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HIV prevention at a crossroads: the promise of an HIV vaccine

We are closer than ever to developing a vaccine against one of the world's most complex pathogens. The coming decade will be a decisive period for the field.

Despite huge progress in HIV prevention, including treatment as prevention and pre-exposure prophylaxis (PrEP), HIV remains a major public health crisis. In 2024 alone, 1.3 million people acquired HIV—more than three times the UNAIDS 2025 target.[1] **Limited access to HIV testing, prevention, and treatment, alongside increasing drug resistance and persistent social, economic, and clinical determinants, undermines efforts to control the epidemic**. This is especially challenging in resource limited settings where adolescent girls and young women and key and vulnerable populations are disproportionately affected.[2]

We still need an HIV vaccine

Vaccines are one of the most impactful and cost-effective public health interventions[3]

We need an effective, durable vaccine to bring a sustainable end to the epidemic.[4,5,6,7] A partially effective vaccine lasting three-to-five years could substantially curtail HIV globally.[4] Considerable economic benefits are predicted in high burden countries, freeing up scarce resources in strained health systems, including reducing the growing need for lifelong treatment.[4,8] Cutting-edge science guided by novel vaccine design is advancing a new generation of promising candidates through clinical testing.[9] Meanwhile, highly effective, long-acting prevention tools such as lenacapavir, a twice-yearly injectable PrEP, are becoming available.[6,10]

No one tool will end the epidemic alone. **A comprehensive prevention toolbox that allows individuals to choose between a vaccine and long-acting prevention options offers the strongest potential to sustainably control the epidemic.**[4-7] Further, an HIV vaccine can help reach people not served by current interventions, such as those with limited access to health facilities who may struggle to return for PrEP refills, people facing stigma when care seeking, or those without stable housing or transportation.[6,7,11] An HIV vaccine can also safeguard against service interruption caused by drug stockouts and funding shortages.[12]

What will we gain from sustained investments in HIV vaccine research?

- Advance existing candidates through clinical development and bring novel candidates based on cutting-edge science into human trials
- Conduct faster, smarter research using innovative approaches to expedite development
- Ensure vaccines meet the needs and realities of communities by prioritizing inclusive, participatory research
- Strengthen regional vaccine research and manufacturing ecosystems, particularly in Africa, to better respond to existing and future health threats
- Support cross-cutting scientific advances that benefit vaccine development for other diseases

A funding crisis at a crucial moment

Dramatic policy shifts move us further from the goal of ending HIV as a public health threat by 2030

Unprecedented funding cuts in 2025 from the U.S. government and other major donors, notably in Europe, are expected to have devastating impacts on the global HIV response.[13,14] Funding for HIV vaccine research, dependent on a limited pool of funders, had already plateaued in recent years, reaching a low of US $671 million in 2023 from a high of $981 million in 2007.[15] While the full scale of the impacts remains unclear, **these decisions are jeopardizing the field at a crucial moment, halting pivotal clinical trials and discovery science.**[16] In South Africa, a research powerhouse

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on the continent, 39 TB and HIV clinical research centers partnering in almost 50 HIV and TB trials are under threat.[17,18]

Such seismic changes risk fragmenting the field and endanger its sustainability. Timelines could be extended by years, especially when infrastructure, partnerships, and trust built tirelessly over decades need to be restored.[19] Critical institutional knowledge, expertise, and leadership are also compromised as people are forced to find work elsewhere.[20] **Replenishing and sustaining the millions in terminated HIV vaccine research dollars requires broad political commitment and diversified, joint investments**.

What will we gain from sustained investments in HIV vaccine research?

Advance novel and existing candidates through development

Promising candidates based on cutting-edge science have transformed the HIV vaccine field

While an HIV vaccine is not yet licensed, researchers have gained crucial insights from HIV vaccine trials to date, helping equip the field with some of the most advanced vaccine science available. Researchers are testing candidates designed to elicit broadly neutralizing antibodies (bnAbs), powerful antibodies able to block a wide range of HIV variants. Complementary efforts are evaluating T cell-inducing candidates targeting vulnerable viral regions, and mRNA platforms are facilitating faster, iterative trials.[21] **It is vital we advance candidates through preclinical and clinical development without delay to bring the most promising candidates to late-stage trials within the next decade**.

