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Global HIV control: is the glass half empty or half full?

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Abstract

The massive scale-up of HIV treatment and prevention over the past two decades has resulted in important reductions in new infections and mortality globally. Reduction in HIV incidence, however, has been unequal, with worsening epidemics in regions where the reach and scale of HIV control programmes have been insufficient, especially in eastern Europe, central Asia, the Middle East, north Africa, and Latin America where HIV epidemics are concentrated among key populations, including people who inject drugs, men who have sex with men, transgender people, and some minority racial and ethnic groups. The global state of the HIV pandemic highlights disparities in HIV control efforts and provides a roadmap for what should be done, including investment to better implement the effective HIV prevention and treatment tools that are available, but whose adoption and scale-up are not yet sufficient to get us close to an AIDS-free generation. To achieve the full potential of global HIV control, we call for urgent, evidence-informed implementation at scale of our existing and novel HIV prevention and treatment strategies in ways that are better, faster, more efficient, and cost-effective, especially in key populations and regions where the HIV pandemic continues to expand.

Introduction

The HIV pandemic and its consequences have caused over 40 million deaths since it was first recognised over 40 years ago. Despite the many successes in HIV prevention and treatment, global efforts to control the pandemic are in jeopardy. In 2021, an estimated 1.5 million adults and 160 000 children became infected with HIV and 552 000 adults and 98 000 children died.^{1,2} 38 million adults and 1.7 million children younger than 15 years have HIV. The negative effects of HIV on individuals, health-care systems, communities, economics, and politics, are felt in nearly every society globally. The early optimism for controlling the HIV pandemic that arose from advances in diagnostics, treatment, and prevention of HIV has been tempered by the continued spread of the virus and the challenge of providing lifelong antiretroviral therapy (ART) and supportive care to a very large number people with HIV. Global ART service scale-up increased from coverage of under 1.0 million people with HIV in 2000 to 7.5 million in 2010; due to concerted effort, commitment, and funding from multilateral, bilateral, and domestic sources, the number of people with HIV on ART increased to 28.7 million in 2021. Consequently, a staggering 16.5 million HIV-related deaths were averted between 2001 and 2021.^{1,2} In 2022, over US\$18 billion was allocated for HIV treatment and prevention, mostly in low-income and middle-income countries (LMICs), from the United States President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund Against AIDS, Tuberculosis and Malaria (GFATM).^{3,4} To control the HIV pandemic, the 2030 UNAIDS 95-95-95 targets specify that 95% of all people with HIV should know their HIV status, 95% of all people with diagnosed HIV infection should be on ART, and 95% of all people receiving ART should have

viral suppression. These 2030 UNAIDS targets note that there is considerable room for improvement to achieve these goals.¹

Some countries have responded to these goals more effectively than others. The good news is that massive ART scaleup worldwide has resulted in effective HIV treatment as prevention causing a 45% decline in mortality since 2010 and a large reduction in HIV transmission.^{1,2} Globally, the estimated number of new HIV infections in 2021 was 54% lower than in 2001. The greatest effect of ART scale-up was observed in sub-Saharan Africa, which has the largest number of people with HIV worldwide (roughly 60% of the world's total). From 2010 to 2021, the number of new HIV infections in sub-Saharan Africa decreased by about 40%. However, the number of new infections increased alarmingly by 33% in eastern Europe and central Asia, where the epidemic is concentrated in people who inject drugs. During the same period, new HIV infections increased by 27% in the Middle East and north Africa and by 11% in Latin America (figure 1).^{1,2} In western and central Europe, although there have been declines in new diagnoses over the past decade, incident cases of AIDS more than halved, with an estimated one in eight people with HIV remaining undiagnosed. In the UK, 20% of people with HIV have a transmissible viral load and an estimated 25% of these people are undiagnosed.¹ Meanwhile, new HIV infections have decreased by 16% in the USA since 2010 (but only 3% since 2016).

