OAR HIV/AIDS Clinical Trials Networks External Review Working Group Recommendations

Preamble

On December 22, 2025, the NIH Office of AIDS Research (OAR) invited 18 external scientific experts, community representatives, and federal implementation partners (*ex officio*) to serve on the HIV/AIDS Clinical Trials Networks (CTN) External Review Working Group. The Working Group was convened to provide strategic recommendations to inform the next funding round of the NIH HIV Clinical Trials Networks (CTNs), led by the National Institute of Allergy and Infectious Diseases (NIAID), Division of AIDS (DAIDS). The first of five virtual meetings was held on January 16, 2026, and the final meeting took place on March 13, 2026.

The charge of the Working Group was to advise the OAR Director on how best to optimize the CTNs' ability to address the highest-priority emerging HIV research questions in the coming funding cycle. In particular, the Working Group was asked to consider how the networks could strengthen their capacity to address implementation science and HIV-associated co-occurring conditions, while maintaining the core scientific strengths that have made the CTNs a cornerstone of global HIV clinical research. The Working Group was also asked to consider how the networks could ensure the meaningful involvement of new investigators with the scientific expertise needed to advance these evolving research priorities.

The Working Group's deliberations occurred under a compressed timeline. Two U.S. government shutdowns (October 1–November 12, 2025, and January 31–February 3, 2026) delayed both the initiation and the progress of the group's work. As a result, the Working Group was unable to fully explore or provide meaningful recommendations for areas related to training and integrating new investigators. Still, the members sought to identify the most critical opportunities and priorities for strengthening the CTNs.

In developing its recommendations, the Working Group considered implementation science broadly, including both implementation research (the study of implementation processes) and implementation science, the broader application of research evidence and methods to improve the adoption, delivery, and sustainability of effective, evidence-based interventions. Similarly, the Working Group interpreted the concept of co-occurring conditions expansively to include coinfections, comorbidities, complications, and syndemic conditions that influence HIV prevention, treatment, and care.

This document summarizes the Working Group's assessment of opportunities to strengthen the CTNs and presents associated recommendations intended to enhance the networks' scientific impact, improve collaboration and efficiency, expand meaningful community engagement, and ensure that the CTNs remain responsive to the evolving needs of the HIV epidemic. The Working Group hopes these recommendations will inform the development of the upcoming

Notices of Funding Opportunity (NOFOs) and support the continued success of the CTNs as a central component of the domestic and international HIV response.

1. Accelerating HIV Research and Real-World Impact Requires Maintaining the Clinical Trials Networks

Opportunity

The CTNs represent a unique and globally recognized infrastructure capable of conducting complex HIV clinical studies, particularly translating biomedical discoveries into clinical and behavioral interventions, and coordinating large-scale studies across diverse populations and settings. Sustaining this infrastructure is essential to continue advancing HIV prevention, treatment, cure, and co-occurring conditions research and the application of its findings in the U.S. and elsewhere.

Recommendations

Recommendation 1: Maintain the CTNs as a core component of the global HIV research infrastructure with a primary emphasis on discovering and evaluating new interventions for HIV prevention, treatment, and cure, as well as interventions addressing HIV-associated conditions. CTN portfolios should include studies evaluating novel antiretroviral agents, prevention technologies, including vaccines, and curative strategies, while also continuing to address associated comorbidities and co-infections, including cardiovascular disease, aging-associated conditions, tuberculosis, viral hepatitis, sexually transmitted infections such as syphilis, and mental health and substance use disorders.

Recommendation 2: Ensure the CTNs maintain a comprehensive research portfolio spanning discovery, development, clinical trials, and implementation science. This balanced approach will maximize scientific impact by enabling the networks to both develop innovative interventions and identify effective strategies for implementing them at scale.

2. Catalyzing a Scientific Agenda that Addresses HIV Prevention, Treatment, Cure, and Co-occurring Conditions Across the CTNs

Opportunity

Maintaining the CTN's coordinated, balanced, and comprehensive scientific agenda spanning HIV prevention, treatment, cure, and related health conditions can maximize the impact of CTN research by ensuring that emerging biomedical and behavioral innovations address real-world needs. Each of these areas of research are critical for ending the HIV epidemic.

