

# An HIV breakthrough in a moment of crisis

## How can we seize this historic opportunity?



### The world's HIV response at a tipping point

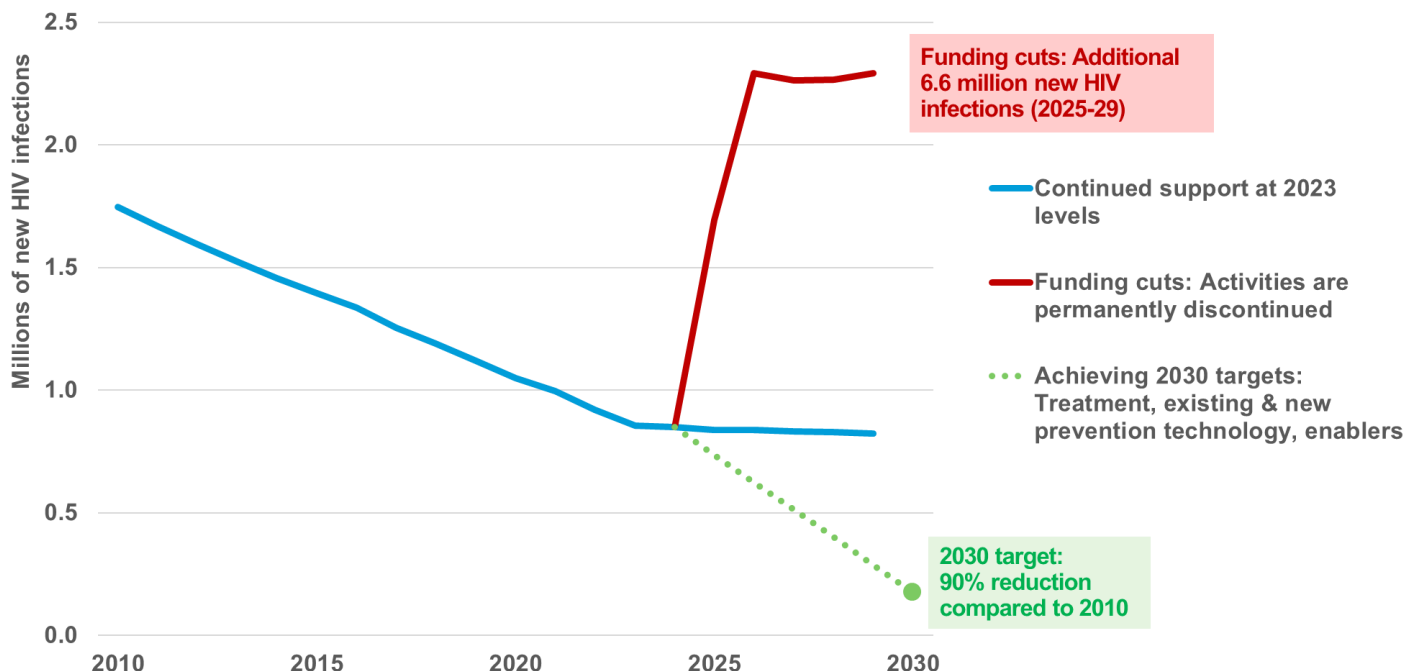
The chances of ending AIDS as a public health threat hang in the balance—between a dramatic reversal of gains if the HIV response is defunded and seizing the huge new opportunity of long-acting injectable HIV prevention.

Decades of hard work, innovation and solidarity have reduced the number of people acquiring HIV to the lowest point in almost three decades. Even then, about 1.3 million people acquired HIV in 2023—much more than the global target of 200 000 new HIV infections in 2030 that would put the world on-track to control the pandemic.

Even optimistic projections forecast that, unless remedied, funding losses would lead to steep rises in the numbers of people acquiring HIV: 6.6 million additional new HIV infections across 55 countries in the next five years, according to one study (Figure 1),<sup>1</sup> and between 4.4 million and 10.7 million new HIV infections in low- and middle-income countries by 2030, according to another.<sup>2</sup> That would erase 20 years of hard-won progress.<sup>3</sup>

Long-acting injectable HIV prevention has shown exceptional efficacy of **95-100%** but can the world translate that into actual public health impact -- quickly, fairly and on a large-enough scale?

**Figure 1. New HIV infections: Trends and projections for three scenarios (55 countries, 2010–2029)**



Source: UNAIDS estimates and projections from Avenir Health April 2025

<sup>1</sup> UNAIDS estimates and projections from Avenir Health April 2025. See also [https://www.unaids.org/sites/default/files/2025-04/JC3144\\_Estimates\\_Funding\\_cuts\\_impact\\_En.pdf](https://www.unaids.org/sites/default/files/2025-04/JC3144_Estimates_Funding_cuts_impact_En.pdf)

<sup>2</sup> For the lower estimate, countries mitigate the impact; for the higher estimate, no such mitigation occurs.