Global disparities in response

Sub-Saharan Africa has been substantially more successful in achieving HIV treatment targets among adults than eastern Europe and central Asia (figure 2A–C),^{1,2} due to successful HIV prevention and treatment programmes among people with HIV and their sexual partners. As of 2022, several GFATM or PEPFAR-supported countries in sub-Saharan Africa (eg, Burundi, Botswana, Eswatini, Malawi, Namibia, Rwanda, and Zimbabwe) have neared or achieved the UNAIDS 95-95-95 treatment targets. Botswana was the first country to be certified by WHO as reaching the agency's silver level of achievement on the path to elimination of HIV, with documented ART coverage of more than 95% among pregnant women in 2021 (up from 77% in 2010) and a mother-to-child transmission rate of 2.2% in 2022 (down from 40% in 1999).^{1,2} Successful ART outcomes among adults in African nations were attributed to public health approaches, such as comprehensive and innovative systems for community outreach, including rapid ART initiation; differentiated service delivery models of HIV care; roll-out of voluntary medical male circumcision that reduces the risk of female-to-male HIV transmission by about 60%; and high levels of commitment from national leaders and international funders.^{3–6} However, obstacles to optimal HIV control in sub-Saharan Africa persist. These obstacles include demographics (eg, 90% of global paediatric HIV infections still occur in sub-Saharan Africa), and persistent gaps in HIV testing among children compared with adults (59% in children *vs* 86% in adults), ART coverage (52% in children *vs* 76% in adults), and HIV viral suppression (41% in children *vs* 70% in adults).^{1,2} Furthermore, HIV incidence in sub-Saharan Africa is still three-times higher among adolescent girls and young women (aged 10–24 years) compared with boys and young men (aged 10–24 years). Additional challenges include economic factors, socio-cultural barriers, and political issues, in particular poverty, stigma, and criminalisation of LGBTQ+ people and lifestyles (table).^{1,2} Data from 65 South African primary care

clinics showed that ART provision was generally maintained during the 2020 COVID-19 lockdown. HIV testing and ART initiation decreased by 46.2% during the first week of lockdown; however, as restrictions eased, these services returned to before-lockdown levels.⁷ The resilience of ART programmes despite the COVID-19 pandemic indicates that the infrastructure and operations are strong and resilient, but they should still be expanded to currently underserved populations.

In contrast to sub-Saharan Africa, the HIV epidemic in eastern Europe and central Asia has continued to expand, reflecting structural impediments to evidence-based HIV prevention, the substantial stigma and discrimination towards people who inject drugs, suboptimal political leadership, and low domestic investment in national HIV responses across much of the region (figure 1). Regional trends are strongly influenced by Russia, which is home to 70% of the people with HIV in the region.¹ Russia has banned the distribution of sterile injecting equipment and opioid agonist therapies such as methadone and buprenorphine, which are essential tools for controlling HIV epidemics concentrated in people who inject drugs.^{8,9} Furthermore, the ongoing armed conflict has disrupted the provision of testing, prevention, and treatment services in Ukraine.^{1,9} Also, the growing HIV epidemics among LGBTQ+ individuals are understudied and unrecognised by several national HIV responses in eastern Europe and central Asia. Russia legislatively banned engagement by governmental and non-governmental agencies with the LGBTQ+ community as they viewed this as promoting homosexuality, with other eastern European and central Asian countries now considering similar legislation. Political, legal, and technical barriers in many national HIV programmes are delaying or preventing the use of new, innovative HIV control approaches and tools. The unique potential of community outreach organisations must be enhanced to reach marginalised populations heavily affected by the epidemic (table).

In the Middle East and north Africa, the HIV epidemic is largely hidden, despite a 20% increase in HIV incidence over the past decade (figure 1, figure 2D).^{1,2} New HIV infections are largely occurring among populations that face high levels of stigma, discrimination, and criminalisation, such as men who have sex with men and people who inject drugs. Almost two-thirds of new HIV infections in this region were in Egypt, Iran, and Sudan. Special efforts are now needed to expand and improve access to HIV testing and to treatment and prevention programmes, including pre-exposure prophylaxis (PrEP) for these populations at high risk.

