Predicting Factors of Detectable Viral Load in HIV infected patients: The PREDICTED-HIV Study

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LONDON
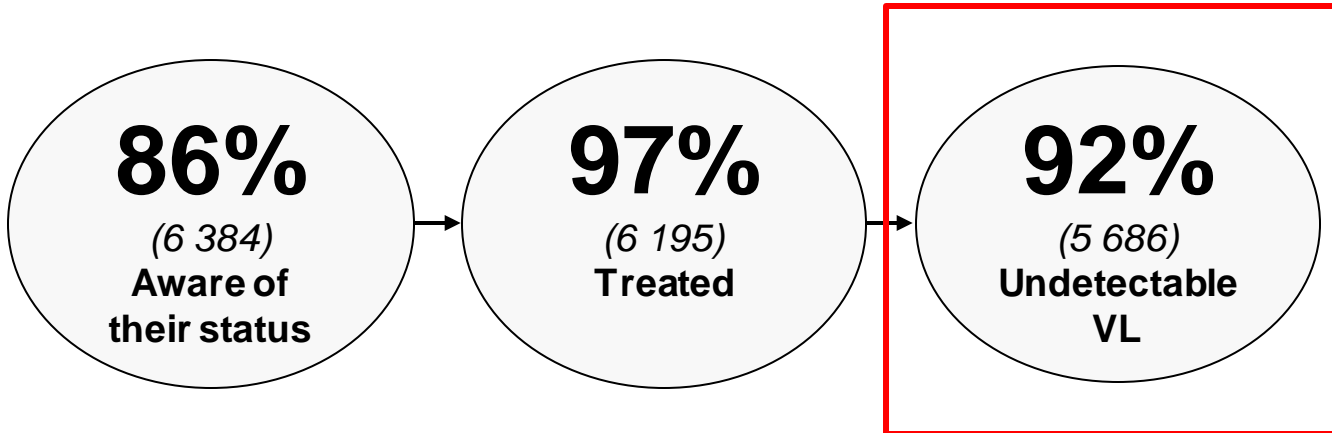FAST-TRACK CITIES 2019

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Introduction

Montreal's statuts on the 90-90-90 UNAIDS target:

86%
(6 384)
**Aware of
their status**

97%
(6 195)
Treated

92%
(5 686)
**Undetectable
VL**

Montréal | Fast-Track Cities [Internet]. [cited 2019 Sep 4

Introduction

Factors associated with detectable VL identified from a review of the literature:

- **Host**-related
    - Place of birth, medication adherence, substance abuse, etc.
- **Treatment**-related
    - Past virologic failure, drug interaction, etc.
- **Virus**-related
    - ART resistance

Lima VD et al. Journal of the International AIDS Society 2017
Gras G, Schneider et al.: JAIDS 2012
Robbins GK et al. Clinical Infectious Diseases 2010
O'Connor J et al. Lancet HIV 2017
Singh A et al. Journal of acquired immune deficiency syndromes (1999)

Objectives

Primary objective:

Identify **predictive factors** of detectable viral load in HIV infected patients on combined antiretroviral therapy (cART)

Secondary objectives:
- Describe the HIV population in 2 major HIV clinics in Montreal
  - Unité hospitalière de recherche, d'enseignement et de soins sur le sida, CHUM
  - Chronic Viral Illness Service, MUHC
- Identify predictive factors for:
  - Virologic failure
  - Low persistent viremia
  - Viral blips

Pending results
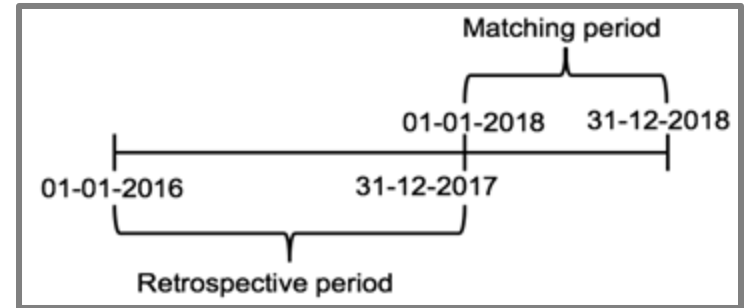
Study Design

Case-control study:

- ▪ Multicentric (CHUM and MUHC)
- ▪ Retrospective period of 2 years
- ▪ 1 : 1 ratio matched on:
  - ○ Sex at birth
  - ○ Year of HIV diagnosis
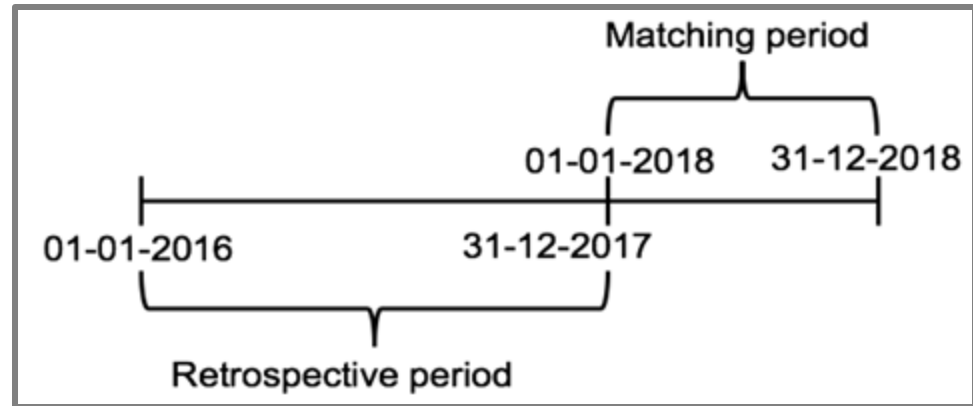
Population

Inclusion criteria:

- ≥ 18 years
- HIV diagnosis
- Same cART > 6 months before matching
- At least 1 follow-up to HIV clinic from 2016 to 2017 and 1 in 2018

Cases → Detectable Viral load (VL) (HIV RNA ≥ 50 copies/mL) at least once in 2018

Controls → Undetectable VL from 2016 to 2018

Population

2938 patients followed

1781 subjects

Cases: detectable VL in 2018
Controls: undetectable VL from 2016 to 2018

1262 subjects

Same cART > 6 months
> 1 follow-up in 2016-2018
Diagnostic date available

200 cases

200 controls

862
(bank of controls left)
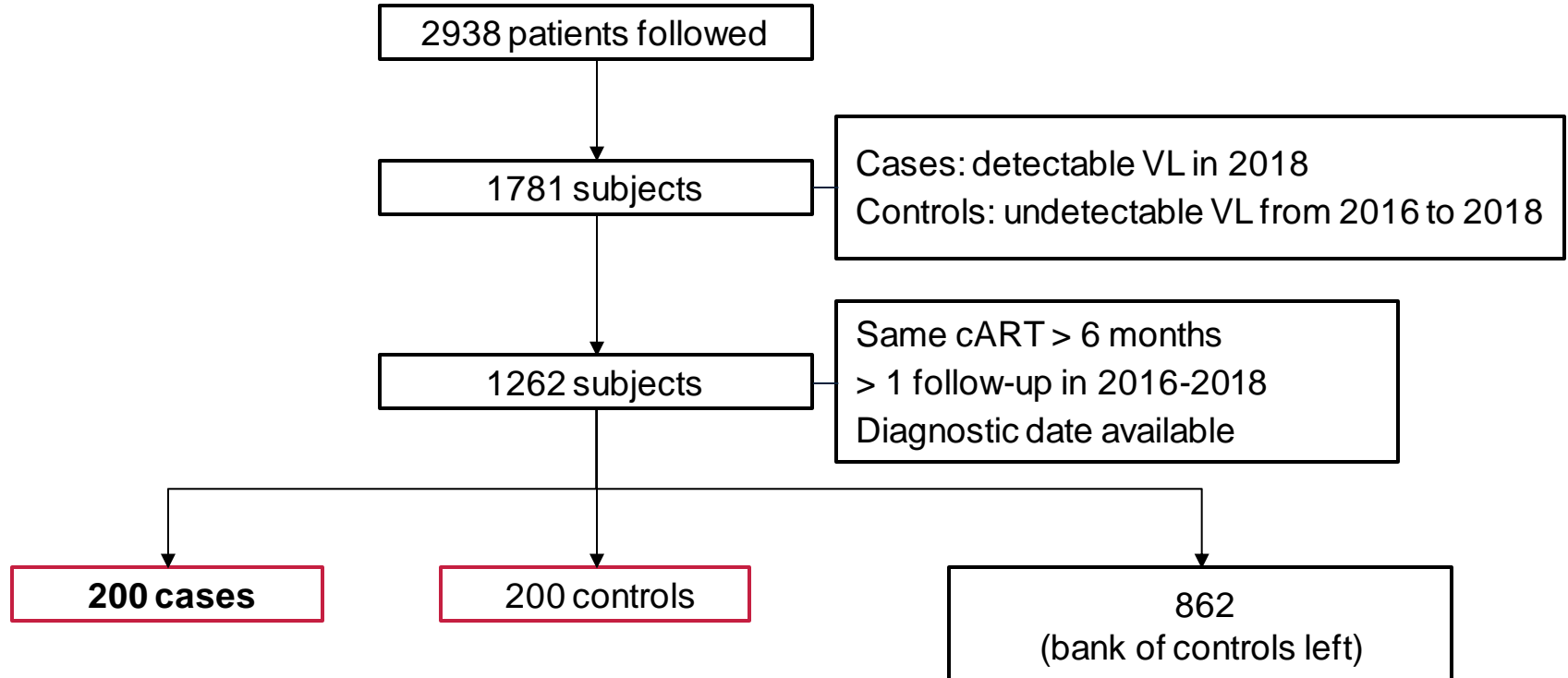
Data collection