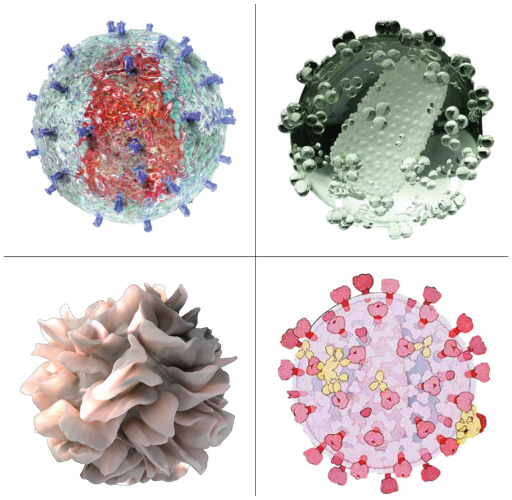
Conduct faster, smarter research

Experts are employing state-of-the-art strategies to expedite HIV vaccine development

Innovations in trial design, experimental medicine, and small-scale manufacturing, alongside emerging technologies like artificial intelligence, are facilitating more efficient identification, testing, and analysis of HIV vaccine candidates.[21,22,23,24]

Strategies that allow pre-planned adaptations to trials and trigger funding release at predetermined milestones can minimise costly delays.[25] Co-creation of strategic guidelines, such as Preferred Product Characteristics (PPC) and a Target Product Profile (TPP), can support joint agenda setting and help streamline development.[5] Modern AI tools, including protein language models, are already helping researchers identify antigen and antibody features that may drive broad and durable immune responses.[24,26] AI is also streamlining clinical trials by automating tasks such as database setup, protocol checks, and document management.[27] Further, the evaluation of vaccine candidates alongside other prevention tools, as seen with the PrEPVacc trial, may better reflect real-world use scenarios, share resources, and explore synergistic effects of interventions.[28,29]

Capitalizing on these efficiencies can reduce delays and strengthen trial reliability, particularly in resource-constrained settings, enabling more local institutions in Africa and elsewhere to run complex trials with greater independence.



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Meet the needs and realities of communities

Communities are calling for HIV prevention research to reflect their priorities and experiences

Developing an accessible HIV vaccine requires inclusive, participatory research that is informed by community needs and builds ownership of and trust in a future vaccine. HIV vaccine development is well placed to build on its strong foundation of close collaboration with affected communities. This includes by embedding socio-behavioural and implementation research across HIV vaccine development efforts to identify trial design issues and ensure community acceptance and participation in vaccine trials by addressing social and structural barriers early, such as medical mistrust, stigma, and vaccine hesitancy.[30] The People's Research Agenda, centered on and led by people living with and at risk of HIV, presents clear, collaboratively developed priorities for how prevention research should be conducted.[31]

Strengthen regional vaccine research and manufacturing ecosystems

HIV vaccine research is a cornerstone of the vaccine development infrastructure in Africa

Decades of investments in HIV science have built world-leading clinical research capabilities and expertise in high burden countries, including in South Africa, Uganda, Zimbabwe and Kenya, that is today supporting infectious disease research beyond HIV.[32] In this way, expanding well established HIV vaccine trial R&D networks, such as Sub-Saharan African Network for TB/HIV Research Excellence, HIV Vaccine Trials Network, and ADVANCE (Accelerate the Development of Vaccines and New Technologies to Combat the AIDS Epidemic) to address other diseases offers a cost-effective approach to expand vaccine development capacities and ensure vaccine candidates meet the needs of local populations.[30,33] Growing regional vaccine production capacities can also be utilized to support a sustainable HIV vaccine pipeline.[34]

Support cross-cutting scientific advances

HIV vaccine science has helped drive vaccinology to the cutting-edge – there are more lessons to be learned