<sup>3</sup> Brink DT, Martin-Hughes R, Bowring AL, Wulan N, Burke K, Tidhar T, et al. Impact of an international HIV funding crisis on HIV infections and mortality in low-income and middle-income countries: a modelling study. *Lancet HIV*. 2025 Mar 26:S2352-3018(25)00074-8. doi: 10.1016/S2352-3018(25)00074-8.

# Long-acting injectables: an exciting breakthrough for HIV prevention

The disparate needs and circumstances of people at risk of HIV acquisition mean that no single prevention approach will suit everyone.

Condoms, for example, work well for some people and situations, but not for others. Oral PrEP is safe and very effective for those who can adhere to pill taking. The monthly dapivirine vaginal ring is a preferred option for some women, as is voluntary medical male circumcision for many men in countries with a high burden of HIV, while clean needles, syringes and opioid agonist treatment are highly effective for people who inject drugs. Long-acting prevention injectables offer solutions for the many people who struggle to protect themselves from HIV and need more convenient and discreet prevention options.

These new long-acting antiretrovirals are highly effective at preventing HIV infection. Hailed by *Science* magazine as one of the “scientific breakthroughs of 2024”, Lenacapavir has been shown to be almost 100% effective in preventing HIV with injections just twice a year.<sup>4</sup> Cabotegravir, another long-acting injectable which is administered once every two months, is already available in some countries.

If long-acting tools like Lenacapavir are made affordable and accessible to the people who need them most and policy barriers are removed to enable that access, they could steeply reduce new infections in communities who are at very high risk of acquiring HIV.

The [Gears of Lenacapavir for PrEP Rollout](#) report outlines this transformative opportunity in greater detail and shows how we can make the most of it.

## The crushing impact of funding cuts

The deep cuts applied to overseas development assistance for HIV put this huge opportunity at risk.<sup>5</sup>

Sudden funding losses in early 2025 have left the prevention programmes of dozens of low- and middle-income countries in crisis. Countries have been increasing their domestic funding and shifting their HIV programmes to more sustainable models. But the abrupt loss of support from overseas development assistance for HIV is upending those processes—and jeopardizing prevention efforts.

### Long-acting PrEP: facts and science

**Long-acting antiretroviral drugs Lenacapavir (LEN) and Cabotegravir (CAB-LA) may be the most exciting HIV prevention tools in decades.**

**High efficacy:** Six-monthly injections of LEN have shown exceptional efficacy in preventing HIV acquisition: 100% efficacy among adolescent girls and young women in the PURPOSE 1 trial in South Africa and Uganda, and 96% efficacy among cisgender men and transgender men and women in the PURPOSE 2 trial in Argentina, Brazil, Mexico, Peru, South Africa, Thailand and the United States. CAB-LA was also highly efficacious and 79% more effective than oral PrEP.

**Safe and well-tolerated:** LEN and CAB-LA are safe and well-tolerated, including during pregnancy.

**Long-lasting protection:** Providing six months (LEN) or two months (CAB-LA) of continuous HIV protection. A once-yearly version of LEN, a four-monthly version of CAB-LA and a once-monthly oral PrEP are being trialed.

**Even with “business as usual”, the number of people living with HIV and requiring lifelong treatment—almost 40 million in 2023—will continue to grow. Funding losses are likely to lead to even higher numbers. This is not sustainable.**

<sup>4</sup> The manufacturer, Gilead, released the encouraging results of the pharmacokinetics and safety of a Phase I trial of the 12-month lenacapavir formulation for prevention (administered intramuscularly) in March 2025. See: Jogiraju V, Pawar P, Yager J, Ling J, Shen G, Chiu A, et al. Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study. *Lancet*. 2025 Apr 5;405(10485):1147-1154. doi: 10.1016/S0140-6736(25)00405-2. Epub 2025 Mar 11.

<sup>5</sup> Jogiraju V, Pawar P, Yager J, Ling J, Shen G, Chiu A, et al. Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study. *Lancet*. 2025 Apr 5;405(10485):1147-1154. doi: 10.1016/S0140-6736(25)00405-2.

