The potential effect of initiating combination antiretroviral therapy with Integrase Inhibitors on HIV transmission risk in British Columbia, Canada

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Background

- Integrase strand-transfer inhibitors (INSTI) represent one of the most efficacious classes of antiretroviral drugs currently available to achieve virologic suppression
- HIV transmission risk is highly dependent on plasma HIV-1 RNA (pVL) levels, which are very high at the early (acute) stage, drop significantly and remain stable during the chronic stage, and again rise in the late stage disease (AIDS)

Objectives

- Determine the difference in time to virologic suppression when initiating cART with INSTI-based regimens versus non-INSTI-based regimes
- Determine the difference in transmission risk during the period between cART initiation and virologic suppression for individuals on INSTI and non-INSTI based regimens

Methods

- The change in pVL from cART initiation to virologic suppression was calculated from a cohort of 1426 naïve individuals who initiated cART between 2011 and 2014 with at least one year of follow-up in BC, Canada; 191 individuals initiated cART with INSTI regimens (Fig. 1)
- HIV transmission risk was estimated as a function of pVL using two previously derived mathematical formulas (see Fig. 2 and references), and applied to a model of the HIV natural history (Fig. 3)
- The cumulative risk of HIV transmission (CRHT) was estimated as the number of days at-risk relative to the chronic stage of HIV from the area under the pVL curves
- Sensitivity analysis on the CRHT was performed by varying the pvL-related transmission risk at each stage of the HIV natural history (Tab. 1)

Figure 1: pVL change from cART initiation in HIV naïve individuals in BC, 2011-2014

