Treatment as prevention—a double hat-trick

Corbis

In the absence of a cure or a vaccine, new HIV infections continue to accumulate 30 years into the pandemic. By contrast, over the past 15 years, highly active antiretroviral therapy (HAART) has prevented progression to AIDS and death for millions of people. More recently, it has become increasingly apparent that HAART has a secondary preventive effect on HIV and tuberculosis transmission. As a result, the International AIDS Society, with the support of key international agencies, organised the International Treatment as Prevention Workshop.[1] At the end of the Workshop, it had become clear that treatment as prevention has progressed from a testable hypothesis to an urgent implementation priority.

Plasma HIV-1 RNA concentration is now accepted as a key driver of HIV transmission, and appropriate use of HAART is highly effective in reducing plasma HIV-1 RNA to undetectable levels, consequently decreasing HIV transmission. This reduction applies to vertical transmission,[2] serodiscordant heterosexual couples,[3] and injection drug use.[4,5] Lower community viral load, caused by the expansion of HAART coverage, has been associated with declining numbers of new HIV diagnoses in Taiwan,[6] British Columbia, Canada,[7,8] and San Francisco, USA.[9]

HPTN 052—a randomised trial of HIV serodiscordant couples—was halted by the data and safety monitoring board after a planned interim analysis.[10] The study[11] included HIV serodiscordant couples in whom the HIV-infected partner had CD4 cell counts between 350 and 550 cells per μL. Participating couples were randomly assigned so that the HIV-infected partner would receive immediate or deferred (defined as started after a CD4 cell count below 250 cells per μL, or an incident AIDS event) HAART. The investigators reported an impressive 96% decrease in the risk of HIV transmission with immediate HAART. Of note, immediate HAART was also associated with a 30% decrease in the combined endpoint of disease progression and death, and an 83% reduction in the incidence of extra-pulmonary tuberculosis.

For the past decade, we have struggled with the substantial tension between those advocating for the need to rigorously pursue every question before implementing treatment as prevention initiatives and those advocating for the research to be done as part of an implementation strategy. Nowadays, particularly in the wake of the compelling—although yet to be reported in detail—HPTN 052 results, we are no longer in equipoise. The evidence is clear: treatment conclusively prevents morbidity, mortality, and transmission. From this point on, these three endpoints should be considered together. Further, we urgently need new normative guidelines that fully incorporate treatment as prevention, without caveats. It would be unethical not to offer immediate HAART to serodiscordant couples.[12]

Starting immediately, we must deploy so-called Smart HAART Roll Out initiatives that incorporate a strong implementation science component so that evidence-based best practices can be adequately delineated. The entire cascade of care must be dissected and assessed as part of these efforts. Seek, Test, Treat, and Retain (STTR) initiatives[13] partially address one dimension of a much more complex picture.

Mathematical modelling has previously suggested that progressive expansion of HAART coverage would lead to proportional decreases in new HIV infections.[14] At the extreme, a universal test-and-treat strategy was suggested as a possible means to eliminate HIV;[15] however, others have contested this view.[16] Research

efforts are currently being deployed to address some of these important questions.[17,18] Unequivocal answers are urgently needed. Moreover, in view of present fiscal challenges and the impracticality of amassing evidence specific to every geographical region, culture, affected group, and population, it will be essential to foster collaboration, data harmonisation, and efficiency at all stages.

The evidence is in: treatment is prevention. Treatment dramatically prevents morbidity and mortality, HIV transmission, and tuberculosis. Furthermore, treatment prevents HIV transmission in vertical, sexual, and injection drug use settings; indeed, a very welcome double hat-trick. The challenge remains to optimise the impact of this valuable intervention. Failure to do so is not an option.

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1 International Treatment as Prevention Workshop. Vancouver, BC, Canada; May 4–6, 2011. http://www.cfenet.ubc.ca/events/international-workshop-treatment-prevention (accessed May 21, 2011).
2 Sturt AS, Dokubo EK, Sint TT. Antiretroviral therapy (ART) for treating HIV infection in ART-eligible pregnant women. *Cochrane Database Syst Rev* 2010; **3:** CD008440.
3 Donnell D, Baeten JM, Kiarie J, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *Lancet* 2010; **375:** 2092–98.
4 Wood E, Kerr T, Marshall BDL, et al. Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study. *BMJ* 2009; **338:** b1649. DOI:10.1136/bmj.b1649.
5 Kirk G, Galai N, Astemborski J, et al. Decline in community viral load strongly associated with declining HIV incidence among IDU. 18th Conference on Retroviruses and Opportunistic Infections; Boston, MA, USA; Feb 27–March 2, 2011: 484 (abstr). http://www.retroconference.org/2011/Abstracts/42134.htm (accessed May 21, 2011).
6 Fang CT, Hsu HM, Twu SJ, et al. Decreased HIV transmission after a policy of providing free access to highly active antiretroviral therapy in Taiwan. *J Infect Dis* 2004; **190:** 879–85.
7 Montaner JSG, Hogg R, Wood E, et al. The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic. *Lancet* 2006; **368:** 531–36.
8 Montaner JSG, Lima VD, Barrios R, et al. Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. *Lancet* 2010; **376:** 532–39.
9 Das M, Chu PL, Santos GM, et al. Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. *PLoS One* 2010; **5:** e11068.
10 National Institute of Allergy and Infectious Diseases. Treating HIV-infected people with antiretrovirals protects partners from infection: findings result from NIH-funded international study. May 12, 2011. http://www.niaid.nih.gov/news/newsreleases/2011/Pages/HPTN052.aspx (accessed May 12, 2011).
11 National Institute of Allergy and Infectious Diseases. The HPTN 052 Study: Preventing Sexual Transmission of HIV with Anti-HIV Drugs. May 12, 2011. http://www.niaid.nih.gov/news/QA/Pages/HPTN052qa.aspx (accessed May 12, 2011).
12 The Lancet. HIV treatment as prevention—it works. *Lancet* 2011; **377:** 1719.
13 Volkow N, Montaner J. Enhanced HIV testing, treatment, and support for HIV-infected substance users. *JAMA* 2010; **303:** 1423–24.
14 Lima VD, Johnston K, Hogg RS, et al. Expanded access to highly active antiretroviral therapy: a potentially powerful strategy to curb the growth of the epidemic. *J Infect Dis* 2008; **198:** 59–67.
15 Granich RM, Gilks CF, Dye C, DeCock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. *Lancet* 2009; **373:** 48–57.
16 Wagner BG, Kahn JS, Blower S. Should we try to eliminate HIV epidemics by using a "Test and Treat" strategy? *AIDS* 2010; **24:** 775–76.
17 International Treatment as Prevention Workshop. WHO references for ART in prevention. http://www.cfenet.ubc.ca/node/5543 (accessed May 21, 2011).
18 Dieffenbach CW, Fauci AS. Universal voluntary testing and treatment for prevention of HIV transmission. *JAMA* 2009; **301:** 2380–82.