

Background paper: Undetectable = Untransmittable

Introduction

Treatment is an important part of any HIV strategy. Antiretroviral therapy (ART)¹ has been proven to not only reduce AIDS-related deaths and adverse health outcomes [1] [2] [3] [4] [5] [6] [7], but also to achieve viral suppression, thus reducing the incidence rate of HIV [1] [4] [5] [7] [8] [9] [10] [11]. The effectiveness of ART is so robust that, according to a recent consensus statement from 13 leading AIDS researchers and AIDS organizations, once an undetectable viral load has been achieved and maintained for six months, the risk of HIV transmission is negligible to non-existent [12]. As part of its vision, the Canadian AIDS Society (CAS) recognizes the importance of prevention strategies in all forms. The availability of ART for all HIV positive individuals is an important part of any prevention strategy and should be taken as one branch of a multi-faceted approach to prevention. The Canadian AIDS Society takes the position that treatment in the form of antiretroviral therapy (ART) is an important part of prevention strategies, and should be taken as one branch of a multi-faceted approach to prevention, and that support from community-based AIDS service organizations is an important factor in facilitating adherence to an ART regime.

However, ART should never be forced upon a person living with HIV for the sake of public health. The person should be given all of the information about benefits (both personal and public health benefits) and risks of ART and be allowed to make the decision about whether or not to start and adhere to their treatment regimen without risk of repercussions for other medical or social services [7] [13] [14].

ART and HIV Prevention

According to *HIV Transmission: Guidelines for Assessing Risk*, there are five conditions which must be met for the transmission of HIV: 1) There must be a source of infection; 2) There must be a means of transmission; 3) There must be a host susceptible to infection; 4) There must be an appropriate route of entry to the target cells of the body; and, 5) There must be a sufficient level of virus delivered to establish infection [15]. ART is effective at reducing transmission because it reduces the HIV viral plasma load and the amount of detectable HIV RNA in “potentially infectious bodily fluids, including semen, cervicovaginal secretions, and anorectal secretions” [7] (p. 74). This limits the level of the virus delivered so that the 5th condition for transmission is difficult to meet.

¹ The terms ART and HAART are often used interchangeably. However HAART involves the use of multiple (sometimes 3 or 4) different ARTs in combination – often referred to as a ‘cocktail’. In general, when discussing prevention the academic and international literatures refer to ART more often than HAART in an effort to capture the full spectrum of ART. Therefore, ART is used here to refer to both ART and HAART.

In order to achieve virologic suppression a person living with HIV must be taking their medication as prescribed at a high level of adherence [7] [9]. Once viral suppression has been achieved and maintained for six months, the person living with HIV can be considered to have a negligible to non-existent risk of transmission [12]. After viral suppression is achieved, testing of viral load and CD4 count should continue at regular intervals to ensure that levels do not change [7] [9] [13] [14].

ART has been proven to be an effective method of prevention in multiple studies. The American Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents states that the current body of evidence “suggests that ART is likely to reduce the risk of transmission regardless of a person’s age, race, ethnicity, sex, gender identity, sexual orientation or HIV transmission risk category” [7] (p.3). In a systematic comparison of 12 mathematical models of the progression of HIV in South Africa, all 12 models showed a linear correlation between increased ART use and decreased HIV incidence [11]. Another two studies, which looked at population-based effects in British Columbia, showed that for every 1% increase in viral suppression among the population using ART, there was a 1% to 1.2% decrease in the number of new infections [1] [10]. Indeed, Montaner, and his colleagues in both studies showed that the effect of ART use was preventative not only in BC, but also internationally in studies in San Francisco, Taiwan, Baltimore, China and Kwazulu-Natal [1] [10]. In fact, the study in rural Kwazulu-Natal cited by Montaner showed that for every 10% increase in ART coverage, there was a corresponding 17% decrease in the rate of infection [16].

The effectiveness of ART as a tool for prevention is so clear that the Joint United Nations Programme on HIV/AIDS (UNAIDS) stated that HIV treatment is “critical to ending the AIDS epidemic and making HIV transmission rare” [3] (p. 3). Treatment is such an important part of the 90-90-90 strategy that UNAIDS has stated that “as a prevention tool, HIV treatment should be seen as a critical component of evidence-based approaches” [3] (p. 4). Indeed, the use of and adherence to ART is the key factor in two of the three main goals for the elimination of AIDS by 2030, which the Government of Canada has endorsed [17]: 90% of HIV positive individuals who know their status will be on treatment; and, 90% of individuals who are on treatment will achieve viral suppression [3].

However, an important part of using ART as a form of prevention is having people living with HIV taking their medication at a high level of adherence [7] [9], and this is difficult to achieve without a support network in place. Community-based AIDS service organizations, which are part of the medical and social delivery model already in place, are a key player in providing that support, especially for those with high CD4 cell counts who may not see immediate benefits to taking ART. The support of the community is so important that it has been noted that implementing a 90% ART adherence rate for people living with HIV will not be possible without focusing more on care models that are “patient-centered, decentralised and outside of health facilities” [5], and that community-based support networks can provide care and a chance to be removed from a potentially stigmatizing environment [5].