Recommendations

Recommendation 3: Maintain a balanced scientific portfolio across HIV prevention, treatment, cure research, and associated health conditions. CTN research agendas should include clinical trials of prevention interventions that expand the range of HIV prevention options, evaluation of novel treatments and new regimens, and studies supporting cure research initiatives. This research should avoid duplication and focus on clear gaps in the prevention, treatment and cure research portfolio.

Recommendation 4: Design clinical trials to reflect real-world contexts and emerging prevention and treatment landscapes. Protocols should incorporate considerations such as ethical control groups, health system constraints, and the availability of existing effective interventions.

Recommendation 5: Integrate behavioral, social, and implementation science perspectives into biomedical research agendas to address barriers to and opportunities for enhanced prevention and treatment uptake. Behavioral and social science research can identify and address sources of mistrust to increase uptake of a biomedical innovation or tailor an intervention to a specific population to ensure a biomedical advance reaches a population confronting the greatest barriers.

3. Strengthening Cross-Network and Other NIH HIV Research Program Collaboration and Coordination

Opportunity

The CTNs collectively represent a broad array of expertise and infrastructure. Coordinating activities across networks can reduce duplication, leverage complementary expertise, enhance efficiency, accelerate scientific discovery, and enable rapid, coordinated responses to scientific and public health priorities.

Recommendations

Recommendation 6: Establish formal, dedicated organizational structures and processes to actively promote collaboration across CTNs. Networks should create joint committees or working groups to coordinate specific research agendas, identify emerging gaps and coordinate operational responses, share infrastructure, and identify opportunities for collaborative trials.

Recommendation 7: Conduct regular cross-network scientific planning meetings. Cross-network planning should occur at least annually to align scientific priorities and assess opportunities for joint initiatives.

Recommendation 8: Encourage sharing of specialized expertise across networks rather than duplicating capabilities within each network. Adult networks should collaborate with the pediatric network to incorporate expertise in studies involving pregnant people, children, or

adolescents. This would also allow the networks to leverage complementary expertise to accelerate prevention, treatment, and cure research.

Recommendation 9: Require Structured Bridging Between Complementary Research Programs. NOFOs should incorporate mechanisms that inten_onally bridge complementary research infrastructures to accelerate transla_on and maximize return on investment. CTNs should be required to forge collabora_ons between established implementa_on science investments—such as, but not limited to, the infrastructure developed through the Centers for AIDS Research (CFARs)—and transla_onal research consor_a such as the Mar_n Delaney Collaboratories. These collabora_ons should be supported by dedicated funds for joint planning and trial development. Embedding implementation expertise early in cure-focused clinical trials will strengthen study design and help ensure that successful interventions can be rapidly and equitably deployed.

4. Strengthening Collaboration with Federal Agencies, Community Organizations, and Public Health Entities

Opportunity

Partnerships with federal agencies, community-based organizations, and public health systems can ensure research addresses real-world needs and accelerate translation of research findings into clinical practice.

Recommendations

Recommendation 10: Strengthen collaboration with other NIH institutes and federal agencies to address HIV-related comorbidities and chronic diseases. Formalize partnerships with institutes such as NHLBI, NIA, NCI, NIDA, NINDS, NICHD, NIDCR, and NIMH to accelerate research on HIV-associated comorbidities, coinfections, and complications, and reinforce collaborations with federal implementing partners, such as the Centers for Disease Control and Prevention (CDC), Health Resources and Services Administration (HRSA), Indian Health Services (IHS), and the State Department, to mobilize coordinated strategies to effectively address chronic diseases.

Recommendation 11: Expand collaboration with federal health programs and community clinic systems. Ryan White clinics, Federally Qualified Health Centers (FHQCs) and community health centers should serve as sites for phase III clinical trials and implementation research, accelerating the deployment and uptake of strategies and intervention once research studies have established their effectiveness.

Recommendation 12: Include public health officials and health system leaders in network governance and scientific agenda setting. This inclusion will give the CTN visibility into real-time public health needs, accelerate the translation of evidence into policy, and strengthen implementation research.

