THE FORUM FOR COLLABORATIVE RESEARCH

THE FUTURE OF HIV PREVENTION CLINICAL TRIALS

Scientific Symposium

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Introduction

The future of HIV prevention clinical trials is marked by both unprecedented scientific opportunity and significant challenges. Advances in biomedical HIV prevention offer promising new tools to reduce HIV infections globally. However, HIV prevention clinical research faces complex trial design, ethical, and funding challenges that require adaptive, inclusive, and efficient research approaches. Navigating this changing landscape requires multi-sector and -regional collaboration, with emphasis on equity and community leadership.

The 13th International AIDS Society Conference on HIV Science (IAS 2025), held in Kigali, Rwanda, July 13th –17th, 2025, convened the global HIV community to address critical issues in HIV treatment, prevention, and related research. Hosting the conference in Kigali, Rwanda, highlighted Africa's leadership in the HIV response and research. Rwanda is also recognized for its strong public health response and notable progress against HIV, having achieved the global UNAIDS 95-95-95 targets ahead of schedule[1].

As part of the conference, the Forum for Collaborative Research at the University of California, Berkeley, organized a scientific symposium on the future of HIV prevention clinical trials. This session built on the Future of HIV Prevention Clinical Trials Summit, held in Johannesburg, South Africa, June 11th-12th, 2025, in collaboration with the Wits RHI at the University of the Witwatersrand[2]. The summit aimed to foster consensus on the future of clinical trial designs that are ethical, inclusive, acceptable, feasible, and efficient. It focused on adapting trial methodologies to the evolving epidemiology, prevention standards, and the changing funding landscape, with special attention to the role of African countries and populations in HIV research. The discussions included specific considerations for various prevention products, such as antiretroviral-based pre-exposure prophylaxis (PrEP), broadly neutralizing antibodies (bnAbs), and HIV vaccines. The summit brought together researchers, regulatory representatives, industry, community advocates, and funders. This report summarizes the key discussions and outcomes from the IAS 2025 satellite session on the Future of HIV Prevention Clinical Trials, highlighting key challenges identified and collaborative strategies proposed to accelerate HIV prevention research.

[1] Rwanda's HIV leadership on display at IAS 2025. (2025, July 16). European AIDS Treatment Group. Retrieved July 21, 2025, from https://www.eatg.org/hiv-news/rwandas-hiv-leadership-on-display-at-ias-2025/

[2] Forum Research. (n.d.). The future of HIV prevention clinical trials summit. https://www.forumresearch.org/hiv-forum/prep-project/meetings/1872-the-future-of-hiv-prevention-clinical-trials-summit

Figure 1: Veronica Miller of the Forum for Collaborative Research speaks at the future of HIV prevention clinical trials scientific symposium at the IAS 2025 conference.

The Future of HIV Prevention Clinical Trials: Challenges and Innovations

The future of HIV prevention clinical trials presents promising advancements in HIV prevention but faces significant challenges, notably by a rapidly evolving research support and funding landscape. A major recurring theme throughout the symposium was the decrease in funding for HIV prevention research. In 2025, the US National Institutes of Health (NIH) terminated 191 HIV-specific grants, cutting over $200 million from critical prevention research portfolios, while United States Agency for International Development (USAID) cancelled funding for numerous pre-clinical and clinical trials[3]. This funding crisis has affected HIV prevention products development and research, and significant concerns were raised about how such disruptions could delay product introduction and equitable access. Therefore, a need for innovative, cost-efficient, and adaptable clinical trial designs was emphasized by symposium attendees. This can be exemplified by the innovative clinical trial design employed by the PURPOSE 1 trial, which used recency assays to estimate the background HIV incidence to use as a counterfactual comparator[4]

An increasing number of HIV prevention products for pre-exposure prophylaxis (PrEP) is becoming available. Notably, lenacapavir, a twice-yearly injectable capsid inhibitor-based PrEP, has been shown to be highly efficacious at preventing HIV, and received US Food and Drug Administration (FDA)

[3] AVAC. (2025). HIV research & development at risk: Tracking the impact of US funding cuts. Retrieved July 22, 2025, from https://avac.org/wp-content/uploads/2025/05/HIVresearchDevelopmentAtRisk.pdf
[4] Parkin N, Gao F, Grebe E, et al. Facilitating Next-Generation Pre-Exposure Prophylaxis Clinical Trials Using HIV Recent Infection Assays: A Consensus Statement from the Forum HIV Prevention Trial Design Project. *Clin Pharmacol Ther*. 2023;114(1):29-40. doi:10.1002/cpt.2830

approval on June 18th, 2025[5]. This long-acting dose schedule has the potential to address challenges with effective use of PrEP products with more frequent dosing. In addition to further PrEP products, such as monthly oral PrEP, symposium participants emphasized that advancing research on broadly neutralizing antibodies (bnAbs) for HIV prevention and HIV vaccines remains an important part of expanding prevention choices, helping to fill critical gaps and offer alternatives that complement existing modalities. Proof-of-concept studies such as the Antibody Mediated Prevention (AMP) trials have demonstrated bnAbs' potential to prevent HIV infection, with ongoing efforts focused on enhancing their potency, breadth, durability, and optimizing delivery methods. Novel production techniques like plant-based expression and mRNA encoding are also being explored to improve scalability and accessibility. Various HIV vaccine approaches are emerging, such as germline-targeting immunogens and mRNA technology. Questions were raised during the symposium as to how regulatory agencies evaluate new HIV prevention products relative to existing ones, highlighting that priority is given to new products that are supplemental, filling gaps and expanding choice rather than duplicating existing options.