Prevention of sexual transmission

Treatment has been proven to have a significant preventative effect on sexual transmission of HIV [1] [2] [6] [7] [8] [9] [10] [11] [12] [16] [18]. The effect of treatment is so strong that, according to a consensus statement signed by 13 highly respected researchers and AIDS organizations, once viral suppression is achieved and sustained for more than 6 months the risk of transmission drops to a negligible rate [12]. One researcher pointed out that in over 10,000 person-years of follow-up during research there were

zero transmissions from people with a suppressed viral load [12]. One study showed that the correlation between the number of individuals on ART and the number of new diagnoses per year was -0.89 ($p < 0.0001$) [1] (p. 534). Mathematically speaking, these values provide very strong evidence that there is a link between the number of people taking ART and the number of new HIV cases, with new cases decreasing when more people take ART.

The randomised control trial HPTN 052 showed a 96% reduction in transmission among serodiscordant couples given early ART, with the results being so significant that the study was stopped early so that all participants could benefit from the effects of early ART [18]. In the consensus statement, the lead researcher in the HPTN study stated that “if people are taking their pills reliably and they're taking them for some period of time, the probability of transmission in this study is actually zero” [12]. These results, and the results of many other studies, support the statement that treatment should be seen as a critical component of evidence based approaches to HIV prevention [3].

Prevention of vertical transmission

ART has been identified as an important tool for reducing transmission from mother to child during pregnancy, childbirth, and breastfeeding [1] [2] [7] [8] [9] [10]. According to health policies in the USA as well as the recommendations of both UNAIDS and the International Antiretroviral Society – USA Panel, pregnant and breastfeeding mothers should be given access to ART to prevent transmission to their unborn child [2] [7] [9].

Prevention of transmission among people who inject drugs

Evidence also exists that use of ART can have a preventive effect in communities of people who inject drugs [1] [7] [10] [19]. Although the evidence of the preventative effects is not as widely studied or as highly significant as the evidence for treatment as prevention for sexual transmission, the evidence is still significant, and adherence to an ART regimen has the added benefit of frequent contact with medical staff to monitor other conditions, and offer support and addiction treatment advice as needed or desired. Montaner et al. [10] note that the progressive drug policies including needle exchange and opioid substitution of British Columbia could have had both a facilitative effect on the expansion of ART, and an effect on decrease in transmission rates. Thus, correlation between higher ART coverage and lower transmission of HIV among people who inject drugs could have had a confounding factor, and more study is needed.

Community involvement in prevention efforts

An important aspect of using treatment as a form of prevention is community buy-in. Treatment regimens cannot be forced onto anyone, and the individual must decide to adhere to the course of ART of their own volition [7]. One of the main “ways forward” to getting back on track to meeting the 90-90-90 targets in [2] is to increase community engagement in HIV testing and treatment programs and offer ART immediately to all HIV positive individuals regardless of CD4 count (p. 54). The importance of the community is also felt strongly in harm-reduction efforts among people who inject drugs with relatively small peer groups able to drive large changes in behaviour for both testing and starting/adhering to treatment [2]. There is interest to use ART as a tool for prevention among people living with HIV, with 45.2% of ART naïve individuals in the UK expressing interest in beginning ART immediately to reduce their infectiousness regardless of whether it would result in health benefits for themselves [20]. Since

using ART to improve Public Health outcomes and reduce incidence of HIV requires that the community agree to adhere to the medication, the ability of relatively small peer groups to drive large change would be very important in increasing the percent of people who are not on ART to start a regime and adhere to it even if they do not see immediate benefits for themselves.

Improving outcomes for people living with HIV along the continuum of care also includes expanding training to non-traditional providers in a patient-centred approach to facilitate ongoing engagement in care [2] [13]. One of the guiding principles of the Canadian AIDS Society is to support the empowerment of communities and the development of organizations that address the needs of people living with and affected by HIV and AIDS. Evidence shows that this is one of the best ways to improve outcomes for both testing and treatment, two branches of any successful prevention strategy. Community members are very well placed to drive change and not only encourage others to get tested but also support their peers during the initiation of ART [1] [2] [10] [13].

Conclusions

Given the body of evidence available, the Canadian AIDS Society takes the position that treatment in the form of antiretroviral therapy (ART) is an important part of prevention strategies, and that support from community-based AIDS service organizations is an important factor in facilitating adherence to an ART regime. As long as the human rights of the individual are respected, and individuals are given the choice to opt out of treatment without repercussions for other forms of therapy (as per the US guidelines [7]), then treatment should be seen as a preventative measure, and offered as such. Policies that support prevention efforts would be remiss to exclude treatment as part of their strategy.