5. Maintaining Investment in International Research

Opportunity

The international infrastructure of the CTNs represents one of the most powerful scientific assets in the global fight against HIV. These networks have generated foundational evidence that has reshaped treatment and prevention guidelines worldwide and they operate at a scale, diversity, and epidemiological richness that cannot be replicated domestically. Moreover, many critical HIV research questions—including those related to prevention trials, maternal and pediatric HIV, and certain co-infections—cannot be adequately addressed within the United States alone. Importantly, clinical trials conducted through the CTNs have informed US Food and Drug Administration (FDA) approvals of pediatric formulations and dosing for key HIV medicines—including dolutegravir-based regimens and fixed-dose combinations such as abacavir/dolutegravir/lamivudine—helping ensure that effective, pediatric-friendly treatments are available for children with HIV in the United States. The bidirectional transfer of knowledge between domestic and international sites has significantly advanced HIV prevention and care everywhere: the tools, protocols, and systems tested and refined in international settings improves care, prevention, and delivery of HIV services in the U.S.

Recommendations

Recommendation 13: Maintain and expand international research sites within the CTNs when they contribute significantly to scientific objectives. International CTN capacity must be preserved, strengthened, and recognized as an indispensable component of the NIH HIV/AIDS research enterprise, not as a peripheral or discretionary capability.

Recommendation 14: Support bidirectional exchange of scientific knowledge between U.S. and international research settings. This exchange can accelerate improvements in prevention and treatment globally. The translational pathway from international trial evidence to U.S. clinical guidelines and FDA approvals should be a part of network evaluations to ensure that the domestic return on international investment is visible and accountable.

Recommendation 15: Invest in workforce development and site capacity in regions with high HIV burden. Strengthening capacity and local scientific leadership at international sites is a long-term asset for ensuring the bi-directional impact of HIV research.

6. Broadening Meaningful Community Engagement

Opportunity

Engaging the broad HIV response community—including people living with HIV, clinicians, community organizations, and public health practitioners—can improve research relevance, strengthen trust, and enhance adoption of interventions.

Recommendations

Recommendation 16: Establish robust organizational structures to support meaningful community engagement across all phases of research. These structures should include sufficient staffing, dedicated funding, fair remuneration, and decision-making authority. Adoption of established frameworks, such as the National Academy of Medicine's (NAM) Meaningful Community Engagement framework or the AVAC and UNAIDS Good Participatory Practice (GPP) guidelines should inform the development of shared minimum standards for community engagement.

Recommendation 17: Position community representatives as partners in research leadership rather than solely as advisory participants. Community members should serve as co-investigators, participate in governance structures and scientific agenda setting, and contribute to protocol development and budget decisions.

Recommendation 18: Expand the definition of "community" to include a broader range of partners in the HIV response. This may include healthcare providers, caregivers, outreach workers, and individuals involved in the everyday care and support of people living with HIV.

Recommendation 19: Develop mechanisms to facilitate participation in community advisory structures. Networks should establish centralized systems to notify individuals of opportunities to participate in advisory and research partnership roles.

7. Maintaining Robust Social and Behavioral Science Research

Opportunity

Social and behavioral factors strongly influence access to prevention and treatment interventions and affect adherence, uptake, and health outcomes. Social and behavioral science projects can inform and be embedded in implementation research and in studies of co-occurring conditions.

Recommendations

Recommendation 20: Integrate social and behavioral research alongside biomedical trials within CTN research portfolios. Studies addressing aging, mental health, substance use, uptake, and adherence behaviors should be conducted in tandem with and/or embded in clinical trials.

Recommendation 21: Incorporate assessments of social determinants of health into clinical trials and implementation research. These should include, but not be limited to, factors such as stigma, housing instability, access to care, and economic barriers. Dedicated budget allocations for these activities will ensure they are adequately resourced and not deferred.

8. Addressing Co-Occurring Conditions

Opportunity

HIV co-occurring conditions--comorbidities, coinfections, and complications--including mental health disorders and substance use disorders, are amplified by social determinants of health and substantially affect HIV outcomes and access to care. Addressing these conditions and their biomedical, behavioral, and social etiologies can improve health outcomes, strengthen prevention and treatment strategies, and support integrated care models.

