
availability of treatment in specific countries can have a significant impact on the overall global situation. For example, South Africa has the largest population of people living with HIV in the world (7.2 million). A radical turn-around in its government’s health policy resulted in the number of South Africans receiving treatment jumping from 4,000 to over 4 million between 2000 and 2017. The country now has the largest HIV treatment programme in the world.

Globally, 61% of all people with HIV live in just ten countries – South Africa, Nigeria, India, Kenya, Mozambique, Uganda, Tanzania, Zimbabwe, the United States of America, and Zambia. While this means that efforts can be focused, these are mostly low-income countries, adding to the challenge.

<table>
<thead>
<tr>
<th>Year</th>
<th>People Living with HIV</th>
<th>People Receiving Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>28.9 million</td>
<td>770,000</td>
</tr>
<tr>
<td>2005</td>
<td>31.8 million</td>
<td>2.2 million</td>
</tr>
<tr>
<td>2010</td>
<td>33.3 million</td>
<td>7.5 million</td>
</tr>
<tr>
<td>2013</td>
<td>35.2 million</td>
<td>13 million</td>
</tr>
<tr>
<td>2014</td>
<td>35.9 million</td>
<td>15 million</td>
</tr>
<tr>
<td>2015</td>
<td>36.7 million</td>
<td>17 million</td>
</tr>
<tr>
<td>2016</td>
<td>36.7 million</td>
<td>19.5 million</td>
</tr>
<tr>
<td>2017</td>
<td>36.9 million</td>
<td>21.7 million</td>
</tr>
</tbody>
</table>

Source: UNAIDS Data 2018

**Ambitious targets and guidelines**

Despite rapid progress, the Joint United Nations Programme on HIV and AIDS (UNAIDS) and the World Health Organisation (WHO) have set global targets that are far more ambitious.

**90-90-90 targets**

UNAIDS is encouraging countries to work towards targets known as 90-90-90. The aim is that by 2020, 90% of all people living with HIV will know their status, 90% of those diagnosed will be on treatment, and 90% of those on treatment will be virally suppressed (where the level of HIV in the blood is below 200ml, indicating successful treatment). This would mean that 73% of the global population of people living with HIV would be virally suppressed by 2020. If this is achieved, then models predict the end of HIV as an epidemic disease by 2030.
Avert.org

**Current guidelines**

Consistent with those targets, the World Health Organisation now recommends that everybody living with HIV, of all ages and in all parts of the world, should receive antiretroviral therapy.\(^{12}\)

Previously, guidelines were more cautious, only recommending treatment to certain groups - for example, individuals with a more depleted immune system (as shown by clinical symptoms or a lower CD4 cell count), people with tuberculosis co-infection or pregnant women who needed to prevent transmission to an unborn child. However the evidence of the benefit of prompt HIV treatment for all has now become overwhelming. Studies have conclusively demonstrated that delaying HIV treatment\(^{13}\) and taking breaks\(^{14}\) from HIV treatment results in greater morbidity and mortality. Research has also shown that effective HIV treatment prevents onward transmission to sexual partners\(^{15}\) and unborn children.

The guidelines have therefore become simpler. WHO recommends that all people living with HIV should begin antiretroviral therapy as soon as possible after diagnosis and continue to take it indefinitely. These ‘treat-all’ guidelines mean that assessment of an individual’s clinical stage or CD4 cell count is not required before initiating HIV treatment.

Nonetheless in situations where resources prevent full implementation of the guidelines, treatment should be prioritised for individuals with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and individuals with a CD4 cell count below 350 cells/mm\(^3\). This is to ensure that people who urgently need treatment are not displaced by people whose need is less pressing.

The AIDSFree Guidance Database details current HIV testing and treatment guidelines for many
Achieving the targets

These changes to the treatment guidelines have called for a dramatic scale up of HIV treatment programmes. It is thought that with the adoption ‘treat all’ approach almost 37 million people will need access to antiretroviral therapy.

Over the last year more and more countries have updated their national guidelines to recommend treatment for all, and as of November 2017, 70% of low- and middle-income countries had adopted the new ‘treat all’ guidelines (compared to just 33% in 2016).

However implementation of these guidelines has been slower. At the end of 2017 only 69% of low- and middle-income countries had put the guidelines fully into practice, at all treatment sites.

Global challenges

Funding

With the global burden of HIV concentrated in low and lower-middle income countries, funding from international donors has been essential to the scale-up of HIV treatment. The contribution of the American government, primarily channelled through the President’s Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund to Fight AIDS, Tuberculosis and Malaria, has been particularly important.