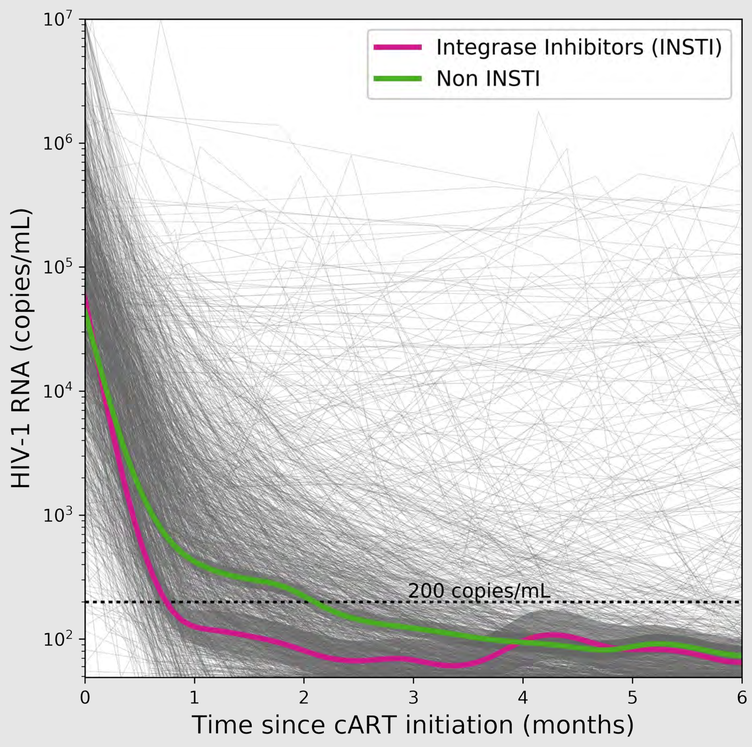


Figure 2: Mathematical models of pVL-related transmission risk

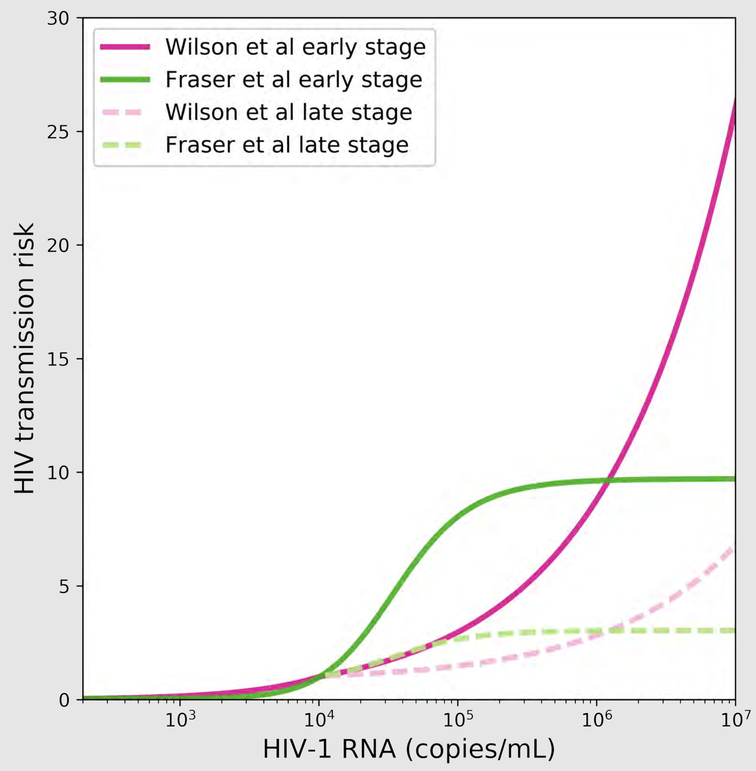


Figure 3: Transmission risk in the Wilson et al and Fraser et al models throughout the HIV natural history

