



The Role of Vaccines and Cures in HIV Elimination

An update from the director of the Basic Science, Vaccines and Cure Project at Treatment Action Group (TAG).

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The development of highly effective approaches to HIV treatment and prevention—in the form of combination antiretroviral therapy (ART) and pre-exposure prophylaxis (PrEP)—stands among the most impressive scientific achievements in human history.

The widespread implementation of these interventions has the potential, at least theoretically, to effectively end the HIV pandemic. However, the practical challenges associated with implementation leave room for even a moderately efficacious HIV vaccine to make a significant additional contribution to halting the virus. And for HIV-positive people, a true end to HIV lies not in an epidemiological calculus, but in a cure.

The first glimmer of hope that an efficacious HIV vaccine can be developed emerged from the RV144 trial in Thailand. A prime-boost regimen comprising an ALVAC canarypox vector followed by AIDVAX B/E (dual HIV Env proteins in adjuvant) reduced the risk of HIV acquisition by 31.2%—a slight, but statistically significant, degree of efficacy.[1] Post-trial analyses provided suggestive evidence that the protective effect may have been higher—around 60%—during the first 12 months, before vaccine-induced immune responses waned.

The encouraging findings from RV144 prompted the design of an efficacy trial with a similar regimen that is now underway in South Africa, which is recruiting a population at higher risk of HIV infection (HVTN 702).[2] Additional booster immunizations are being administered after 12 months in hopes of achieving and sustaining efficacy of 50% or greater.

More recently, a combination of an adenovirus serotype 26 (Ad26) vector prime and HIV Env protein boost entered efficacy testing among women in five southern African countries (HVTN 705/HPX2008). In preclinical macaque studies, the vaccine led to a 94% diminution in per-exposure risk of simian immunodeficiency virus (SIV) acquisition, with complete protection being observed in 66% of animals after a series of six weekly SIV exposures.[3]

These two large ongoing trials offer at least some cause for optimism that a partially effective HIV vaccine could become available in the relatively near term.

In a paper published last year in the Proceedings of the National Academy of Sciences, Jan Medlock and colleagues modeled the possible effect of an HIV vaccine that reduced the risk of HIV infection by 50% when implemented in tandem with efforts to achieve UNAIDS diagnosis, treatment, and viral load suppression targets across 127 different countries.[4]

In a variety of scenarios, vaccination had a synergistic beneficial impact. Even if current levels of diagnosis, treatment, and viral suppression remained unchanged, rolling out a vaccine with 50% efficacy starting in 2020, with scale up proceeding at 25% coverage annually up to a maximum of 70% coverage, was estimated to reduce the number of people living with HIV by 36% and HIV-related mortality by 11%. Analyses in which vaccine availability was delayed to 2025 and/or scale up slowed to 10% per year still predicted significant benefit. A vaccine with a higher efficacy of 70% was estimated to have the potential to avert 24 million HIV infections between now and 2035.

In an opinion piece published in the Journal of the American Medical Association last October, Anthony Fauci (director of the National Institute of Allergy and Infectious Diseases) drew on the work of Medlock and others to articulate the view that “development of a moderately effective vaccine, together with optimal implementation of existing treatment and prevention modalities, could end the current HIV pandemic.”[5]

At the 2015 edition of the International AIDS Society’s annual Towards an HIV Cure Symposium, longtime HIV-positive community activist Matt Sharp gave a plenary address highlighting that talk of “Ending AIDS” can seem empty without the promise of curative interventions on the horizon. Sharp advocated powerfully that cure research is a vital component of the effort to vanquish HIV.[6]

Although efficacy trials of candidate cures still appear to be a long way off, researchers have brought models to bear on the question of how hypothetical approaches might affect HIV at the population level. Andrew Phillips and colleagues, in a paper published in the Journal of Infectious Diseases in 2016, concluded that an intervention that allowed ART-free viral suppression in a majority of recipients could reduce both the costs and the burden of disease; however, they noted that “given the effectiveness and cost of ART, such interventions would have to be inexpensive and highly effective.”[7]

The research group of Rochelle Walensky has similarly found that model outcomes are extremely variable, depending on the estimated effectiveness and cost of a cure intervention.⁸ But Walensky and colleagues also articulate the profound benefits that may elude modeling studies, albeit using the dry and understated language of academia. “This analysis does not account for the psychosocial benefits of being cured. Studies show that stigma, even among HIV-infected people on ART, decreases health-related quality of life. By failing to account for the intangible (but nonetheless real) benefits of complete disease eradication, we may have undervalued cure.”

At the most basic level, HIV will not have entirely ended if daily treatment is still required for the majority of HIV-positive people.

The take home message is that, although it’s essential that the benefits of the tools available to

tackle HIV are maximized as quickly as possible, this will not obviate the need for sustained long-term investment in the development of effective vaccines and cures. Thus, advocates need to push back against efforts to slash HIV research funding at the National Institutes of Health (or elsewhere) based on a false narrative that the interventions needed to stop the pandemic have already been created.

Continued community engagement with the vaccine and cure research fields remains essential to ensure that there is dialogue and input regarding the challenges that arise—such as the appropriate provision of PrEP to participants in HIV vaccine efficacy trials or the use of ART interruptions to test the effect of cure-related therapeutic approaches.

Ultimately, if success can be achieved in these fields, it has the potential to deliver the coup de grace necessary to finally consign HIV to history.

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