In Latin America, no countries have reached the 2020 UNAIDS 90-90-90 targets (figure 2E).^{10,11} In most of this region, the HIV epidemic remains concentrated in large urban centres and in vulnerable populations, with men who have sex with men and transgender people having the highest burden.^{1,2} Between 2016 and 2020, HIV prevalence in the region was estimated at 13.9% for men who have sex with men and 25.9% for transgender people, with differences among and within countries.^{12,13} Barriers to HIV control include inadequate access to HIV services that are not decentralised, stigma, discrimination, and human rights violations (table). The HIV continuum of care in Latin American countries has slowly improved, including expanded ART coverage, which has resulted in modest decreases in AIDS-related mortality, but retention in care efforts have been thwarted by highly centralised treatment services. However, over a third of people with HIV are still

diagnosed with advanced HIV infection, and AIDS-related conditions remain the leading causes of death among this group. Despite high PrEP awareness and willingness to use it, its adoption and scale-up is suboptimal and access and availability are generally low. This region represents only 10% of PrEP users globally, most of whom are in Brazil, which has the largest PrEP programme.

In the USA, continued challenges for HIV diagnosis, treatment, and prevention include barriers at the societal, health-care system, and individual levels, such as stigma, racism, fragmented care, housing and food insecurity, poverty, mental illness, and substance use (table).¹⁴ Major health inequities result in HIV bearing a disproportionate effect on specific US populations and, despite considerable resources, HIV prevention and treatment programmes do not adequately reach the most vulnerable groups, such as men who have sex with men, people who inject drugs, transgender people, and minority racial or ethnic groups. The proportion of people with HIV who are members of minority racial or ethnic groups represents an increasing share of all people with HIV and of people newly diagnosed with HIV. Although African Americans represent only 13.6% of the US population, 45% of all HIV-associated deaths occur in this population, the highest of all sub-groups.¹ Further, the intertwined opioid and HIV epidemics have the potential to undermine several years of successful prevention. Mitigating these large health disparities and reducing drug epidemics through scale-up of opioid agonist therapies and syringe services programmes are essential for further control of HIV.¹⁵

In 2019, a new US HIV strategy was launched to reduce infections by 75% in 5 years and by 90% in 10 years, termed *Ending the HIV epidemic: a plan for America*. This plan is based on early diagnosis, rapid and effective treatment, multipronged prevention, and outbreak response.¹⁴ The provision of HIV care in the USA, however, is dependent on medical insurance status and health-care access. To address this gap, the Ryan White HIV Program provides a comprehensive system of primary HIV medical care, medication, and essential support services to people with HIV, including a specific focus on health equity, addressing social determinants of health, and supporting community needs. In 2020, 89.4% of those who received continuous HIV care through the Ryan White HIV Program had suppressed HIV viral loads, compared with 65.5% of patients receiving care outside of the programme (figure 2F). Ryan White services, however, are not fully accessible to all who need them, especially in rural settings. Innovative approaches like the Ryan White HIV Program, which provide wrap-around services and whole person care, need expansion to many more people with HIV if we are to succeed in further reducing HIV deaths and transmission in the USA.

HIV prevention gap

Globally, there is an urgent need to address the HIV prevention gap arising from underuse of PrEP and the challenges associated with long-term adherence to both PrEP and ART. Intramuscular injections of long-acting cabotegravir and long-acting rilpivirine are a novel ART combination approved for use as a fully suppressive regimen for people with HIV (table) by the US Food and Drug Administration and other regulatory agencies in high-income countries and a few LMICs.^{16–19} Long-acting cabotegravir and rilpivirine ART has substantially reduced the required dosing frequency from once daily to monthly or

bimonthly injections, resulting in low (<2%) virological failure rates in clinical trials.²⁰ However, data from real-world clinical experience of long-acting cabotegravir and rilpivirine are needed and demonstration projects that include populations at risk for poor ART adherence are ongoing.^{21–23} Long-acting cabotegravir alone is approved for PrEP in a variety of populations after confirming its superiority relative to oral PrEP.^{24,25} The effectiveness of long-acting cabotegravir as PrEP outside of high-income settings will be challenging to evaluate due to its prohibitive annual cost (US\$22 200), over 185-times higher than the \$60–119 estimated cost-effectiveness threshold for LMICs.²⁶ Following civil society pressure, ViiV Healthcare provided access to generic versions of ART medication in 90 countries with the Medicines Patent Pool, including all African nations. However, a real challenge is expanding access to many other LMICs outside Africa, where the HIV epidemic is continuously expanding. Therefore, for long-acting cabotegravir to have a significant global impact on the HIV pandemic, its affordability needs to be expanded to all in need.²⁷ WHO added long-acting cabotegravir to its HIV prevention guidelines in July, 2022, but combined long-acting cabotegravir and rilpivirine has not been added to its global antiretroviral treatment guidelines, perhaps partly due to cost considerations.²⁸

