The value of achieving optimal adherence with long-acting directly observed antiretroviral therapy (LA DOT ART) amongst patients living with HIV-1 infection: a modelling study

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Introduction

- Human Immunodeficiency Virus (HIV) is a human retrovirus infecting CD4+ cells which can lead to development of Acquired Immune Deficiency Syndrome (AIDS), a clinical condition developed at late stages of HIV infection. HIV and AIDS represent a significant global economic, clinical and humanistic burden [1, 2].
- Despite advances in antiretroviral therapies (ARTs) and improved access to treatment, over 35 million people were living with HIV/AIDS worldwide in 2017, with over 900,000 deaths attributed to HIV-related illnesses [3].
- Virologic suppression, the primary objective of ART treatment, reduces HIV-related morbidity and mortality, leading to increased quality of life, life years (LYs) and health outcomes, in addition to a significant reduction in the risk of onwards disease transmission [4, 5].
- Adherence to treatment is vital for ensuring HIV patients remain virally suppressed [6-8], with poor adherence a major determinant of virologic failure, drug resistance, disease progression, hospitalisations, mortality and health care costs [9, 10].
- The control and prevention of HIV infection therefore rely on adherence to treatment, with a proportion of people living with HIV (PLWH) failing to achieve optimal levels of adherence [9, 11-13].
- Several factors are involved in non-adherence to ART, with pill burden, dosing frequency, dietary restrictions and adverse effects most frequently reported [6, 14-17].
- Parenteral long-acting (LA) ART administered by healthcare professionals monthly or every two months are in development and will facilitate directly observed therapy (DOT) for HIV [18, 19].
- By removing the need for adherence to daily oral dosing and offering improved patient choice through alternative modes of treatment administration, the proportion of PLWH who are receiving and adhering to treatment may be improved, positively contributing to the UNAIDS 90-90-90 target to eliminate HIV.
- This study models the potential impact of improved treatment adherence and reduced subsequent HIV transmission with LA DOT.

Methods

- A decision tree and Markov cohort state transition model was adapted to model the impact of treatment adherence and disease transmission (Figure 1) [20-22].
- In order to focus on the impact of adherence in isolation, parity pricing and efficacy equivalence between LA DOT and oral therapy was assumed.
- Health states were defined by viral load and CD4 cell count.
- As LA DOT does not require adherence to daily dosing, the efficacy of LA DOT was modelled independently of adherence, assuming optimal adherence as observed in clinical trials.
- An 8.12% reduction in adherence to daily oral regimens in Canada was derived using published data reporting the proportion of patients experiencing at least one treatment interruption as well as average follow-up and average time to treatment resumption [23].
- Data on the relationship between treatment adherence and virologic suppression from Ross et al. were used to adjust virologic suppression in the standard of care arm (Figure 2, adapted from [24]).
- A Canadian perspective was adopted, with costs and quality-adjusted life-years (QALYs) discounted annually at a rate of 1.5%.

Figure 1. Model flow diagram

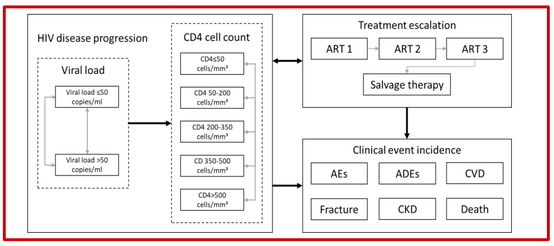
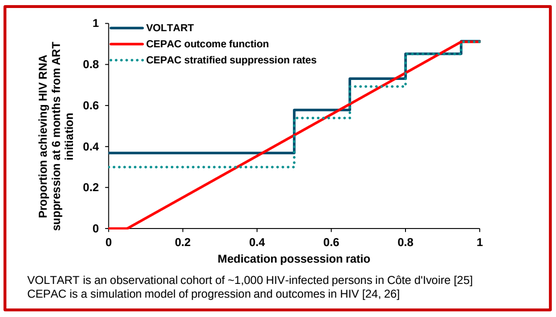


