The potential to avert HIV incidence in MSM initiating ART with Integrase Inhibitors

Ignacio Rozada, Michelle Lu, Julio S.G. Montaner, and Viviane D. Lima

British Columbia Centre for Excellence in HIV/AIDS, Vancouver, British Columbia, Canada

Background

- Integrase strand-transfer inhibitors (INSTI) represent one of the most efficacious classes of antiretroviral treatments (ART) 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)
- Individuals can also be at risk of HIV transmission due to behavioral and biological determinants of risk, or the composition of their sexual networks

Objectives

- Determine the difference in time to virologic suppression when initiating ART with INSTI-based regimens versus non-INSTI-based regimes
- Estimate the amount of potential averted HIV incidence from ART-naïve men who have sex with men (MSM) initiating ART with INSTI regimens, considering different risk profiles and accounting for the stage of HIV infection at ART initiation

Methods

- HIV transmission risk due to the stage of HIV at ART initiation was estimated using two mathematical models (see Fig. 1 and references), and applied to a model of the HIV natural history (Figure 2)
- The change in pVL from ART initiation to virologic suppression was calculated from a subset of the HOMER cohort: 1743 naïve individuals who initiated ART between 2011 and 2015 with at least one year of follow-up in BC; 326 individuals initiated ART with INSTI regimens (Figure 3)
- HIV transmission risk due to individual risk behaviour was based on Momentum cohort data by dividing a simulated population into 4 groups based on HIRI-MSM scores (Table 1)
- Averted infections due to ART initiation on INSTI regimens were estimated for both mathematical models, by stage of HIV at ART initiation and by individual risk behaviour