Conclusion

In summary, the early successes in scale-up of HIV treatment and prevention, which changed the global inflection point on HIV-related mortality and transmission, have slowed in the past 10 years, with unequal progress depending on the geographic setting, at-risk population, or demographic groups. Although current projections and the absence of an effective HIV vaccine and cure do not support the possibility of complete HIV eradication in the near future,^{29,30} new HIV infections can be reduced in African countries and other regions with an increased focus on sustainable HIV treatment and prevention services. Whereas several tools for HIV prevention and treatment are effective, their adoption and scale-up has been inadequately implemented in some regions and for some populations, especially those who experience social and health inequities that make effective implementation challenging.³¹ Our future efforts should be reinvigorated through the expansion of targeted strategies that can be effectively implemented in each context, especially for those at increased risk for health inequities. In our vision for the future, we call on public-health and political leaders to urgently intensify global efforts to scale-up safe, convenient, and effective options for ART (including for pregnant women, children, and hard to reach populations); expand access to syringe services programmes to support safer injection practices and opioid agonist therapies that are key to controlling the HIV epidemic among people who inject drugs; implement a range of combination prevention strategies, including PrEP; and continue research towards an effective HIV vaccine and a durable ART-free method for immune control of HIV. Guided implementation of these evidence-based strategies should more quickly reach a larger number of individuals with or at risk for HIV, work better than the current strategies, and remain cost-effective. With evidence-based, generalisable, and cost-effective patient-based and community-based innovative HIV/AIDS programmes, implemented and sustained at scale and for all affected populations, including in sub-Saharan Africa where the largest number of people with HIV reside, through compassionate and effective leadership, the world could finally realise its

full potential to reduce HIV incidence and the human burden of HIV. Without unwavering commitment to achieve this goal, the glass will remain half empty for too many people with HIV and for those at risk of HIV long into the future.

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Declaration of interests

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Search strategy and selection criteria

We searched PubMed using MeSH. We focused on HIV-related terms (MeSH terms “HIV infections” and “HIV”). We used a person keywords search to capture specific populations that included “adolescent”, “adult”, “children”, and “pregnant women” AND “global epidemiology”. The term AND was used to combine the HIV and persons search. We sorted results by region. We added terms about key populations, health equity, and health disparities with a focus on HIV prevention, testing, and antiretroviral treatment (MeSH terms “anti-retroviral agents”, “antiretroviral therapy”, “highly active”, “Anti-HIV agents” including sub-headings on “therapeutic use”, “therapy”, and “control”). We reviewed articles that were published in English from database conception until December, 2022. Authors also recommended specific articles to review. The final reference list was generated based on originality of the articles and relevance to the broad scope of this Viewpoint.

