

*Medicine and society***The use of highly active retroviral therapy to reduce HIV incidence at the population level**

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In this article, we will argue that the widespread use of highly active antiretroviral therapy has the potential to reduce the incidence of HIV at the individual and population level (Table 1). However, this approach has been overlooked by public health specialists as a viable prevention strategy. Other practical interventions such as education and the use of condoms and clean needles have helped to reduce the transmission of HIV worldwide. Once proven effective, safe and culturally accepted, biomedical interventions such as vaccines, topical microbicides, pre- and post-exposure prophylaxis and male circumcision offer further potential to prevent HIV transmission. Despite such advances, the global number of new HIV infections continues to increase at an alarming rate. It is therefore timely to explore other possible means to curb the growth of the epidemic.

Clinicians and researchers have long recognized the role that highly active antiretroviral therapy can play in preventing HIV/AIDS. High-quality clinical trials have demonstrated that highly active antiretroviral therapy successfully prevents mother-to-child transmission by lowering maternal plasma concentrations of HIV type 1 (HIV-1) RNA.¹ As a consequence of widespread access to highly active antiretroviral therapy, mother-to-child transmission of HIV in industrialized nations has become exceedingly rare.² Observational studies have also reported that this therapy can decrease the risk of HIV transmission from percutaneous exposure and between serodiscordant couples by reducing the concentration of HIV RNA in infected people.²

Highly active antiretroviral therapy has also been shown to reduce the concentration of HIV-1 RNA in semen, the rectum and the female genital tract.² Furthermore, in a major study from Uganda, no cases of HIV transmission were identified among couples in which the index case had a level of HIV-1 RNA less than 1500 copies/mL.² A dose-response effect was also reported in a Thai study, in which no cases of HIV transmission were observed if the index case's serum level of HIV-1 RNA was less than 1100 copies/mL.³ Finally, an observational study of serodiscordant couples in Spain showed that no HIV seroconversions took place in the sexual partners of patients who had received highly active antiretroviral therapy.⁴ This therapy was independently associated with an 80% reduction in HIV transmission.⁴

At the population level, access to highly active antiretroviral therapy has been temporally associated with substantial reductions in HIV incidence.⁵ For example, population-based research in Taiwan found a 53% (95% confidence interval [CI] 31%–65%) reduction in new positive HIV test results after the introduction of free access to highly active

Key points

- Expanded access to highly active antiretroviral therapy for patients with a medical indication will reduce AIDS-related morbidity and mortality and may reduce HIV incidence.
- "Treatment as an aid to prevention" has been overlooked as a viable public health strategy.
- The biological impact of highly active antiretroviral therapy on HIV transmission has been demonstrated at the patient level.
- There is a need to prospectively validate and quantify the preventive impact of highly active antiretroviral therapy on the incidence of HIV at the population level.

antiretroviral therapy.⁶ There was no change in the rate of syphilis infections, which was used as a surrogate marker for sexual risk behaviour during the study. In Uganda, expanded access to all clinically eligible people was projected to decrease HIV incidence by 11.2% (interquartile range 1.8%–21.4%).⁷ In Canada, new yearly HIV infections in British Columbia decreased by about 50% after the introduction of highly active antiretroviral therapy between 1995 and 1998 and has remain unchanged since then despite a noticeable increase in the rate of syphilis infections.⁵ It has been also been suggested that the preventive impact of expanded access to highly active antiretroviral therapy increases along with the number of people treated.⁷

The use of "treatment as an aid to prevention" is not new in the context of public health management of infectious diseases. For example, treatment of pulmonary tuberculosis and recurrent genital herpes prevents disease progression and reduces the risk of transmission.⁸ However, public health policy-makers and program managers have been reluctant to accept this strategy as viable for preventing the growth of the HIV/AIDS epidemic. Critics have argued that the preventive impact of expanded access to highly active antiretroviral therapy may be overridden by increases in HIV risk behaviours. This notion is supported by an ecological study that found widespread access to this therapy among men who have sex with men did not reduce HIV incidence and was associated with elevated risk behaviours.⁹ However, a recent meta-analysis evaluating the impact of highly active antiretroviral therapy use on sexual behaviours found no statistically significant increase in sexual risk behaviours among people receiving treatment (odds ratio 0.92, 95% CI 0.65–1.31).¹⁰

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Table 1: Potential challenges and successes of expanded access to highly active antiretroviral therapy to all people with a medical indication

Potential challenges	Potential successes
<ul style="list-style-type: none"> Limited knowledge of HIV status among infected people 	<ul style="list-style-type: none"> Decreased AIDS-related morbidity
<ul style="list-style-type: none"> Extensive and innovative strategies for vulnerable and hard-to-reach populations 	<ul style="list-style-type: none"> Decreased AIDS-related mortality
<ul style="list-style-type: none"> Increases in risk behaviour while receiving highly active antiretroviral therapy (e.g., treatment optimism, risk compensation) 	<ul style="list-style-type: none"> Reduced HIV incidence
<ul style="list-style-type: none"> Incomplete adherence to highly active antiretroviral therapy 	<ul style="list-style-type: none"> Reduced HIV prevalence in the long term
<ul style="list-style-type: none"> Increases in population-level drug resistance and adverse events 	<ul style="list-style-type: none"> Intermediate and long-term decrease in health care costs
<ul style="list-style-type: none"> Increased short-term health care costs 	<ul style="list-style-type: none"> Health care cost savings because of fewer HIV infections

Some have argued that successful treatment is too difficult for patients to initiate at a comparatively early stage of their illness. Indeed, we agree that people with HIV should be encouraged to initiate treatment only when clinically eligible. Yet even though some infections occur in the acute stages of a patient's infection, often before HIV infection is diagnosed, many exposures occur when patients are already aware of their serostatus and when patients are eligible for therapy. Furthermore, the reality is that highly active antiretroviral therapy coverage in Canada is suboptimal. It is estimated that over 50% of Canadians infected with HIV access treatment either late or not at all. Thus, increasing access to highly active antiretroviral therapy in Canada will result in decreased AIDS-related morbidity and mortality as well as potentially fewer infections.

Concerns have also been raised to suggest that treatment as an aid to prevention might cause a rise in population-level viral drug resistance, thus reducing the preventive benefit of highly active antiretroviral therapy on HIV transmission. Yet, population-based mathematical modelling suggests that expanded access would only be associated with a small increase in population-level drug resistance and would therefore have a limited adverse impact on HIV transmission.¹¹ Adding to this finding, studies suggest that transmission of HIV from people with drug-resistant viral strains to serodiscordant contacts is reduced compared with people with wild-type HIV strains.¹²

The Swiss National AIDS Commission recently put forward a statement suggesting that people with HIV who adhere to highly active antiretroviral therapy, who have undetectable viral loads and who have no sexually transmitted infections are not infectious.¹³ As a result, the need to prospectively validate and quantify the effect of this therapy on HIV prevention has grown substantially. Treatment as an aid to prevention should be explored in diverse settings, including in developed and developing countries. There are several research strategies that could help inform this debate. For instance, serodiscordant couples could be randomized to initiate highly active antiretroviral therapy at different CD4 thresholds to determine if greater periods of plasma viral load suppression are related to reduced HIV transmission. Community-based trials could also be used to measure longitudinal patterns of plasma HIV RNA and HIV incidence associated with expanded uptake of highly active antiretroviral therapy. Evidence derived from these

research efforts will decrease AIDS-related morbidity and mortality and inform policy-makers about the role of treatment as an aid to prevention.

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