Treatment Action Group

TAG HIV Research Network Statements: HIV Prevention Trials Network (HPTN)

Background and Achievements

The HPTN plays an essential role assessing non-vaccine biomedical HIV prevention interventions. Among many achievements, the network has conducted studies demonstrating HIV treatment also prevents onward transmission (leading to the Undetectable = Untransmittable [U = U] public health campaign) and that community testing and treatment significantly reduce HIV incidence. These are examples of robust, high quality science with a transformative effect on the implementation of HIV prevention and public health practice, with U=U additionally serving to ameliorate harmful stigma surrounding transmission risk.

Furthermore, evidence from studies conducted by the network has led to demonstration of high efficacy of antiretroviral-based pre-exposure prophylaxis (PrEP) to prevent HIV acquisition. In large part attributable to several large taxpayer-supported, NIH-funded clinical trials, there are now four (4) FDA-approved methods of PrEP – with the first (oral) PrEP intervention approved in 2012 and the most recent (injectable) intervention approved in 2025.

Two large efficacy trials of long-acting cabotegravir were conducted by the HPTN, leading to FDA approval under the trade name Apretude, and the research infrastructure also supported efficacy studies led by Gilead Sciences of the breakthrough twice-yearly PrEP drug lenacapavir. HPTN is also working collaboratively with Gilead Sciences to investigate the implementation of lenacapavir PrEP in cisgender women and people who inject drugs in the United States.

Significant early research included the demonstration that a short course of nevirapine could reduce the risk of HIV transmission from mothers to newborns, and highlighted the centrality of HIV testing to prevention.

The network has worked with multiple populations in urgent need of prevention, including pregnant women, serodiscordant couples (primarily heterosexual) in the HPTN 052 study that demonstrated that HIV treatment is prevention (designated scientific breakthrough of the year by the journal *Science* in 2011), Black men in HPTN 073 (which demonstrated the value of care coordination for optimizing PrEP adherence), and people who inject drugs (e.g. demonstrating that treatment and support reduces HIV incidence).

HPTN's essential work to date encompasses a total of 78 completed and ongoing trials that have enrolled more than 172,000 participants, with results reported in more than 800 scientific publications.

Collaborative research with other NIH-supported networks has provided key information regarding the levels of broadly neutralizing antibodies (bNAbs) required to protect against HIV acquisition in the Antibody-Mediated Prevention (AMP) trials. Conducted in partnership with the HIV Vaccine Trials Network (HVTN), these studies have informed both efforts to design bNAb-inducing vaccines and strategies for using direct delivery of bNAbs for HIV prevention. Collaborations between HPTN, HVTN, and Advancing Clinical Therapeutics Globally (ACTG) are exploring whether receipt of bNAbs is associated with an improved capacity to control HIV viral load after antiretroviral therapy (ART) interruption (work toward strategies that can reduce the need for ART).

TAG recommendations on research priorities

Six-monthly injectable lenacapavir does not mark the end of the need for a comprehensive and broad-based HIV prevention agenda in search of better tools and strategies for their effective integration in communities where they're needed. This requires:

- The development of biomedical HIV prevention options that accommodate the preferences of all people who stand to benefit, including preferences that are population-specific and those that may change based on age and life circumstances (e.g,. extent and mode of possible risk of acquisition, during pregnancy).

- Investigation of both new approaches and optimal implementation of existing biomedical prevention interventions in populations at highest risk of HIV acquisition and HIV-associated comorbidities, including (but not limited to): Black and Latino/x men who have sex with men, cisgender and transgender women, persons who inject drugs, people ages 50 and older who are living with HIV; as well as young cisgender women and heterosexual cisgender men on the African continent.

- Continued investigation of on demand systemic and topical biomedical PrEP options as alternatives to continuous PrEP.

- Assessment of integrated strategies to prevent both HIV and other sexually transmitted infections (STIs).

- Continued collaborative research with other NIH-supported research networks e.g. research into the preventive potential of broadly neutralizing antibodies (bNAbs) with the HIV Vaccine Trials Network (HVTN) and Advancing Clinical Therapeutics Globally (ACTG).

- Continued integration of social and behavioral sciences research into biomedical research protocols, particularly in the context of implementation science projects focused on maximizing efficiency, cost-effectiveness, reach and impact of existing biomedical interventions.

- Hybrid implementation/efficacy research that tests clinical economic models (interventions) for improving financial sustainability of the integration of current and future long-acting PrEP products, with the goal of enhancing the practical translation of biomedical innovations in the real world. This is an important area of opportunity that could also potentially involve collaboration with implementation stakeholders such as third-party payors.

- Expansion of the example set by HPTN 096 by working more directly with community-based clinical practice organizations to understand and influence the factors which affect real world implementation of biomedical innovations, including collaboration outside of the traditionally university-based HPTN US sites.

- Use of more adaptive trial designs that account for the dynamic nature of human behavior and its interaction with changing socioeconomic conditions in communities most impacted by HIV.

- Advancement of the use of human-centered design principles in the development of multi-level integrated intervention strategies to improve the adoption (at the clinical practice organization level) and uptake (at the patient level) of long-acting and combination prevention modalities — which includes deep and extensive community engagement from concept development through to protocol closure.