Host related		Treatment related	Virus related
Gender at birth	Payment card	Number of cART since diagnosis	Resistance data available
Year of HIV diagnosis	Children at charge	History of virological failure	Genotypic sensitivity score
Detectable viral load	Homeless status	Antiretroviral experienced	
Virologic failure	Transmission mode	PI based containing	
Viral blip	History of psychiatric disease	NNRTI containing regimen	
Low persistant viremia	History of depression	INI containing regimen	
Absolute CD4 count	Pill burden	NRTI containing regimen	
Age (years)	Non adherence to clinic follow-up	Drug interaction with cation	
Continent of birth	Medication adherence	Drug interaction with gastric acid modifying agent	
HIV clinical stage	Incarceration / trouble with the law	Drug interaction with inducers	
Asylum seeker	ART starting date		
Medication coverage plan	Substance abuse		
Seeking for healthcare services	Sexual habits		

➔ Data were collected by medical chart review

# Statistical Analysis

- Multiple Imputation by Chained Equation (MICE) was applied for missing data
- Forward stepwise model selection by AIC for identifying predictors
  - Addition/Withdrawal of variables from models generated through bootstrapping
  - AIC used to select the best «fitting» model

Predictors found in at least 75% of the final models were considered strongly related to the outcome

Descriptive Data

Characteristic	Case (n=200)	Control (n=200)	Total (n=400)
Sex (male, %)	136 (68,0)	136 (68,0)	272 (68,0)
Age (years, range)	53 (21-82)	54 (22-83)	54 (21-83)
Date of diagnosis (%)			
≤ 2010	173 (86,5)	173 (86,5)	346 (86,5)
2011-2017	27 (13,5)	27 (13,5)	54 (13,5)
CD4 (cells/ml, range)	500 (0-1620)	600 (50-2102)	565 (0-2102)
MSM (%)	70 (35,0)	89 (44,5)	159 (39,8)
Substance abuse (%)	66 (33,0)	43 (21,5)	109 (27,3)
Homeless status (%)	17 (8,5)	5 (2,5)	22 (5,5)
History of cART regimens since diagnosis (%)			
1-2	46 (23,0)	64 (32,0)	110 (27,5)
3-4	37 (18,5)	40 (20,0)	77 (19,3)
5 and more	77 (38,5)	62 (31,0)	139 (34,8)