Advances from HIV vaccine development are now shaping the broader vaccine field, including rational immunogen design using reverse engineering of viruses, understanding the role of viral surface proteins in immune recognition, and applications of novel vaccine platforms, such as viral vectors.[35,36,37] HIV vaccine development also played an integral role in developing the mRNA platform.[38] These insights, alongside those from research in diseases like influenza and respiratory syncytial virus, made the speed and success of COVID-19 vaccine development possible.[36,37] Beyond vaccines, HIV research has contributed to treatments for chronic hepatitis B and C, using drugs initially developed for HIV, and laid the groundwork for cancer immunotherapies, such as CAR-T cells and immune checkpoint inhibitors.[39] **Integrated research approaches that leverage synergies between HIV and other infectious diseases can better prepare us to tackle current and future epidemics, while accelerating the efficient development of safe and effective interventions across disease areas.**

Innovate funding to fulfil the promise of the science

Realizing the potential of the hard-won advances in HIV vaccine development requires long-term global collaboration and funding. **Sustaining this research infrastructure represents a strategic investment to secure regional capacities, leadership, and autonomy to develop vaccines for HIV from discovery to access, as well as for existing and emerging health threats.** A joint financing approach that brings together investments from funders in high- and low-and-middle-income countries will be crucial to this end. Advocates, civil society, and regional policy makers can play a critical role in ensuring that investments are sustained and coordinated. In high burden regions, particularly in Africa, policy makers and funders should prioritize sustainable funding strategies for vaccine development that leverage domestic investments, diversified public-private partnerships, and create incentives for local investment.[30]

References

1 UNAIDS. Domestic revenues, debt relief and development aid: Transformative pathways for ending AIDS by 2030 - Report on Eastern and Southern Africa, 2024. 2024 Available at https://www.unaids.org/en/resources/documents/2024/domestic-revenues-debt-relief-development-aid-esa

2 Key and vulnerable populations include sex workers, men who have sex with men, transgender women, people who inject drugs, and people deprived of liberty. In: UNAIDS. Key populations. [Accessed 5 August 2025] Available from: https://www.unaids.org/en/topic/key-populations

3 Ozawa S, Clark S, Portnoy A, Grewal S, Stack ML, Sinha A, et al. Estimated economic impact of vaccinations in 73 low- and middle-income countries, 2001–2020. Bulletin of the World Health Organization. 2017 Jun 27;95(9). doi:10.2471/BLT.16.178475

4 Adamson B, Dimitrov D, Devine B, Barnabas R. The Potential Cost-Effectiveness of HIV Vaccines: A Systematic Review. *PharmacoEconomics Open*. 2017;1(1). doi:10.1007/S41669-016-0009-9

5 Tatoud R, Lévy Y, Le Grand R, Alcami J, Barbareschi G, Brander C, et al. In danger: HIV vaccine research and development in Europe. *PLOS Global Public Health*. 2025;5(4):e0004364-e. doi:10.1371/JOURNAL.PGPH.0004364

6 Jatt LP, Mgodi NM, Buchbinder SP, Gray GE, Kublin JG. An HIV Vaccine in the Era of Twice-Yearly Lenacapavir for PrEP — Essential or Irrelevant? *NEJM*. 2025;392(16):1561-3. doi:10.1056/NEJMP2415893

7 Beyrer C, Tomaras GD, Gelderblom HC, Gray GE, Janes HE, Bekker LG, et al. Is HIV epidemic control by 2030 realistic? *The Lancet HIV*. 2024;11(7):e489-e94. doi:10.1016/S2352-3018(24)00098-5

8 Bozzani FM, Terris-Prestholt F, Quaife M, Gafos M, Indravudh PP, Giddings R, et al. Costs and Cost-Effectiveness of Biomedical, Non-Surgical HIV Prevention Interventions: A Systematic Literature Review. *PharmacoEconomics*. 2023;41(5):467-80. doi:10.1007/S40273-022-01223-W