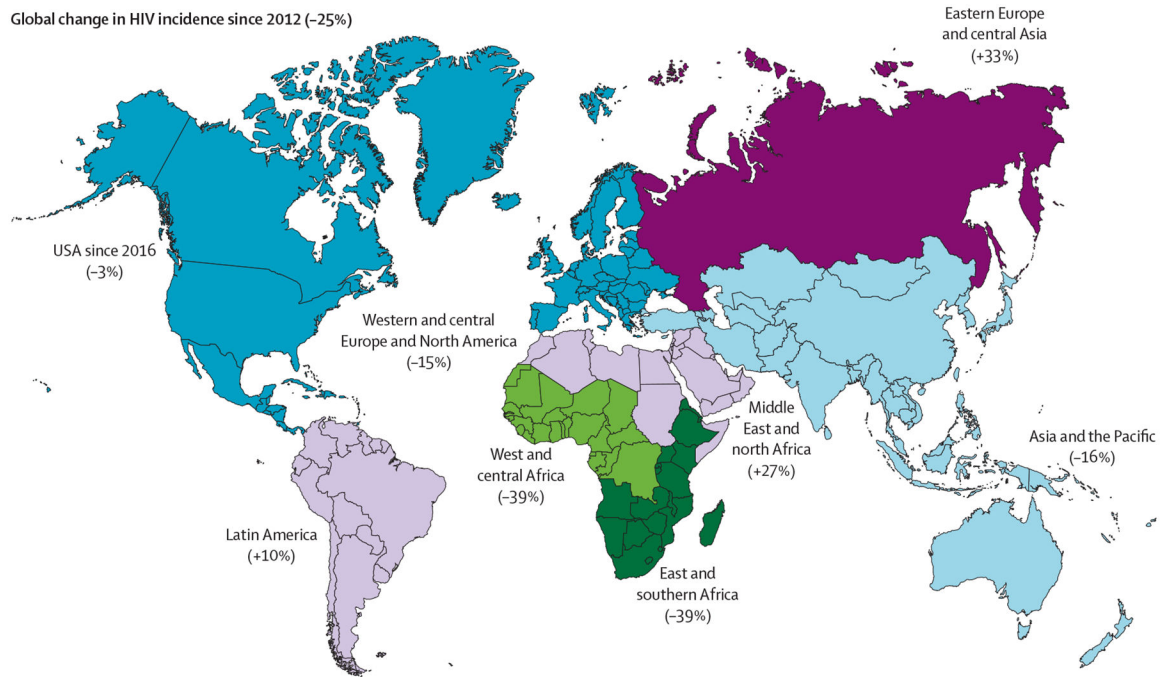


Figure 1: UNAIDS 2022 estimates of percentage change in HIV incidence since 2012¹