References

- [1] J. S. G. Montaner, V. D. Lima, R. Barrios, B. Yip, E. Wood, T. Kerr, K. Shannon, P. R. Harrigan, R. S. Hogg, P. Daly and others, "Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study," *The Lancet*, vol. 376, pp. 532-539, 2010.
- [2] UNAIDS, Prevention Gap Report, Geneva, Switzerland: UNAIDS, 2016.
- [3] UNAIDS, 90-90-90 An ambitious treatment target to help end the AIDS epidemic, Geneva, Switzerland: UNAIDS, 2014.
- [4] R. Granich, S. Gupta, B. Hersh, B. Williams, J. Montaner, B. Young and J. M. Zuniga, "Trends in AIDS deaths, new infections and ART coverage in the top 30 countries with the highest AIDS mortality burden; 1990--2013," *PloS one*, vol. 10, p. e0131353, 2015.
- [5] S. Vella, "Addressing barriers to the end of AIDS by 2030," *The Lancet HIV*, vol. 2, pp. e360--e361, 2015.

- [6] M. S. Cohen, Y. Q. Chen, M. McCauley, T. Gamble, M. C. Hosseini, N. Kumarasamy, J. G. Hakim, J. Kumwenda, B. Grinsztejn, J. H. S. Pilotto and others, "Prevention of HIV-1 infection with early antiretroviral therapy," *New England journal of medicine*, vol. 365, pp. 493-505, 2011.
- [7] Panel on Antiretroviral Guidelines for Adults and Adolescents, Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents, Available at <http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf>: Department of Health and Human Services, 2014.
- [8] WHO; UNICEF; UNAIDS, Global update on HIV treatment 2013: Results, impact and opportunities, World Health Organization, 2013.
- [9] H. F. Günthard, M. S. Saag, C. A. Benson, C. Del Rio, J. J. Eron, J. E. Gallant, J. F. Hoy, M. J. Mugavero, P. E. Sax, M. A. Thompson and others, "Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2016 recommendations of the International Antiviral Society-USA panel," *JAMA*, vol. 316, pp. 191-210, 2016.
- [10] J. S. G. Montaner, V. D. Lima, P. R. Harrigan, L. Lourenço, B. Yip, B. Nosyk, E. Wood, T. Kerr, K. Shannon, D. Moore and others, "Expansion of HAART coverage is associated with sustained decreases in HIV/AIDS morbidity, mortality and HIV transmission: the "HIV Treatment as Prevention" experience in a Canadian setting," *PloS one*, vol. 9, p. e87872, 2014.
- [11] J. W. Eaton, L. F. Johnson, J. A. Salomon, T. Bärnighausen, E. Bendavid, A. Bershteyn, D. E. Bloom, V. Cambiano, C. Fraser, J. A. C. Hontelez and others, "HIV treatment as prevention: systematic comparison of mathematical models of the potential impact of antiretroviral therapy on HIV incidence in South Africa," *PLoS Med*, vol. 9, p. e1001245, 2012.
- [12] Prevention Access Campaign, *Consensus Statement*, Washinton, DC: Available at <http://www.preventionaccess.org/consensus>, 2016.
- [13] World Health Organization, Consolodated Guidelines on the use of Antiretroviral drugs for Treating and Preventing HIV Infection, Geneva, Switzerland: World Health Organization, 2016.
- [14] British HIV Association, British HIV Association guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy (2016 Interim update), London, UK: British HIV Association available online at <http://www.bhiva.org/documents/Guidelines/Treatment/2016/treatment-guidelines-2016-interim-update.pdf>, 2016.
- [15] Canadian AIDS Society, HIV Transmission: Guidelines for assessing risk, 5th Edition, Ottawa, Canada: Canadian AIDS Society, 2004.
- [16] F. Tanser, T. Bärnighausen, E. Grapsa, J. Zaidi and M.-L. Newell, "High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa," *Science*, vol. 339, pp. 966-971, 2013.

- [17] Government of Canada, "World AIDS Day - December 1, 2015 [Official Statement]," 01 12 2016. [Online]. Available: <http://news.gc.ca/web/article-en.do?nid=1022689>. [Accessed 14 11 2016].
- [18] The INSIGHT START Study Group, "Initiation of antiretroviral therapy in early asymptomatic HIV infection," *N Engl J Med*, vol. 2015, pp. 795-807, 2015.
- [19] E. Wood, T. Kerr, B. D. L. Marshall, K. Li, R. Zhang, R. S. Hogg, P. R. Harrigan and J. S. G. Montaner, "Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study," *British Medical Journal*, vol. 338, p. b1649, 2009.
- [20] A. J. Rodger, A. Phillips, A. Speakman, R. Gilson, M. Fisher, E. Wilkins, J. Anderson, M. Johnson, R. O'Connell, S. Collins and others, "Attitudes of people in the UK with HIV who are antiretroviral (ART) naive to starting ART at high CD4 counts for potential health benefit or to prevent HIV transmission," *PLoS one*, vol. 9, p. e97340, 2014.