



A Failure to Disseminate Transformative Science — HIV Treatment as Prevention, 10 Years On

Jacob Bor, S.D., Dorina Onoya, Ph.D., Bruce Richman, J.D., and Kenneth H. Mayer, M.D.

August 2021 marked a decade since the HIV Prevention Trials Network (HPTN) 052 trial showed that HIV treatment prevents sexual transmission of the virus.¹ Hailed as a game changer,

HPTN 052 altered scientific discourse and HIV policy. But has it changed minds?

The global scale-up of HIV treatment is one of the great public health success stories of the 21st century. Millions of people with HIV are living longer and healthier lives because of the substantial resources that have been deployed to increase access to medication. Despite widespread awareness of treatment's therapeutic benefits, however, recent research revealed large global disparities in knowledge about the efficacy of treatment as prevention (TasP).² Knowledge of TasP is particularly limited in sub-Saharan Africa, which is home

to two thirds of all people with HIV. The science supporting TasP has not been widely disseminated, despite growing evidence that sharing this information has clinical and public health benefits.

In HPTN 052, investigators randomly assigned people with HIV in serostatus-discordant couples to immediate or deferred antiretroviral therapy (ART) and compared HIV incidence among the originally HIV-negative partners. The results, published in August 2011, demonstrated what many clinicians and scientists had long suspected: that HIV treatment leading to viral suppression is highly effective in preventing HIV transmission.¹ Large cohort studies —

PARTNER, PARTNER 2, and Opposites Attract — confirmed this result, finding no transmissions associated with a combined 126,000 condomless sex acts: in other words, zero risk.

HPTN 052 catalyzed a sweeping revision of HIV policy goals. Starting treatment for people with HIV became a central pillar of HIV-prevention efforts, which had previously focused on promoting condom use, abstinence, monogamy, and circumcision. Treatment policy changed, too. Whereas access to ART was previously rationed to people with low CD4+ lymphocyte counts, in 2015 the World Health Organization (WHO) recommended that all people with HIV start ART at the time of diagnosis, an approach known as “test and treat.” Nearly all countries have adopted this strategy. Although the WHO recommendation was precipitated by the

publication of the INSIGHT START and TEMPRANO trials, which showed that early treatment reduces HIV-related morbidity, it was the preventive benefits of ART that justified the allocation of scarce resources to early ART and placed the test-and-treat approach at the center of contemporary HIV policy.

Since 2016, activists have popularized and clarified the science of TasP under the slogan “undetectable equals untransmittable,” or “U=U.” The U=U consensus statement has been endorsed by governments and organizations in more than 100 countries.

The U=U campaign promotes the message that “all people living with HIV have a right to accurate and meaningful information about their social, sexual, and reproductive health.” When it comes to TasP, however, global and national policymakers haven’t delivered on this promise. Treating HIV is among the most effective ways to prevent transmission. Yet in many countries, TasP isn’t broadly emphasized in public health information campaigns, HIV-education curricula, or HIV counseling. A review of 40 recorded HIV post-test counseling sessions in South Africa found that none mentioned prevention as one of the benefits of treatment.³ The 2020 UNAIDS Global AIDS Update relegated U=U to a brief mention before dismissing the approach as impractical and potentially harmful, if people believe they are virally suppressed when they are not.

Failure to disseminate the data on TasP has led to global knowledge gaps. In a systematic review of 72 studies published between 2008 and 2020,² we found that awareness of TasP was greatest

among men who have sex with men living in the Global North; yet even in this population, there are misperceptions about transmission risks. Data from sub-Saharan Africa suggest that many patients, clinicians, and members of the public aren’t aware of TasP. Students at an urban South African university believed the annual risk of transmission in a mixed-status couple in which the partner with HIV had suppressed virus was 73%, on average. Men in Uganda thought it was very unlikely that a mixed-status couple could remain so, even with ART that suppresses the virus. There are also knowledge gaps in the Global North: just 2% of women in a U.S. study named TasP as an effective HIV-prevention strategy.²

Beyond the ethical arguments supporting increased promotion of TasP, holding back information about this strategy may limit the effects of test-and-treat efforts on HIV incidence, morbidity, and mortality. UNAIDS estimates that 5.3 million people know they have HIV but aren’t on treatment. For some people diagnosed with early-stage HIV infection — the target population for the test-and-treat approach — the clinical benefits of ART, though substantial, may not outweigh the perceived costs, including psychosocial costs associated with status acceptance, stigma, and disclosure. The preventive benefits of ART could be a strong source of motivation to start and stay on therapy. However, many people with HIV are counseled to start ART solely for their own health, without mention of the opportunity, once the virus is suppressed, to protect their sex partners from infection and to


have condomless sex without fear of HIV transmission (including transmission to children, in the case of pregnancy).