Figure 1: Mathematical models of pVL-related transmission risk

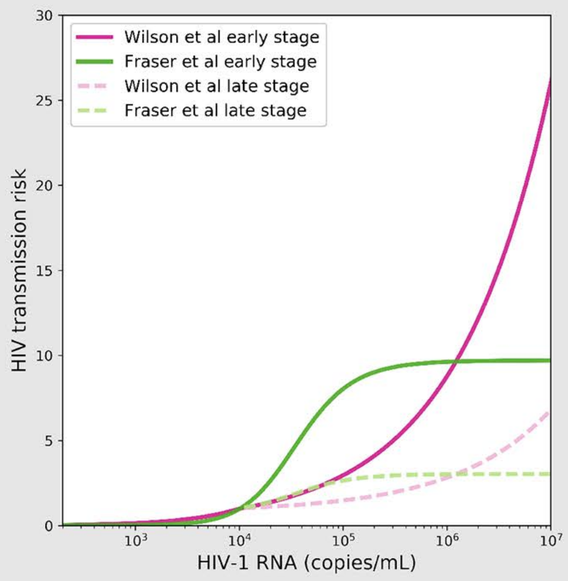

Figure 2: Relative transmission risk along the HIV natural history

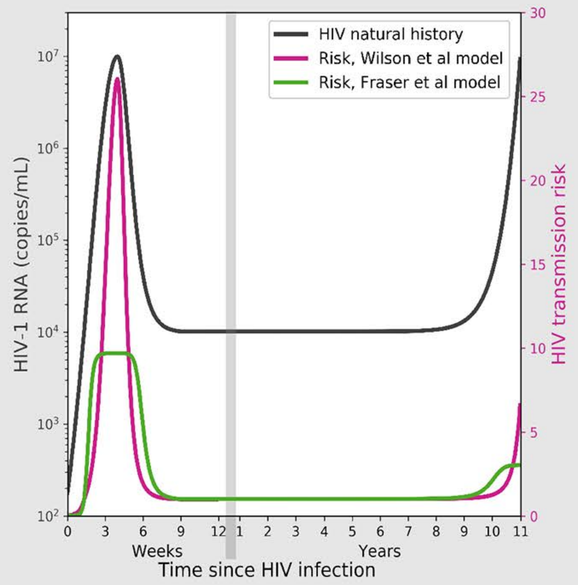

Table 2. Averted infections (per 1000 PY) by stage of HIV and risk group

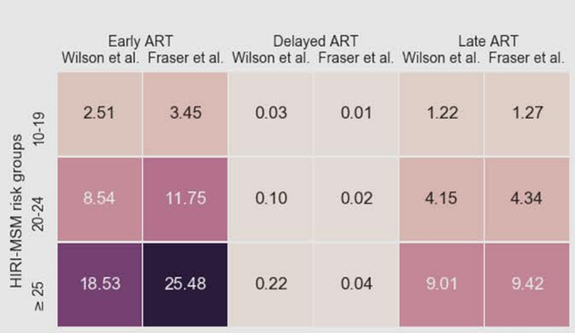

Table 3: Sensitivity analysis on transmission risk by stage of HIV

	INSTI-based regimens				Non INSTI-based regimens			
	Wilson et al.		Fraser et al.		Wilson et al.		Fraser et al.	
	Days 95% CI	% Diff.	Days 95% CI	% Diff.	Days 95% CI	% Diff.	Days 95% CI	% Diff.
Early ART initiation								
Status quo	167.3 (158.9-176.2)	--	168.7 (157.5-179.5)	--	287.8 (270.1-305.7)	--	383.5 (344.7-419.9)	--
+ 20%	191.3 (182.0-201.3)	14%	192.9 (180.0-205.2)	14%	322.4 (302.9-342.1)	12%	438.4 (394.1-480.0)	14%
- 20%	142.3 (134.9-150.1)	-15%	143.6 (134.0-152.8)	-15%	251.4 (235.6-267.3)	-13%	326.4 (293.4-357.3)	-15%
Delayed ART initiation								
Status quo	4.5 (4.3-4.7)	--	1.7 (1.7-1.7)	--	7.5 (7.1-7.9)	--	2.2 (2.1-2.3)	--
+ 20%	4.7 (4.5-5.0)	7%	1.9 (1.9-2.0)	14%	8.2 (7.8-8.7)	9%	2.5 (2.5-2.6)	14%
- 20%	4.1 (4.0-4.3)	-7%	1.4 (1.4-1.5)	-15%	6.8 (6.4-7.1)	-10%	1.9 (1.8-1.9)	-15%
Late ART initiation								
Status quo	54.7 (51.4-58.4)	--	55.6 (51.7-59.5)	--	113.7 (106.7-120.8)	--	134.9 (123.1-146.0)	--
+ 20%	134.2 (127.0-142.3)	145%	82.4 (76.0-89.9)	48%	247.0 (232.3-262.6)	117%	228.2 (211.4-244.0)	69%
- 20%	27.6 (25.9-29.4)	-50%	32.7 (30.7-34.7)	-41%	60.4 (54.8-66.0)	-47%	61.9 (56.5-67.9)	-54%

Figure 3. pVL change in ART-naïve individuals in BC, 2011-2015

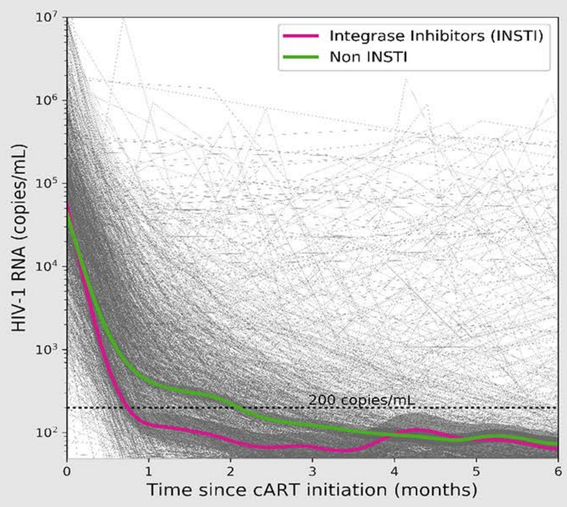

Table 1. Estimated risk characteristics of the HIV positive MSM population in BC in 2017

HIRI-MSM risk groups	<10	10 – 19	20 – 24	>= 25
Proportion	43.0%	30.7%	11.7%	14.5%
MSM Population (N)	17102	12210	4653	5767
MSM PLWH (N)	-	1199	1645	3562
Incident cases	-	42.1	57	119.5
Relative contact rate	-	1.0	3.4	7.4
Transmission cases	-	7.9	36.9	173.8
Transmissions per 1000PY	-	6.6	22.5	48.8

Results

- Time to first virologic suppression for INSTI regimens was 22.7 days (95% credible interval (CI) 20.7-25.4), compared to 64.4 days (95% CI 60.8-69.0) for non-INSTI (Figure 3)
- There was no statistically significant difference between the populations that achieve virologic suppression, whether on INSTI or non-INSTI regimens
- INSTI-Initiating HIRI-MSM$\geq$25 individuals are estimated to avert 0.04 (chronic stage), 9 (late stage), and 25 (early stage) incident cases per 1000 PY
- HIRI-MSM<20 individuals would avert less than 4 incident cases per 1000 PY independent of stage of HIV at ART initiation
- Individuals in the chronic stage would avert less than 0.3 incident cases per 1000 PY independent of HIRI-MSM risk group (Table 2)
- Estimates for the late stage of HIV were the most sensitivity to the transmission risk assumptions (Table 3)
- Number need to treat with INSTI to avert one incident case is $\simeq 40$ for high risk individuals that initiate ART in the early stage, but > 500 for individuals initiating ART in the chronic stage, independent of risk behaviour

Conclusions

- INSTI regimens achieve faster virologic suppression than other regimens
- Initiating high risk individuals on INSTI-based regimens has the potential to avert incident cases when compared to other regimens
- The potential gains are highly dependent on risk behavior and the stage of HIV at ART initiation

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

Ethics: H05-50123
I have no conflicts of interest
Contact: Ignacio Rozada, irozada@cfenet.ubc.ca