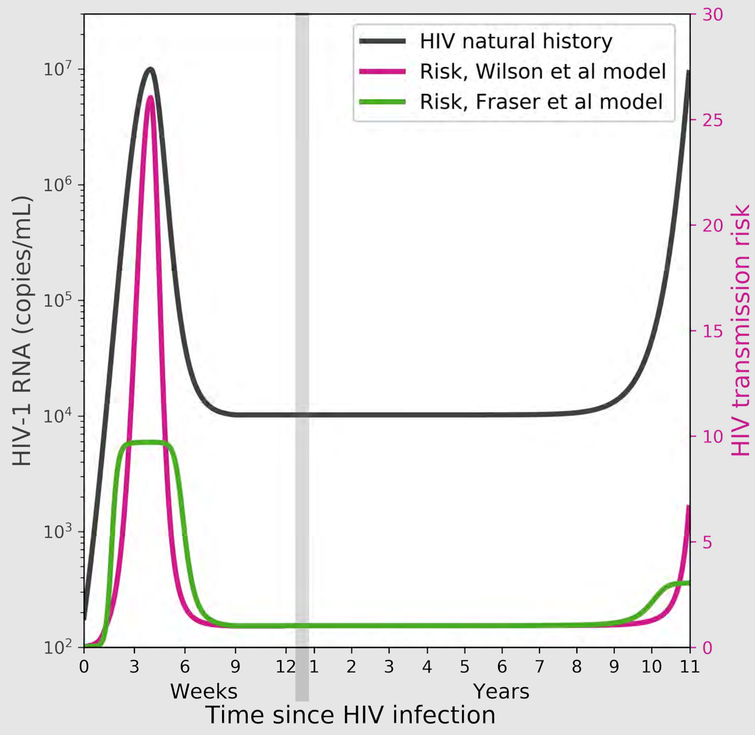


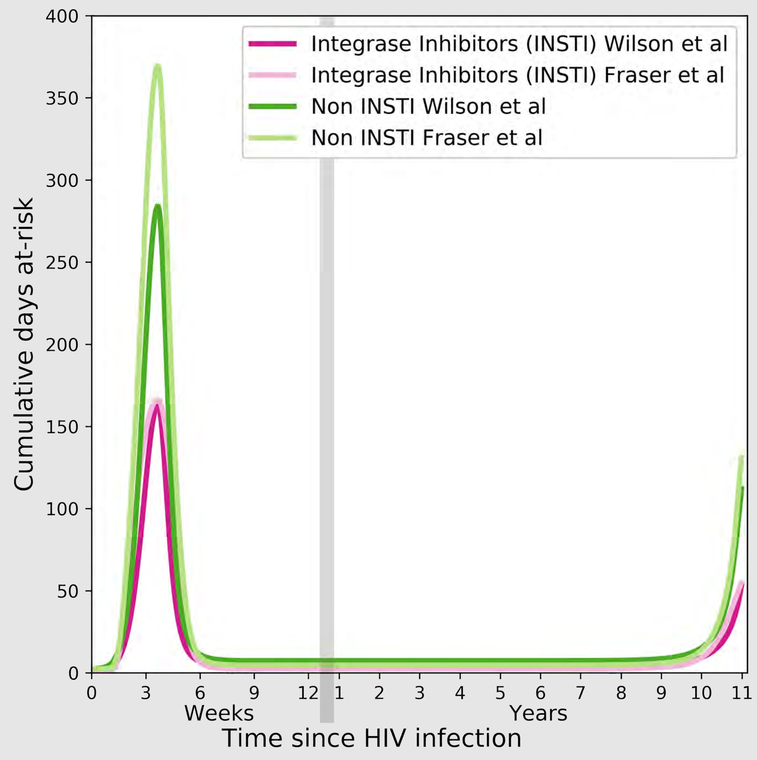
Table 1: Sensitivity Analysis on transmission risk at the acute, chronic and AIDS stages

Stage at ART initiation	INSTI regimens (Wilson/Fraser)			Non INSTI regimens (Wilson/Fraser)		
	Acute	Chronic	AIDS	Acute	Chronic	AIDS
Status quo	163.1/165.5	4.3/1.7	53.6/54.6	284.1/367.0	7.5/2.2	112.3/130.5
Risk, Acute stage						
+ 20%	186.4/189.0	4.3/1.9	58.7/60.1	318.5/419.1	7.5/2.5	119.8/142.4
- 20%	138.8/141.0	4.3/1.4	48.2/48.9	248.0/312.7	7.5/1.9	104.3/118.0
Risk, Chronic stage						
+ 20%	163.1/165.7	4.6/1.7	53.6/54.7	284.2/367.4	8.2/2.2	112.4/130.6
- 20%	163.0/165.3	4.0/1.6	53.6/54.6	284.0/366.5	6.7/2.2	112.2/130.4
Risk, AIDS stage						
+ 20%	163.1/165.5	4.3/1.7	113.0/73.5	284.1/367.0	7.5/2.2	216.5/201.8
- 20%	163.1/165.5	4.3/1.7	28.5/35.3	284.1/367.0	7.5/2.2	60.8/65.8

Results

- Time to virologic suppression for INSTI regimens was 22.5 days (95% confidence interval (CI) 19.8-26.3), compared to 64.0 days (95% CI 59.5-68.5) for non-INSTI regimens (Fig. 1)
- There was no statistically significant difference between the populations that achieve virologic suppression, whether on INSTI or non-INSTI regimens
- Averaged over the two models, CRHT when initiating cART in the chronic stage was estimated to be 3.0 days at-risk for INSTI regimens, compared to 4.9 days for non-INSTI regimens (Fig. 4)
- If cART were initiated in the acute stage, CRHT can be up to 164.3 days at-risk for INSTI regimens, compared to 325.6 days for non-INSTI regimens (Fig. 4)
- If cART were initiated in the AIDS stage, CRHT can be up to 54.1 days at-risk for INSTI, compared to 121.4 days for non-INSTI regimens (Fig. 4)

Figure 4: Cumulative risk of HIV transmission from cART initiation to virologic suppression



Conclusions

- INSTI regimens achieve faster virologic suppression than other regimens
- The difference in cumulative risk between INSTI and other regimens is small in patients initiating cART in the chronic stage of HIV
- Cumulative risk averted with INSTI regimens would be very high for individuals initiating cART in the acute stage, and still significant in the AIDS stage

References and Contact

- Wilson DP et al, Lancet 2008; 372 (9635):314-20
- Fraser C et al, Proc. Nat. Acad. Sci. 2007; 104 (44):17441-6

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