There is growing evidence that sharing information on TasP leads to clinical benefits. Two randomized trials in the United States found significant improvements in treatment adherence and viral suppression when information on TasP was added to counseling interventions.² A South African randomized trial found that messaging related to U=U increased uptake of HIV testing among men invited to test by community outreach workers.⁴ Several qualitative studies have revealed lower internalized stigma among people with HIV after they learned about TasP.

Perhaps the greatest potential for benefit is in disseminating information about TasP at the community level. In a cluster-randomized trial in Malawi,⁵ villages received an educational workshop on TasP or a general HIV-education workshop excluding this information. Community dissemination of TasP information resulted in increased knowledge, lower stigma, and higher rates of HIV testing. Behavioral effects were driven not by people’s own beliefs about TasP, but by their perceptions of what other community members believed. The trial was conducted before Malawi implemented a test-and-treat strategy. TasP may provide even stronger motivation for people to learn their HIV status, now that all people with HIV are eligible for treatment. To date, there has been no rigorous evaluation of the effects of community-level dissemination of TasP information on ART uptake or viral suppression.

Why hasn't the science of TasP been disseminated more aggressively? One factor is the fear of unintended consequences. Clinicians worry that people may misinterpret the science or not know their true viral load and inadvertently transmit HIV. People who have condomless sex are also at risk for other sexually transmitted infections and unintended pregnancy. In places where people don't have access to viral-load monitoring, it may be difficult to rely on TasP as a sole HIV-prevention strategy. Acceptability also depends on the extent to which people without HIV trust their partners to adhere to therapy.

U=U also challenges deeply held beliefs about HIV. For 40 years, public health messaging has emphasized that people with HIV must use condoms or abstain from sex to avoid transmitting HIV. Perversely, this message has discouraged HIV testing, disclosure, and ART uptake among people who wish to

 An audio interview with Prof. Bor is available at [NEJM.org](https://www.nejm.org)

have condomless sex. The science supporting TasP breaks this link: people with HIV can have condomless sex without fear of transmission so long as the virus is suppressed. In populations in which people understand that viral suppression eliminates transmission risk, acceptability of TasP is high.²

Sharing information on TasP and U=U is important not only from an ethical standpoint; there is growing evidence that it's good clinical and public health practice. Countries around the world are now seeing the potential of U=U. For example, the South Africa Department of Health is launching a national campaign in 2022. The HPTN 052 trial established TasP as a cornerstone of the global HIV policy response. In the second decade of TasP, we believe it's essential to ensure that the science is disseminated to all who stand to benefit.

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From the Department of Global Health, Boston University School of Public Health

(J.B.), and the Fenway Institute (K.H.M.) — both in Boston; the Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg (D.O.); and the Prevention Access Campaign, New York (B.R.).

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E66.01 and Our Culture of Shame

Scott Hagan, M.D.

“You’re going to be disappointed in me!” was how he opened our visit.

The problem list included non-alcoholic steatohepatitis, atrial fibrillation, and a body-mass index (BMI) of 42 standing in the way of his candidacy for knee replacement. Having faithfully committed to a structured weight-loss program for the previous year, my patient had initial success, but most of the pounds came back. “I know, I know, it’s no good. I

have been bad lately,” he confessed with a sheepish grin.

Metabolic surgery was off the table. One of his relatives had had a severe complication, and he didn’t want to take that risk. We discussed the promising new option of an injectable glucagon-like peptide 1 (GLP-1) analogue. “A shot to lose weight?” he asked skeptically, but eventually he agreed to try it.

The request for a nonformulary drug required an associated

International Classification of Diseases, 10th Revision (ICD-10) diagnosis. Groaning as I typed “obesity,” I knew the search result I would select: “morbid (severe) obesity due to excess calories” (E66.01). Although “other obesity” (E66.8) and “obesity, unspecified” (E66.9) were also options, they lacked a more precise obesity classification, and I worried that they might not be convincing enough to justify an authorization for an expensive drug.