Figure 2. Relationship between adherence and viral suppression



VOLTART is an observational cohort of ~1,000 HIV-infected persons in Côte d'Ivoire [25]
CEPAC is a simulation model of progression and outcomes in HIV [24, 26]

Results

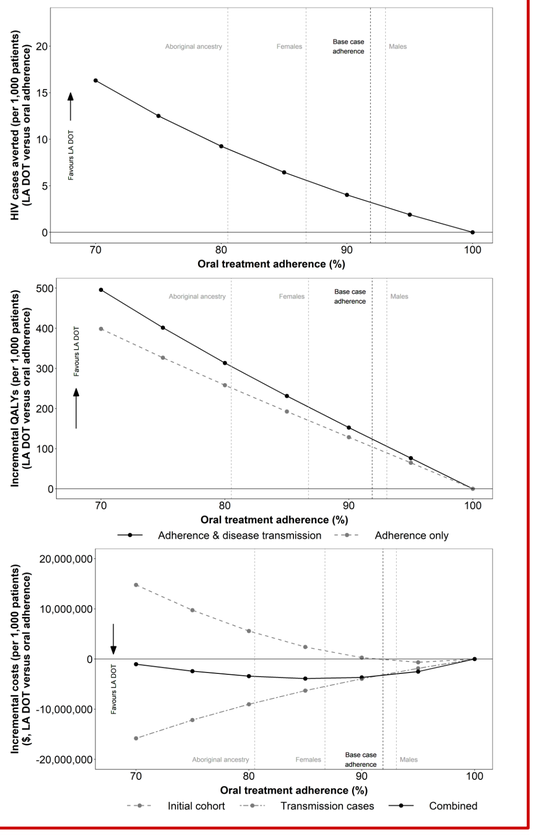
- Eliminating suboptimal adherence among PLWH in Canada in the model averted three new HIV cases, achieved lifetime cost-savings of $3.3 million as well as QALY and LY gains of 124 and 157, respectively, per 1,000 persons treated.
- Extrapolating these results to the Canadian prevalent HIV population, over the lifetime model horizon, resulted in 201 new HIV cases averted, lifetime cost savings of $211 million and QALY and LY gains of 7,816 and 9,917, respectively (Table 1).
- Figure 3 shows how variation in the level of adherence to oral treatment impacted the model results. As adherence to oral treatment decreases, LA DOT was found to result in increased numbers of HIV cases averted, increased incremental QALYs as well as a small increase in incremental costs.
- Greater benefits were estimated when assessing the impact in subgroups with lower adherence; such as women and people with aboriginal ancestry.
- Reduced adherence results in reduced viral suppression and increased rates of viral discontinuation. Patients who discontinue for virologic reasons progress more rapidly towards less effective and more costly salvage therapies. Patients who are not virally suppressed are also more likely to transmit HIV to others, leading to additional costs incurred and QALYs lost.

Table 1. Benefits of LA DOT extrapolated to the HIV-infected population of Canada

Population	Number of patients	Future transmission avoided	QALYs gained	LYs gained	Cost savings ($; CAD)
Canadian HIV prevalence (2016)					
Total	63,110	201	7,816	9,917	211,038,174
Aboriginal ancestry	6,055	54	1,847	2,319	21,113,702
Females	14,520	81	2,849	3,551	70,529,640
Males	48,590	130	5,177	6,605	139,978,013

CAD: Canadian dollar; LY: life year; QALY: quality-adjusted life-year

Figure 3. Impact of average baseline population treatment adherence on the incremental number of transmissions, QALYs and total costs (LA DOT vs oral adherence, per 1,000 patients)



Conclusions

- The elimination of suboptimal adherence to daily oral dosing in Canada is estimated to result in the avoidance of 201 new HIV cases averted in addition to cost savings of $211 million as well as substantial QALY and LY gains.
- In order to accurately quantify the benefits of HIV therapies with the potential to improve treatment adherence, such as LA DOT ART, the impact of treatment adherence needs to be accounted for.
- Providing PLWH and healthcare providers with novel modes of ART administration that enhance individualisation of treatment, leading to improvements in treatment adherence, may facilitate achievement of UNAIDS 90-90-90 objectives.

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