Doctopic: Analysis and Interpretation

thelancethiv-D-25-00277 S2352-3018(25)00193-6

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## Comment

## The imperative for increased investment for an HIV cure



The transformation of HIV from a fatal disease to a manageable condition represents one of medicine's greatest achievements. However, without a cure, HIV remains an urgent global health challenge. Despite widespread availability of prevention tools and treatments in high-income countries, globally, in 2024, 40-8 million people were living with HIV, 1-3 million people newly acquired HIV, and 630 000 people died from AIDS-related illnesses.¹ These numbers represent people facing daily psychological, social, and physical burdens associated with lifelong therapy, persistent stigma, economic hardship, and uncertain access to care.

Antiretroviral therapy suppresses viral replication and eliminates sexual transmission but cannot cure HIV. Lifelong treatment remains essential, as interruption leads to viral rebound due to persistent latent reservoirs. This requirement presents a growing burden for people living with HIV and health-care systems, and is particularly concerning given ongoing infections among adolescents, children, and infants.

The recent decision by the US administration to halt most foreign aid funding2 threatens millions of additional infections and deaths by 2030.3 Other donors, including France, Germany, the Netherlands, and the UK, have reduced their HIV response commitments. This drop in funding underscores the urgent need for alternative interventions for millions of people who are dependent on aid agencies. We stand at a crucial juncture. These changes in the donor landscape make finding a cure for HIV an urgent imperative. Recent scientific breakthroughs show that an HIV cure is biologically possible. However, translating these isolated successes into broadly applicable therapies requires sustained research backed by substantial resources. New public-private models of investment must advance innovations to market, achieving commercial sustainability and broad accessibility.

The past decade yielded extraordinary advances redefining possibilities in HIV cure research. Since Timothy Ray Brown's cure in 2007 through haematopoietic stem cell transplantation,<sup>4</sup> ten people have achieved long-term remission or cure through similar interventions, including two new reports this year.<sup>5,6</sup> Although not scalable due to risk profiles, these patient outcomes provide crucial proof-of-concept,

driving investment into safer, scalable strategies. Moreover, hundreds of individuals have been identified who, either naturally or after treatment interruption, are able to maintain undetectable viraemia for decades in the absence of antiretroviral therapy.

Current research advances along several promising avenues: therapeutic vaccines, gene editing technologies such as CRISPR-Cas9 to modify immune cells or target viral genomes, and approaches focused on reducing HIV reservoirs by activating latent virus for elimination or permanently suppressing replication. Highly potent broadly neutralising antibodies show strong potential for killing infected cells and preventing latent virus replication.7 Technological breakthroughs single-cell analysis, enhanced immune monitoring, drug delivery advancements, and artificial intelligence I integration—have created an exceptionally favourable landscape for rapid advancement. However, funding should align with this transformative potential.

HIV cure research presents a compelling economic case. Lifelong antiretroviral therapy creates global costs for health-care systems that are difficult to sustain. Estimated lifetime medical costs of a person living with HIV range from US\$5221 in low-income settings8 to over €500000 in high-income settings.9 Globally, maintaining and expanding care and treatment access requires annual investments amounting to billions of euros. Even optimistic estimates project a nearly 50% increase in sub-Saharan African infections over 5 years, with a 300% increase highly plausible given the rapidly growing youth population.3 Donor withdrawal, economic uncertainty, and expanding treatment needs threaten to reverse all HIV response progress by 2030: the effect will be felt first and disproportionately affecting sub-Saharan Africa but also, in the longer term, high-income countries, particularly key populations, will be affected. Although long-acting pre-exposure prophylaxis-and in particular, lenacapavir-could transform prevention efforts, it cannot end the epidemic without an HIV cure. Importantly, HIV cure innovation investments offer compounded benefits for other unmet medical needs. These platforms could cure other chronic infections, genetic diseases, and neurological conditions. This market potential highlights the value of public-private investments advancing technological

innovation, presenting opportunities for long-term health system savings, and strategic health technology autonomy.

Despite this transformative potential, HIV cure research remains significantly underfunded. In addition, until now, nearly 90% of global funding came from US Government sources, with National Institutes of Health as the largest funder. These resources face severe reduction due to shifting political priorities and foreign aid cuts. Private sector commitment remains limited, deterred by the nature of cure-related science. Consequently, promising approaches remain in early stage development, clinical trials are underpowered, and research capacity of low and middle income countries is underutilised.

Diversification of the funding ecosystem is urgently needed. This disparity has created significant constraints on HIV research pace and scope. All HIV-affected countries should contribute equitably to expeditiously advance the cure agenda. The EU together with low and middle income countries should assume prominent leadership roles through increased investment and structural mechanisms supporting innovation and derisking the cure pipeline. We recommend the following steps to facilitate progress in cure development: expanded public funding for early stage, investigatorled research and development; establishment of an HIV cure impact fund, a public-private blended finance mechanism supporting late-stage development; greater inclusion of institutions from low and middle income countries in research consortia, trials, and leadership roles; a coordinated global agenda anchored by International AIDS Society, WHO, and UNAIDS in articulation with funders, ensuring strategic alignment and resource pooling, working together with communities to develop HIV cures that fit people's real needs.

Decades of foundational work created unprecedented understanding of HIV biology, and technological innovations provide powerful tools to address viral persistence. Simultaneously, treatment-only approach limitations have become increasingly apparent, particularly for resource- limited settings and marginalised populations in an area of resources constraints. We possess scientific tools to pursue HIV cure with reasonable prospects of success: political and financial commitment commensurate with the urgency

and feasibility of achieving this goal are required. Having long championed global health leadership, the EU is now positioned to help shape the final phase of the global HIV response. With foresight, partnership, and investment, the EU and its allies can deliver a future where HIV no longer defines lives.

SRL has received investigator-initiated grant funding from Gilead, Merck, and ViiV Healthcare, and has been a paid member of advisory boards to Abbvie, Gilead, Immunocore, and Esfam. JM-P declares institutional grants from Merck Sharp and Dohme, ViiV Healthcare, and Grifols, MD declares grants from Gilead Sciences, ViiV Healthcare, and Merck Sharp and Dohme, and is advisory board member of ILGA-Europe and Council for Global Equality. OSS declares participation in scientific advisory boards for Immunocore, ViiV Healthcare, Merck Sharp and Dohme, Gilead Sciences, and AbbVie, and is (unpaid) board member and treasurer for the Nordic Scoiety for Clinical Microbiology and Infectious Diseases. RvL declares to be inventor of an pending international patent application P137348EP00 for treatment of immune paralysis, is a member of the Advisory Committee on Public Health Emergencies of the European Commission (unpaid) and member of the Joint Industrial Cooperation Forum of the Health Emergency Response Agency of the European Commission, as well as board Member and Vice President of the Riotech companies from Europe innovating in Anti-Microbial resistance research Alliance (unpaid), representing European biotechs on working on antimicrobials, and is a founder and stock holder of biotech company SurvivX, which is working on treatment of immune paralysis. All other authors declare no competing interests.

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