A Made-in-Canada Strategy to Stop HIV and AIDS

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TREATMENT OF HIV/AIDS

While an outright cure and a preventive vaccine for HIV/AIDS remain elusive, remarkable advances have taken place over the last two decades with regard to HIV therapeutics.[1] Most significant among them has been the development of Highly Active Anti–Retroviral Therapy (HAART).[2] HAART refers to a combination of antiretroviral drugs, typically three, that can fully suppress HIV replication.[3] With the use of HAART, the number of HIV–1–viral copies in plasma rapidly becomes undetectable, as measured by the most sensitive commercially available plasma HIV–1–viral load assays. This allows immune reconstitution to take place, arresting the otherwise fatal course of the disease. HIV disease can therefore be put into remission on a long–term basis. Dramatic HAART–related reductions in morbidity and mortality in HIV–infected patients have been shown in clinical trials and observational studies.[4,5] By 2006, it was estimated that at least three million years of life were saved in the United States as a direct result from the roll out of HAART.[6]

TREATMENT AS PREVENTION

Recently, a rapidly growing body of evidence has suggested that expansion of HAART coverage can offer a substantial positive synergy towards the reduction of HIV transmission.[7-13] HAART and effectively suppresses viral replication rendering the plasma HIV–1–viral load undetectable on a sustained basis. As a result, HAART also decreases HIV–1–viral load in other biological fluids; including semen and vaginal secretions.[14,15]

Strong proof of principle regarding the impact of HAART on HIV transmission is found in the vertical transmission setting.[16] In this scenario, HIV transmission is virtually eliminated when HAART is appropriately used.[17]

A preventive role of HAART has also been demonstrated in HIV sero–discordant heterosexual couples. Attia *et al* completed a meta–analysis involving over 1000 person years (the sum of actual observation times for each patient) from five different cohorts, which showed that no events of HIV transmission were documented when the index patient was receiving antiretroviral therapy and had a viral load below 400 copies/mL.[18]

More recently, we were interested in evaluating the potential secondary benefit of HAART on HIV transmission among injection drug users.[14] Our results showed, for the first time, that the "community plasma HIV–1–-RNA level" directly correlated with HIV incidence in this community. Further, we showed that increased HAART uptake in this community was a major driver for decreasing the community plasma HIV–1–RNA level.

At the population level, the effect of the initial roll out of HAART on HIV transmission has also been reported. In Taiwan, this was associated with a 53% reduction in new HIV–positive diagnoses between 1996 and 1999.[20] In British Columbia, Canada, new yearly HIV diagnoses decreased by approximately 50% between 1995 and 1998 following the introduction of HAART.[8] Of note, while the changes described in Taiwan occurred against a background stable syphilis rate, which serves as a marker of high–risk sexual behavior in the community, syphilis rates steadily increased in British Columbia over the same period.[21]

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Based on the British Columbia experience described above, Lima et al estimated the potential decrease in HIV incidence that would be associated with stepwise increases in HAART coverage.[22] Overall, the model suggested that increased HAART coverage leads to proportional decreases in HIV transmission, which is not overwhelmed by decreasing adherence or increasing resistance rates.

Our proposed "Treatment as Prevention" strategy was initially regarded as controversial; however, this notion has

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gained the support of the international community in recent years. In fact, as recently as January 2009, investigators based at the World Health Organization's AIDS program published a paper in The Lancet,[13] which independently validated this approach. Further, in February 2009, an International Summit co–convened by the International AIDS Society, the World Bank and the Global Fund in Vancouver, called for further expansion of HAART in the developing world centered on the proposed "Treatment as Prevention" initiative.[23]

COLLATERAL BENEFITS OF HAART

As discussed above, the benefit of HAART on AIDS–related morbidity and mortality is quite clearly established. HAART is widely accepted to be highly cost–effective based on its effect on reducing AIDS–related morbidity and mortality. In addition, appropriate use of HAART can substantially decrease HIV transmission, rendering HAART potentially cost–averting. Several other significant collateral benefits of HAART have also been described, which further enhance the individual and public health value of this intervention.[24]

HAART has been shown to substantially reduce tuberculosis burden.[25] Of note, this benefit has the potential to impact not only those infected with HIV but also the community at large. HAART has also been shown to substantially enhance maternal health, which is particularly crucial in the African context, where families are currently being devastated by the effect of the HIV pandemic. Specifically, "motherless children" are ten times more likely to die within two years of their mother's death.[26] In a recent study, HAART programs in this context were associated with a 95% decrease in mortality in HIV–infected adults, an 81% reduction in mortality in their uninfected children and a 93% decrease in the number of orphans, in a Ugandan cohort.[27] Additionally, antiretroviral therapy use in HIV–infected mothers after delivery allows for safe breast–feeding which simultaneously can prevent HIV infection in the newborn as well as prevent diarrhea attributed to formula feeding with contaminated water, which is frequent in that setting.[28]

Other collateral benefits of expanded HAART coverage have been reported, including its ability to preserve the integrity of the health care system by protecting the health work force.[29] HIV infection is estimated to already afflict 20% of the nursing force in South Africa.[30] Even greater impact can be seen in other work forces; notably among them is the mining force where the death toll from HIV is currently estimated at 60% in those aged thirty to fourty-four years. As a result, HIV has led to decreased productivity and lower exports. It is estimated that the AIDS pandemic has reduced the average national gross domestic product growth rates across fourty-one African countries by 2–4% per year.[31]

HAART therefore represents a powerful tool to decrease not only AIDS related morbidity and mortality, but also to decrease HIV transmission, prevent orphans, reduce tuberculosis burden, preserve the integrity of the population pyramid, and specially protect the productive demographic groups. As a result, HAART contributes significantly towards maintaining social stability and therefore prevents social unrest.

CONCLUSION

HAART has been associated with dramatic decreases in AIDS related morbidity and mortality. These benefits can be demonstrated regardless of the route of HIV infection. More recently, a secondary benefit of HAART has been demonstrated in its ability to decrease HIV transmission. Further, many other collateral benefits of HAART have been reported at the individual and societal level.

Based on the available evidence we urge for the immediate implementation of an aggressive strategy aimed at rapidly[32] expanding antiretroviral therapy coverage to all those in medical need, based on a liberal interpretation of current medical guidelines. This should be done with full respect of human rights, including the need to respect the privacy, and autonomy of HIV infected individuals.[33] Additionally, the expansion of HAART should be carried out within a comprehensive "combination prevention" framework.[34] It should also include enhanced case finding, as well as supportive and culturally sensitive strategies to promote, facilitate and support engagement and maintenance in care, particularly among hard to reach populations.

Implementation of this strategy will dramatically decrease AIDS–related morbidity and mortality, eliminate neonatal HIV infection, prevent orphanhood, decrease HIV transmission and maximize individual and societal collateral benefits of HAART, as described above. As such, the expansion of HAART here proposed represents a cost–averting proposition. In fact, the recognition of the dramatic direct and indirect benefits of expanded HAART use should serve as a strong motivation to strengthen the roll out of HAART in resource–limited settings.

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