Detectable Viral Load analysis
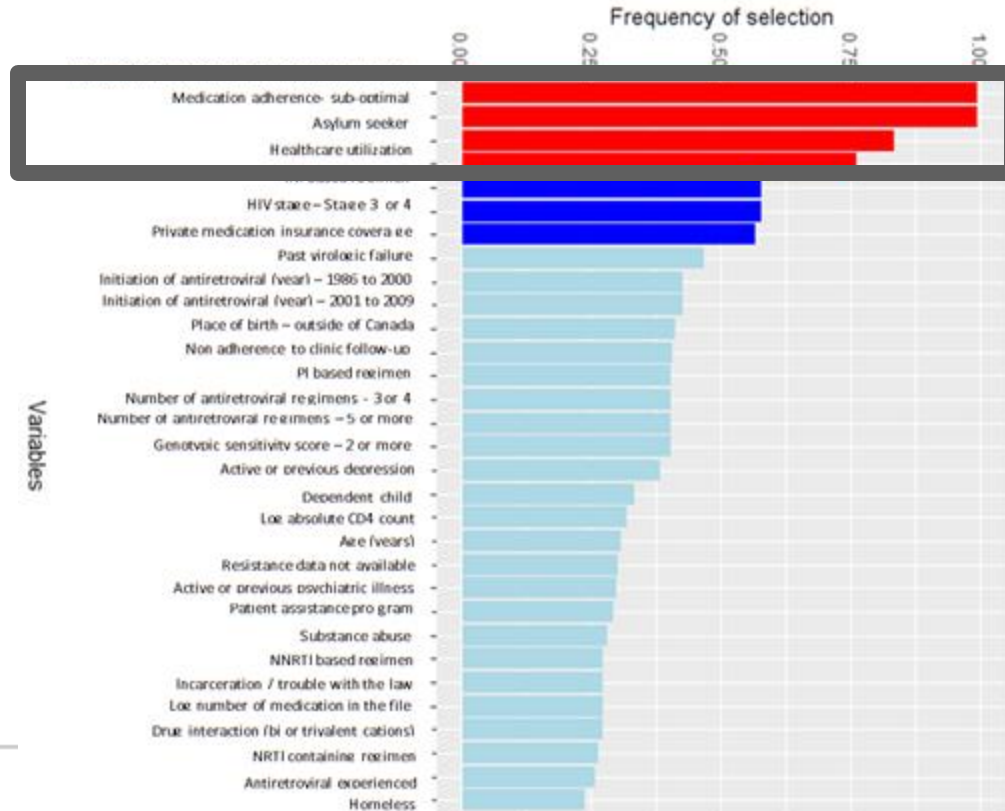
Detectable Viral Load analysis

Figure 2 : Frequencies of variable selection

Frequency of selection (%)
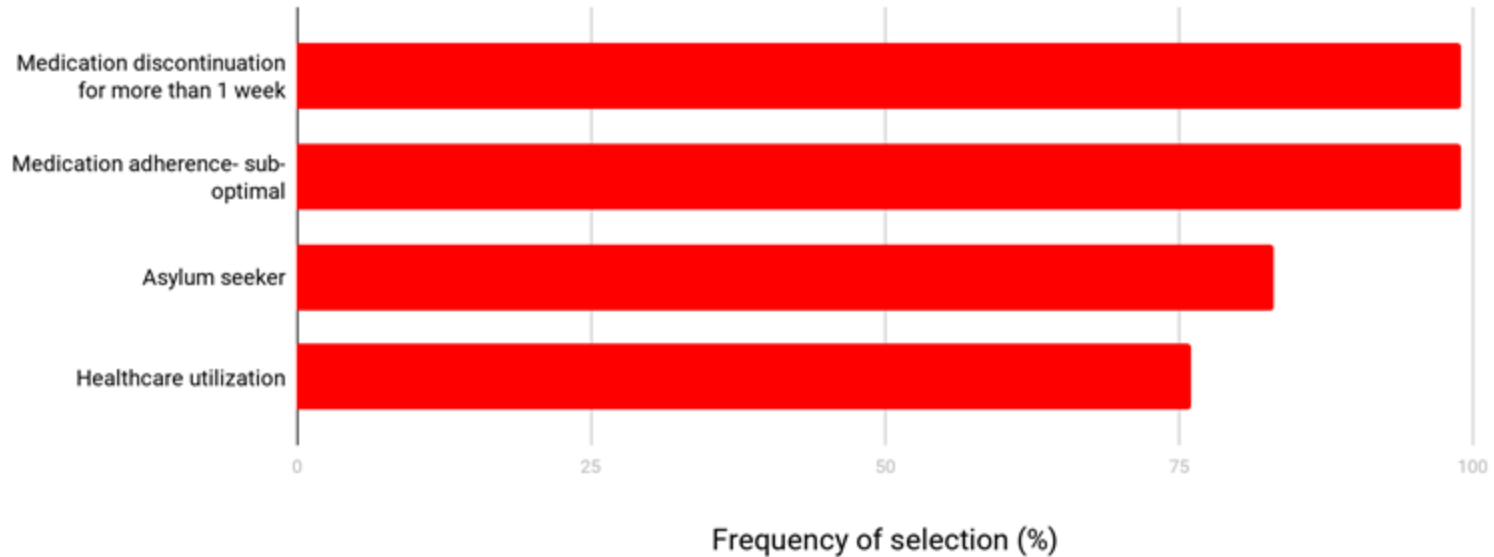
Multivariate regression fit after variable selection