9 Jefferys R. 2025 Pipeline Report: HIV Vaccines and Passive Immunization. *Treatment Action Group*. August 2025. https://www.treatmentactiongroup.org/wp-content/uploads/2025/08/Pipeline_HIV_Vaccines_2025.pdf

10 Bekker LG, Das M, Abdool Karim Q, Ahmed K, Batting J, Brumskine W, et al. Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women. *NEJM*. 2024;391(13):1179-92. doi:10.1056/NEJMOA2407001/

11 Richterman A, O'Brien C, Ghadimi F, Sumners E, Ford A, Houston N, et al. Acceptability, facilitators, and barriers to a hypothetical HIV vaccine in the pre-exposure prophylaxis era. *AIDS care*. 2024;36(11). doi:10.1080/09540121.2024.2372715

12 UNAIDS. Country updates on the impact of US funding cuts on the global HIV response 2025. [Accessed 4 November 2025] Available from: https://www.unaids.org/en/impact-US-funding-cuts/country-updates.

13 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. *The Lancet HIV*. 2025;12(5):e346-e54. doi:10.1016/S2352-3018(25)00074-8

14 Lahiri I. From Finland to the UK, European countries are slashing aid. What does it mean for climate funds? *Euro News*. 3 March 2025. https://www.euronews.com/green/2025/03/30/from-finland-to-the-uk-european-countries-are-slashing-aid-what-does-it-mean-for-climate-f.

15 G-FINDER Data Portal: HIV Vaccines [Internet]. *G-FINDER*. 2025. [Accessed 14 August 2025]. Available from: https://gfinderdata.impactglobalhealth.org/pages/data-visualisations/allNeglectedDiseases. Note: *The amount cited takes into account inflation and the value of the investment in relation to its purchasing power (i.e., the actual goods or services for which it can be exchanged at a given time.*

16 MacPhail K. USAID freeze halts effort to develop HIV vaccine in Africa. *STAT*. 26 February 2025. https://www.statnews.com/2025/02/26/trump-usaid-freeze-halts-hiv-vaccine-trial-in-africa-qa-glenda-gray/

17 Treatment Action Group & Medecins Sans Frontières. U.S. Funding Cuts Threaten 39 Research Sites in South Africa Putting Scientific Advancements and Hard Won Progress Against TB and HIV at Risk. 15 May 2025. https://www.treatmentactiongroup.org/statement/u-s-funding-cuts-threaten-39-south-african-research-sites/

18 Nolen S. South Africa Built a Medical Research Powerhouse. Trump Cuts Have Demolished It. *The New York Times*. 17 June 2025. Available at https://www.nytimes.com/2025/06/17/health/south-africa-medical-research-trump.html?

19 Bieske L, Zinner M, Dahlhausen F, Truebel H. Critical path activities in clinical trial setup and conduct: How to avoid bottlenecks and accelerate clinical trials. *Drug Discovery Today*. 2023/10/01;28(10). doi:10.1016/j.drudis.2023.103733

20 Murray LW, Venter F. The impact of United States Government cuts to funding on South African Healthcare and Research. Wits *J Clin Med*. 2025-07-07;7(2). doi:10.18772/26180197.2025.v7n2a8

21 Haynes BF, Saunders KO, Hahn BH, Wiehe K, Baden LR, Shaw GM, et al. Status of HIV vaccine development: progress and promise. *J Int AIDS Soc*. 2025;28(5):e26489-e. doi:10.1002/JIA2.26489

22 Prudden H, Tatoud R, Slack C, Shattock R, Anklesaria P, Bekker L-G, et al. Experimental Medicine for HIV Vaccine Research and Development. *Vaccines.* 2023;11(5). doi:10.3390/vaccines11050970

23 Global HIV Vaccine Enterprise Strategic Plan 2022-2027. *International AIDS Society*. 2021. https://www.iasociety.org/sites/default/files/IAS-VE-Strategic-plan-22-27.pdf

24 Jin R, Zhang L. AI applications in HIV research: advances and future directions. *Front Microbio*. 2025;16. doi:10.3389/fmicb.2025.1541942