The availability of efficacious PrEP has led to a shift in HIV prevention clinical trials from placebo-controlled to active-controlled trial designs, underscoring the complexity of evaluating new interventions in the context of existing prevention options. This shift includes the need for larger sample sizes and longer follow-up periods to establish the non-inferiority of new products. Innovative trial methodologies, such as adaptive designs, single-arm studies, and the use of external controls, are becoming increasingly necessary to address these challenges. Trial design experts also noted challenges in choosing appropriate comparators, especially when comparing different prevention modalities, such as long-acting injectable versus oral PrEP. Recently, the PURPOSE trials on lenacapavir incorporated an external control group to address ethical and practical issues in HIV prevention research[6]. During the symposium, regulatory representatives expressed openness to these alternative trial approaches, including the use of external control groups, as traditional placebo arms become less viable due to existing prevention standards. Regulatory agencies are also encouraging the harmonization of standards and the adoption of adaptive and innovative trial designs.

Digital health infrastructure, artificial intelligence (AI), and real-world data integration emerged as essential tools for enhancing trial efficiency, participant monitoring, and product rollout. These technologies can streamline study workflows through automated data collection, patient enrollment, and data management. There is a need for investments in infrastructure alongside careful protection for data privacy and ownership. The inclusion of AI and digital health experts in future discussions was suggested to deepen understanding of these tools' potential and limitations in HIV research.

[5] Gilead Sciences, Inc. Yeztugo® (Lenacapavir) is now the first and only FDA-approved HIV prevention option offering 6 months of protection [Internet]. Foster City (CA): Gilead Sciences, Inc.; 2025 [cited 2025 Jul 10]. Available from: https://www.gilead.com/news/news-details/2025/yeztugo-lenacapavir-is-now-the-first-and-only-fda-approved-hiv-prevention-option-offering-6-months-of-protection

[6] Parkin N, Gao F, Grebe E, et al. Facilitating Next-Generation Pre-Exposure Prophylaxis Clinical Trials Using HIV Recent Infection Assays: A Consensus Statement from the Forum HIV Prevention Trial Design Project. *Clin Pharmacol Ther*. 2023;114(1):29-40. doi:10.1002/cpt.2830

Community Engagement, Stigma Reduction, and Equitable Access

The symposium highlighted that community engagement and leadership is vital for ethical and effective trials. Community advocates demanded complex scientific jargon to be translated into clear, contextualized, and culturally appropriate messaging to build trust and informed participation. Communities expect transparency about trial progress and outcomes, as well as assurance of post-trial access to successful products. Patient advocates also voiced concerns about persistent stigma impeding trial participation and HIV prevention access. Best practices to combat stigma include education and training, stigma-free trial designs (e.g., avoiding clinic layouts that reveal HIV status), collaboration with trusted community-based organizations (CBOs), and tactics like “decoy” visits to protect confidentiality.

Figure 2: Panel session at the future of HIV prevention clinical trials scientific symposium at the IAS 2025 conference.

Key Takeaways

Need for Innovation and alternative funding sources: There is a need to develop more cost-efficient and adaptable trial designs that can sustain progress amidst reductions in global research funding.

Evolving clinical trial designs: There is need for scientifically robust innovations in HIV prevention clinical trials, such as adaptive trial designs, alternative external or historical control groups, and utilizing real-world data.

Community engagement and equity: Meaningful and sustained community involvement is essential for ethical and successful trials. Trial designs must provide participants with genuine choice of prevention options and address the inclusion of underrepresented populations.

Strengthening South-to-South collaboration: Strengthening South-to-South collaboration is essential to enhance scientific capacity, regional ownership, and responsiveness to local epidemiological and social realities.

Expanding the HIV prevention options: Continued research into novel HIV prevention products and ensuring access to new products is essential to ensure access to a variety of HIV prevention products, giving individuals the option to choose that best suits their needs and preferences.

Conclusion and Next Steps

This scientific symposium captured the dynamic landscape of HIV prevention clinical research, highlighting how scientific innovation, regulatory evolution, funding realities, and community engagement intersect to shape the future of HIV prevention. Embedding community voices, embracing innovative trial designs, expanding inclusivity, and fostering regional leadership are imperatives to develop interventions that are not only scientifically robust but also equitable, accessible, and impactful worldwide.

The Forum plans to collaborate on a manuscript to be published in a peer-reviewed journal to publicize the deliberations and recommendations from the IAS 2025 symposium and Future of HIV Prevention Clinical Trials Summit. Additional in-person or virtual meetings will be considered. The summit concluded with participants expressing their appreciation for the vision and significance of the symposium, as well as gratitude for everyone’s commitment to advancing HIV prevention research.