Characteristics	Odds ratio
Asylum seeker	0.31
Medication adherence - Discontinuation for more than 1 week	15.94
Medication adherence - Forgetting punctual doses	3.87
Seeking healthcare services (emergency visit and/or hospitalization)	1.91

Discussion

Suboptimal adherence to HIV medication → inadequate exposure
- ❖ Stopping for > 7 days
- ❖ Forgetting punctual doses

Seeking healthcare services
- ❖ Surrogate for severity/complexity/social precariousness

Asylum seeker → Protective
- ❖ Facilitate access to cART

Strengths	Limitations
Selection of the study population	Sample size
Case-control design	Missing data
Medical chart review	Retrospective design

Conclusion

In this cohort from 2 large hospital HIV clinics in Montreal, **inadequate adherence** to cART and **seeking healthcare services** were identified as predictors of detectable VL. **Asylum seeker** seemed to be a protective factor.

Acknowledgements

- CHUM : Stéphanie Matte
- MUHC : Costas Pexos
- Patients in both clinics

Supplementary Material

	Case (n=200)	Controls (n=200)	Total (n=400)
Gender at birth(male %)	136 (68,0)	136 (68,0)	272 (68,0)
Age (years, range)	53 (21-82)	54 (22-83)	54 (21-83)
Year of HIV diagnostic(%)			
≤ 1990	26 (13,0)	26 (13,0)	52 (13,0)
1991-2000	75 (37,5)	75 (37,5)	150 (37,5)
2001-2010	72 (36,0)	72 (36,0)	144 (36,0)
2011-2020	27 (13,5)	27 (13,5)	54 (13,5)
Type of detectable VL (%)			
Virologic failure	79 (39,5)	N/A	79 (19,8)
Viral blip	86 (43,0)	N/A	86 (21,5)
Persistent low-level viremia	27 (13,5)	N/A	27 (6,8)
Not identified	8 (4,0)	N/A	3 (0,8)
absolute CD4 count (cells/ml, range)	500 (0-1620)	600 (50-2102)	565 (0-2102)
Born outside of Canada (%)	83 (41,5)	84 (42,0)	167 (41,8)
Continent of birth (%)			
North America	126 (63,0)	118 (59,0)	244 (61,0)
Africa	32 (16,0)	32 (16,0)	64 (16,0)
South America	30 (15,0)	28 (14,0)	58 (14,5)
Caribbean	5 (2,5)	9 (4,5)	14 (3,5)
Europe	5 (2,5)	6 (3,0)	11 (2,8)
Asia	2 (1,0)	6 (3,0)	8 (2,0)
Oceania	0 (0,0)	1 (0,5)	1 (0,02)

Table 1. Descriptive Data

	Case (n=200)	Controls (n=200)	Total (n=400)
Transmission (%)			
IDU	43 (21,5)	26 (13,0)	69 (17,3)
MSM	70 (35,0)	89 (44,5)	159 (39,8)
Heterosexual	59 (29,5)	61 (30,5)	120 (30,0)
Mother to child	7 (3,5)	5 (2,5)	12 (3,0)
Others	36 (18,0)	35 (17,5)	71 (17,8)
Missing data	14 (7,0)	12 (6,0)	26 (6,5)
Sexual orientation (%)			
MSM	70 (35,0)	89 (44,5)	159 (39,8)
Heterosexual	109 (54,5)	94 (47,0)	203 (50,8)
Others	6 (3,0)	4 (2,0)	10 (2,5)
Missing data	15 (7,5)	13 (6,5)	28 (7,0)
HIV stage (%)			
1	83 (41,5)	92 (46,0)	175 (43,8)
2	17 (8,5)	32 (16,0)	49 (12,3)
3	39 (19,5)	31 (15,5)	70 (17,5)
4	61 (30,5)	45 (22,5)	106 (26,5)
Number of medication in the file (median, range)	5 (1-22)	5 (1-28)	5 (1-28)
substance abuse (%)	66 (33,0)	43 (21,5)	109 (27,3)
Missing data	8 (4,0)	4 (2,0)	12 (3,0)
IDU (%)	25 (12,5)	11 (5,5)	36 (9,0)
Methamphetamines (%)	7 (3,5)	3 (1,5)	11 (2,8)
Alcohol (%)	28 (14,0)	22 (11,0)	50 (12,5)
Others	41 (20,5)	31 (15,5)	72 (18,0)