25 Bethe U, Pana ZD, Drosten C, Goossens H, König F, Marchant A, et al. Innovative approaches for vaccine trials as a key component of pandemic preparedness - a white paper. *Infection*. 2024;52(6). doi:10.1007/s15010-024-02347-1

26 El Arab RA, Alkhunaizi M, Alhashem YN, Al Khatib A, Bubsheet M, Hassanein S. Artificial intelligence in vaccine research and development: an umbrella review. *Front Immun*. 2025;16. doi:10.3389/fimmu.2025.1567116

27 Contreras B. AI Set to Speed Up HIV Vaccine Research and Trials, Focusing on Fair Access - IAS 2025. *Managed Healthcare Executive*. 15 July 2025. https://www.managedhealthcareexecutive.com/view/ai-set-to-speed-up-hiv-vaccine-research-and-trials-focusing-on-fair-access

28 HIV vaccines tested in PrEPVacc fail to reduce infections. *MRC Clinical Trials Unit*. 2024. [Accessed 22 September 2025]. Available from: https://www.mrcctu.ucl.ac.uk/news/news-stories/2024/july/hiv-vaccines-tested-in-prepvacc-fail-to-reduce-infections/

29 Dawson L, Garner S, Anude C, Ndebele P, Karuna S, Holt R, et al. Testing the waters: Ethical considerations for including PrEP in a phase IIb HIV vaccine efficacy trial. *Clinical trials (London, England)*. 2015;12(4). doi:10.1177/1740774515579165

30 Ndembi N, Karuna S, Cowden J, Cagigi A, Pilorget A, Moodley A, et al. Accelerating vaccine development in Africa: lessons from HIV research. *The Lancet*. 2025;405(10491). doi:10.1016/S0140-6736(25)00564-1

31 AVAC. People's Research Agenda: Community & Advocacy Priorities in HIV Prevention Research and Development. December 2024. https://avac.org/wp-content/uploads/2024/10/peoplesResearchAgenda_dec2024.pdf

32 Read SW, Kim P, Marovich M, Dieffenbach CW, Fauci AS. Forty years of investment in HIV research: progress towards ending the HIV pandemic and preparation for future pandemics. *J Int AIDS Soc*. 2022;25(12). doi:10.1002/jia2.26039

33 Nyirenda T, Bockarie M, Machingaidze S, Nderu M, Singh M, Fakier N, et al. Strengthening capacity for clinical research in sub-Saharan Africa: partnerships and networks. *Int J Infect Dis*. 2021;110. doi:10.1016/j.ijid.2021.06.061

34 Gray G, Williamson C, Bekker LG, Daniels B, Smidt W, Garrett N, et al. Africa is an Essential Partner in the Research and Development of an HIV Vaccine. *Current HIV research*. 2025;23. doi:10.2174/011570162X361496250627004203

35 Schwetz TA, Fauci AS. The Extended Impact of Human Immunodeficiency Virus/AIDS Research. J Infect Dis. 2019;219(1). doi:10.1093/infdis/jiy441

36 Calder T, Tong T, Hu DJ, Kim JH, Kotloff KL, Koup RA, et al. Leveraging lessons learned from the COVID-19 pandemic for HIV. *Communications Medicine*. 2022;2(1). doi:10.1038/s43856-022-00175-8

37 Bok K, Sitar S, Graham BS, Mascola JR. Accelerated COVID-19 vaccine development: milestones, lessons, and prospects. *Immunity*. 2021;4(8). doi:10.1016/j.immuni.2021.07.017

38 Harris JE. The repeated setbacks of HIV vaccine development laid the groundwork for SARS-CoV-2 vaccines. *Health Pol Tech*. 2022;11(2). doi:10.1016/j.hlpt.2022.100619

39 Corey L, Ratevosian J, Beyrer C, Currier J, Eron J, Cohen MS, et al. How HIV research drives health innovation in multiple diseases. *Nature Medicine*. 2025. doi:10.1038/s41591-025-04019-5

Translating science into global health impact

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