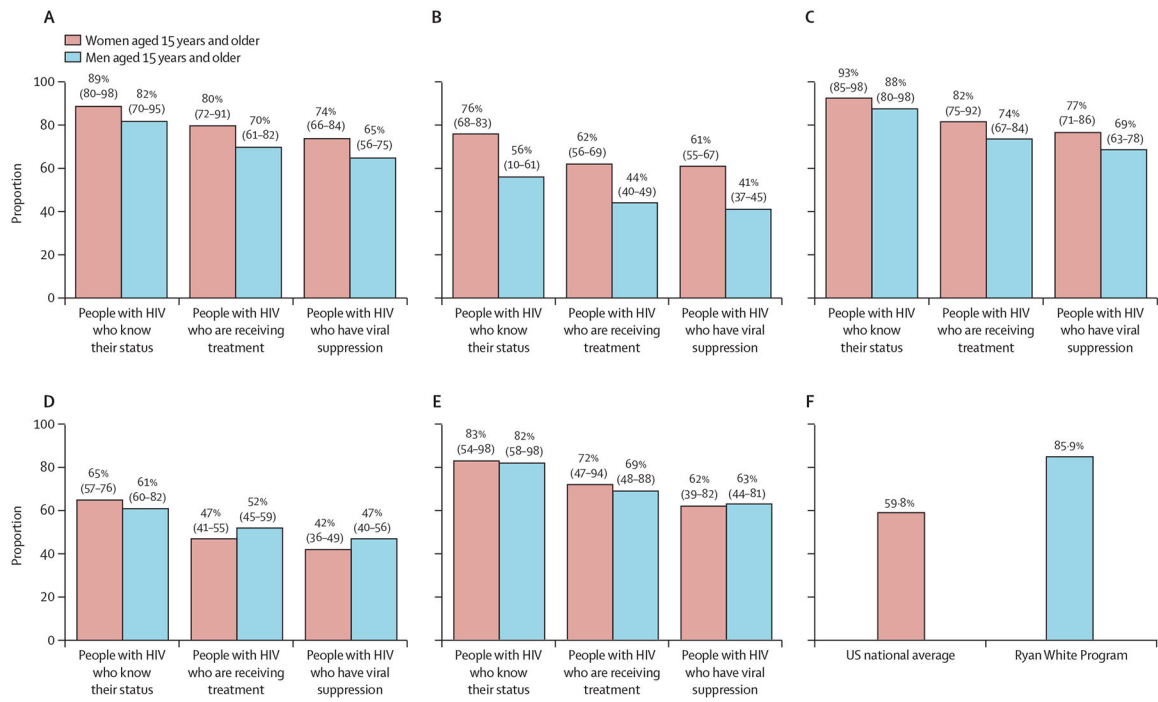


Figure 2: UNAIDS 2022 estimates of HIV testing and treatment cascade
 (A) Global. (B) Eastern Europe and central Asia. (C) Eastern and southern Africa. (D) Middle East and north Africa. (E) Latin America. (F) Rate of viral suppression in people with HIV in the USA. Numeric data are point estimate (95% CI). Source: Health Resources and Services Administration.

Table:

Global HIV control—target regions, remaining challenges, and solutions²

	Remaining challenges	Priority solutions
Sub-Saharan Africa (25.6 million people with HIV)	Gaps in HIV testing between children and adults, ART coverage, and viral load suppression; HIV incidence is still 3-fold higher among adolescent girls vs boys and young men; missed opportunities for early infant diagnosis; insufficient paediatric antiretroviral drug formulations and paediatric ART coverage; poor antepartum and postpartum adherence and retention; rebound in viraemia, particularly during postpartum period; fear of HIV status disclosure; low social and male-partner support; postpartum depression; criminalisation of LGBT people; and stigma	Implement novel interventions to address social, cultural, and structural barriers to HIV service access, uptake, and continuity; provide point-of-care virological diagnostic testing; improve access to newer antiretroviral drugs in paediatric formulations; prioritise viral load testing in pregnant and breastfeeding women; provide peer-based psychosocial support; assist with disclosure and improving male-partner involvement; screen for depression and substance misuse; provide case management; provide long-acting antiretroviral agents; advocate for human rights; and scale up PrEP and male circumcision
Western and central Europe and North America (2.3 million people with HIV)	Reaching men who have sex with men (40%), heterosexual men (19%), and migrants (from sub-Saharan Africa, Latin America and Caribbean); PrEP underused; and stigma. In the USA: racism; fragmented health care; housing and food insecurity; poverty; mental illness; and substance misuse.	Improve prevention, treatment, and care interventions targeting men who have sex with men at risk of infection need to be scaled up and strengthened together with linkage to immediate care and ART for those found to be positive; improve testing, prevention, and care services for migrants with HIV or who are at risk of HIV; provide long-acting antiretroviral agents; and scale up PrEP. In the USA: advocate for human rights focused on early diagnosis; scale up PrEP; provide long-acting antiretroviral agents; expand the Ryan White Program; scale up opioid agonist therapies; and scale up syringe services programmes
Latin America (2.2 million people with HIV)	Reaching men who have sex with men, transgender people, sex workers, and people who inject drugs; stigma; discrimination; and criminalisation of LGBTQ+ people	Advocate for human rights; improve the HIV testing and treatment and prevention programmes including scaling up PrEP; enable safer injection practices; integrate and link HIV and drug misuse treatment; and provide long-acting antiretroviral agents
Eastern Europe and central Asia (1.8 million people with HIV)	Insufficient access to sterile injecting equipment and the unavailability of opioid substitution therapy; stigma; and criminalisation of key populations making them targets of violence in some countries; and armed conflicts (eg, Ukraine)	Make safer sex possible; advocate for human rights; produce decentralised, community-based differentiated service delivery models including testing, access to ART, adherence counselling, and viral load monitoring; scale up PrEP and long-acting antiretroviral agents; scale up opioid agonist therapies; and scale up syringe services programmes
Middle East and north Africa (180 000 people with HIV)	Reaching key populations; stigma; and criminalisation of key populations in some countries	Advocate for human rights; adapt services including outreach for testing and ART; make adherence support targeted; integrate and link HIV and drug misuse treatment; scale up PrEP; scale up opioid agonist therapies; and provide long-acting antiretroviral agents

ART=antiretroviral therapy. PrEP=pre-exposure prophylaxis.