Table 1. Descriptive Data

	Case (n=200)	Controls (n=200)	Total (n=400)
Asylum seeker (%)	16 (8,0)	20 (10,0)	36 (9,0)
Medication insurance coverage (%)			
Private insurance	28 (14,0)	36 (18,0)	64 (16,0)
Public or governmental insurance	153 (76,5)	126 (63,0)	279 (69,8)
Missing data	19 (9,5)	38 (19,0)	57 (14,3)
Payment card (%)	22 (11,0)	18 (9,0)	40 (10,0)
Children at charge (%)	27 (13,5)	29 (14,5)	56 (14,0)
Homeless (%)	17 (8,5)	5 (2,5)	22 (5,5)
Active or previous psychiatric illness (%)	87 (43,5)	69 (34,5)	156 (39,0)
Active or previous depression(%)	47 (23,5)	45 (22,5)	92 (23,0)
Healthcare utilization (%)	96 (48,0)	61 (30,5)	157 (39,3)
Non adherence to clinic follow-up (%)	87 (43,5)	77 (38,5)	164 (41,0)
Medication adherence (%)			
Optimal	69 (34,5)	132 (66,0)	201 (50,3)
Forgetting punctual doses of ART medication	66 (33,0)	35 (18,0)	101 (25,3)
Stopping ART medication for over a week	49 (24,5)	8 (4,0)	57 (14,3)
Missing data	16 (8,0)	25 (12,5)	41 (10,3)
Incarceration / trouble with the law (%)	31 (15,5)	13 (6,5)	44 (11,0)
Antiretroviral experienced (%)			
Yes	179 (89,5)	168 (84)	347 (86,8)
No	19 (9,5)	29 (19,5)	48 (12,0)
Unable to evaluate	2 (1,0)	3 (1,5)	5 (1,3)

Table 1. Descriptive Data

	Case (n=200)	Controls (n=200)	Total (n=400)
initiation of antiretroviral(%)			
1986-2000	55 (27,5)	57 (28,5)	112 (28,0)
2001-2009	57 (28,5)	56 (28,0)	113 (28,3)
2010-2017	43 (21,5)	56 (28,0)	99 (24,8)
Unable to evaluate	45 (22,5)	31 (15,5)	76 (19,0)
number of antiretroviral regimens since diagnosis (%)			
1-2	46 (23,0)	64 (32,0)	110 (27,5)
3-4	37 (18,5)	40 (20,0)	77 (19,3)
5 and more	77 (38,5)	62 (31,0)	139 (34,8)
Unable to evaluate	40 (20,0)	34 (17,0)	74 (18,5)
Past virologic failure (%)			
Yes	74 (37,0)	38 (19,0)	112 (28,0)
No	73 (36,5)	99 (49,5)	172 (43,0)
Unable to evaluate	53 (26,5)	63 (31,5)	116 (29,0)
ART therapy at matching date (%)			
IP	69 (34,5)	53 (26,5)	122 (30,5)
INNTI	39 (19,5)	52 (26,0)	91 (22,8)
INI	145 (72,5)	122 (61,0)	267 (66,8)
INTI	189 (94,5)	190 (95,0)	379 (94,8)
Interaction with CYP3A4 inductors (%)	0 (0,0)	0 (0,0)	0 (0,0)
Interaction with cation (%)	44 (22,0)	36 (18,0)	80 (20,0)
Interaction with acid modifying drug(%)	3 (1,5)	3 (1,5)	6 (1,5)
genotypic sensitivity score (%)			
Under 2	8 (4,0)	3 (1,5)	11 (2,8)
2 and more	150 (75,0)	142 (71,0)	292 (73,0)
Unable to evaluate	42 (21,0)	55 (27,5)	97 (24,3)

Table 1. Descriptive Data

Clogit model fit after variable selection

Characteristics	Odds ratio
Asylum seeker	0.31
Medication adherence - Discontinuation for more then 1 week	15.94
Medication adherence - Forgetting punctual doses	3.87
Healthcare utilization	1.91
Private medication insurance coverage	0.59
INI based regimen	1.67
HIV stage - Stage 3 or 4	1.64