Recommendations

Recommendation 22: Establish dedicated organizational structures to integrate co-occurring condition research into CTN scientific agendas. These structures should systematically identify research opportunities and incorporate co-occurring condition research into clinical trials when appropriate.

Recommendation 23: Prioritize research on key co-infections and health conditions affecting people with HIV. Priority areas should continue to include tuberculosis, viral hepatitis, sexually transmitted infections such as syphilis, cardiovascular disease, aging-associated conditions, and mental health and substance use disorders.

9. Integrating Implementation Science

Opportunity

Implementation science can accelerate the adoption, delivery, translation, and sustainability of effective interventions into real-world practice and ensure that innovations reach populations most affected by HIV.

Recommendations

Recommendation 24: **Incorporate implementation science as a core component of CTN research while preserving the networks' primary mission of development and evaluation of methods and tools for HIV prevention, treatment, cure, and co-occurring conditions.** This will require adequate, dedicated funding so networks do not have to choose between discovery research and implementation science.

Recommendation 25: Establish dedicated implementation science organizational structures within and across CTNs. Networks should create implementation science committees and embed implementation science expertise into protocol development and research planning.

Recommendation 26: Embed implementation science questions within clinical trials where appropriate. This should include evaluating feasibility, acceptability, cost and affordability, access, health systems constraints, scalability, and sustainability of interventions to inform the translation of prevention and treatment interventions into practice.

Recommendation 27: Apply implementation science lens across the research continuum, including pre-clinical and basic science work, when appropriate. Considering implementation early helps move promising discoveries more efficiently from the laboratory to clinical use and early attention to delivery, cost, and feasibility can reduce delays between discovery and widespread adoption.

Recommendation 28: Develop centralized implementation science expertise and resources shared across networks. Explicitly including expertise in both statistical analysis and sample size estimation for complex implementation trial designs and standardized review of designs and protocols for appropriateness and quality will be critical to promoting the quality and generalizability of CTN research.

10. Supporting Training and Capacity Building

Opportunity

Sustaining the future HIV research workforce requires continued investment in training and mentorship programs for early-career investigators.

Recommendations

Recommendation 29: Develop and deploy comprehensive programs to train and mentor early-stage investigators within the CTNs. These programs should include structured training, mentoring, leadership opportunities in clinical trials, and support for investigators from communities disproportionately affected by HIV.

11. Aligning Budgets

Opportunity

Expanding research activities—including community engagement, implementation science, and collaboration—requires appropriate funding structures.

Recommendations

Recommendation 30: Ensure that CTN budgets provide adequate resources for all required scientific and operational activities. Budget structures should include dedicated funding for

community engagement, implementation science, social and behavioral research and community collaboration without compromising core scientific research.

12. Evaluating Network Activities and Performance

Opportunity

Regular evaluation can help ensure that CTNs remain responsive to evolving scientific priorities and maintain high performance across sites.

Recommendations

Recommendation 31: Establish formal processes for evaluating CTN operations, performance, and scientific impact. These evaluations should assess network coordination, research outcomes, community engagement practices, and the integration of new activities such as implementation science.

Recommendation 32: Implement transparent processes to assess site performance and address underperforming sites. This should include mechanisms for addressing sites before and after clinical research has begun as well as onboarding new sites when needed to support emerging research priorities.

Recommendation 33: Establish independent advisory committees to conduct mid-cycle reviews of network core facilities and services. The committees should provide recommendations to network leadership on core priorities, performance, and emerging technology needs.

Concluding Summary Statement

The Working Group believes the NIH HIV Clinical Trials Networks remain uniquely posi_oned to advance the domes_c and interna_onal fight against HIV and co-occurring conditions. By strengthening collabora_on, integra_ng implementa_on and social science perspec_ves, expanding and resourcing meaningful, representa_ve involvement of the en_re HIV response community—including people living with HIV, clinicians, community organizations, and public health practitioners—and sustaining the networks' scien_fic capacity, the CTNs can con_nue to accelerate progress toward ending the HIV epidemic.