In the current geopolitical and fiscal context, increased funds for HIV—whether domestic or external—may not be a realistic prospect for many low- and middle-income countries. Worse, to keep their HIV treatment programmes running, countries may feel compelled to *reallocate* funding from prevention and community systems to antiretroviral treatment. Doing so risks degrading their prevention efforts. The current funding cuts have already severely disrupted access to oral PrEP in low- and middle-income countries. Oral PrEP, daily pills that prevent HIV transmission, were used by only about 2.8 million people in 2023—far fewer than the estimated annual need of approximately 20 million.<sup>6</sup>

**Maintaining treatment programmes is a clear priority everywhere. But treatment alone will not overcome the AIDS pandemic. Primary prevention and the removal of barriers to prevention are crucial.**

The new long-acting PrEP versions are easier to use and show even greater efficacy than oral PrEP. They could catapult HIV prevention forward—if they are universally available and affordable, their roll-out is fully financed, and regulatory and structural barriers are removed. But PrEP programmes have suffered significant setbacks in recent months.<sup>7</sup>

Affordable pricing will be essential and feasible. Progress has been made, but the financing challenge looms large. The Global Fund and the United States President’s Emergency Plan for AIDS Relief (PEPFAR) announced their intention to finance the roll-out of Lenacapavir for two million people over three years. For economies of scale, even larger volumes are needed, which will require middle-income countries to be part of a provision arrangement.

## Prevention is essential for sustainability

HIV prevention efforts are in transition—evolving from fragmented, short-term projects to integrated, nationally owned programmes.<sup>8</sup> Countries are working hard to take ever-greater ownership of their HIV programmes by turning donor-reliant programmes into self-sustaining ones. But that process requires time and continued collaboration and solidarity during their transitions.



In the current geopolitical and fiscal context, large increases in domestic HIV funding are not realistic options for many lower income countries. Several countries will need external support to sustain and transition their HIV programmes.

Given the financing context, the roll-out will have to prioritize populations and places where the risk of acquiring HIV is very high. For example, for young women who struggle to consistently negotiate condom use, key populations in countries where they face criminalization, replacing pills with periodic injections can offer the autonomy they need to stay safe from HIV.

And finally, these new technologies should not be seen as a quick fix for weak prevention efforts. To work best, they need well-functioning HIV programmes and capable health and community systems.

<sup>6</sup> Beyrer C. The global HIV/AIDS pandemic: where are we now? Abstract 17. Conference on Retroviruses and Opportunistic Infections, San Francisco, 9–12 March 2025.

<sup>7</sup> For more information, see: Impact of PEPFAR Stop Work Orders on PrEP, which outlines disruptions to global PrEP programming (<https://www.prepwatch.org/pepfar-stop-work/>).

<sup>8</sup> Mutale W, Semeere A, Bukusi EA, Ojji D, Venter F, Odeny T, et al. How can Africa sustain its HIV response amid US aid cuts? *Lancet HIV*. 2025 Mar 20:S2352-3018(25)00071-2. doi: 10.1016/S2352-3018(25)00071-2. Epub ahead of print.

# A call to action: Expand access to HIV prevention options

## The challenge

Where we are:	1.3 million new HIV infections per year
Where we should be:	Fewer than 200 000 new HIV infections in 2030

## The historic opportunity

Change the trajectory of the HIV epidemic by boosting access to prevention tools that work, including new long-acting tools.

Ensure that 20 million people access antiretroviral-based prevention options by 2030 (as an additional option to existing effective, lower-cost prevention and harm reduction choices).

## Now is the time to act

### Countries can

- Develop truly country-led and well-prioritized, sustainable HIV prevention plans in 2025 and evolve them from fragmented projects to integrated, nationally owned programmes.
- Roll out long-acting PrEP as part of a prevention package that includes oral PrEP and lower-cost, effective options—thereby getting the most out of limited resources and catering to people’s different preferences and shifting needs.
- Sustain investments in condoms and other self-care products by using “total market” approaches.
- Create an enabling legal and policy environment to ensure people most affected can access HIV prevention.
- Make HIV prevention more accessible outside the health sector including through multisectoral government and private sector activities.

### Funding partners can

- Support a phased transition to sustainability that will achieve impact (instead of abrupt defunding).
- In their own interest, sustain investment in HIV prevention for most-affected populations in low- and middle- income countries: a pandemic cannot be stopped only in some countries.
- Reinvest savings from declining HIV commodity prices in prevention programming to ensure 2 million people are using long-acting PrEP by 2027, and provide support to countries, including through the Global Fund and technical partners.

### Communities and civil society can

- Actively promote access to and use of highly effective HIV prevention options.
- Lead in the development of trusted access programmes for key populations, young people and women, and work to remove barriers to access.
- Identify gaps and advocate for equitable access to all context-relevant HIV prevention options, including new long-acting PrEP.

### Technical partners can

- Support granular data collection and analysis to develop prevention needs estimates and an optimal mix of prevention options.
- Engage countries and draw on country experiences to reimagine prevention. Provide guidance, tools and technical support to develop programmes; build demand; and use new delivery strategies to achieve sustained access to prevention options.
- Work with governments, industry and communities to ensure affordability, licensing and rapid regulatory approval in countries, as well as the inclusion of new prevention options as part of Universal Health Coverage.