A rapid scale-up of international funding from $1.2 billion in 2002 to $7.8 billion in 2008 allowed many countries’ treatment programmes to expand in that period. But international donors have curtailed or capped their contributions since the 2008 financial crash. With $8.6 billion provided in 2014, funding is little different to that available six years earlier. A scale-up in line with either WHO treatment guidelines or UNAIDS’ 90-90-90 targets is extremely challenging in this context.

In response, funding from domestic governments has become increasingly important for HIV programmes in many countries. By 2014, domestic funding comprised about 57% of total resources available for HIV programmes in low- and middle-income countries. In the five previous years, 84 countries increased their domestic spending on AIDS, including 35 which more than doubled it.

Such shifts are dependent on countries’ economic growth and on political leadership. In too many countries, leaders are unwilling to fully support HIV programmes or they limit their support to specific elements. Provision for key affected populations such as sex workers or people who inject drugs is often seen as politically unpalatable.

Drug prices and generics

While staffing and infrastructure costs are important, the biggest single element influencing the affordability of HIV treatment programmes is the price of antiretroviral drugs. Generic manufacturers now supply more than 95% of all ARVs in low- and middle-income countries, at a cost of less than US$ 150 per person per year for a person’s first treatment regimen. But if a person needs to switch to an alternative regimen, its price may be around $300 a year and third-line regimens (rarely available from generic manufacturers) may cost 15 times more than the standard first-line regimen. Further patent restrictions and a weakening of competition from generic manufacturers could restrict access to newer medicines.

Moreover economic growth in many countries may move them into the middle-income bracket, meaning that they are no longer permitted to use generic drugs and may also become ineligible for
The effective scale-up of HIV treatment is made more challenging by weak health services and health systems in many countries. In places where health services are difficult to access, understaffed or poorly organised, uptake of testing and treatment is suboptimal, with too many people dropping out of care when faced with difficulties.

A very concrete example is stock-outs, when antiretrovirals or other medical supplies cease to be available in clinics. Poor planning, forecasting and budgeting; delivery delays; and corruption are described as the most common reasons for stock-outs. When stock-outs occur, individuals may simply take a forced break from their treatment and wait for supplies to be replenished, risking the development of drug resistance, treatment failure and a switch to a more expensive drug combination.

Civil society movements have been vital in placing HIV high up on the public health agenda and in finding solutions to challenging problems. Further pressure from civil society may be needed for the next scale-up of treatment to be achieved.

To look at an historical example, South Africa’s treatment access movement linked street protests and community activism with court challenges and high-level lobbying. Campaigners focused on social justice and linked with activists across the world, ultimately achieving a relaxation of intellectual property restrictions. Campaigning eventually led to a change in the South African government’s approach to HIV and the world’s largest HIV treatment programme.

Activism has also spurred innovations in the health sector. For example, ‘task-shifting’ involves redistributing human resources so that, for example, a nurse rather than a doctor initiates patients on antiretroviral therapy. This means that shortages of qualified doctors do not stop people from receiving treatment as nurses can be trained for specific tasks and are less costly.

People living with HIV have also been involved in delivering care to their peers – sometimes as a counsellor, but sometimes with a more extensive role. For example rather than requiring patients to make a lengthy visit to the clinic each month, they may be seen in between clinic visits by a trained peer who assesses adherence and conducts basic health checks, referring patients to the clinic in the case of any abnormalities. In southern Africa, patients who are stable on therapy sometimes form groups in which members distribute medication to each other.

Such projects particularly respond to the challenge of an ever increasing number of people who are stable on HIV treatment and will need an ongoing supply of ARVs for the rest of their lives. Without innovation, they will fill up existing health facilities and reduce capacity for patients who are unwell or newly diagnosed.

‘Decentralisation’ of HIV care to a wider range of health services can also make HIV treatment more accessible. HIV treatment may be integrated with services for tuberculosis, maternal and child health, hepatitis, or other health conditions. For example South Africa made ART available at virtually every public health facility in the country.
Improving the efficiency of treatment services will mean that more patients can be treated for the same financial resources. Wide variations in the cost of providing treatment between facilities demonstrate that some facilities are less efficient whereas others may be benefiting from economies of scale (providing ART to more patients while fixed costs remain the same) or economies of scope (integrating ART delivery with other health services). Other efficiency gains are possible through improving procurement systems so as to lower the cost of commodities and introducing new technologies (such as point-of-care diagnostic tests).

Addressing stigma and discrimination

Finally, addressing the stigma and discrimination faced by people living with HIV – especially that which occurs in health services - may encourage more people to test and to start treatment. Many people living with HIV, especially those who belong to key populations such as people who use drugs or men who have sex with men, report stigmatising attitudes from health workers which discourage them from using health services. Revising laws which discriminate against key populations, protecting the rights of people living with HIV and making legal services available so that people can seek redress may ultimately have an impact on the uptake of antiretroviral therapy.

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