

Antiretroviral Prescription and Adherence in a Portuguese Cohort of HIV-1 Infected Subjects: an overall analysis of changes over the years 2005 – 2008

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Background

The prescription of Highly Active Antiretroviral Therapy (HAART) has been changing over the years. On the other hand, high levels of adherence are still required to achieve the best response to treatment, preventing drug resistances, disease progression and death [1].

Knowledge on which HAART is used on HIV infection may provide useful information for clinical evaluation with regard to safety and effectiveness. Drug utilization studies may be used to promote appropriate drug use through education and other interventions, since “without a knowledge of how drugs are being prescribed and used, it is difficult to initiate a discussion on rational drug use or to suggest measures to improve prescribing habits” [2].

Objectives

- To evaluate the trends in adherence to HAART in a cohort of HIV-1 infected adults, and
- To characterize the HAART prescription pattern, over the period 2005-2008.

Methods

Retrospective data collection from a random sample of HIV-1 adult infected subjects, from the total of 2861 subjects followed-up at the HIV outpatient clinic of Hospital de Santa Maria (HSM, Lisbon, Portugal), and presenting at least one HAART refill between 01-01-2005 and 31-12-2008 (Figure 1).

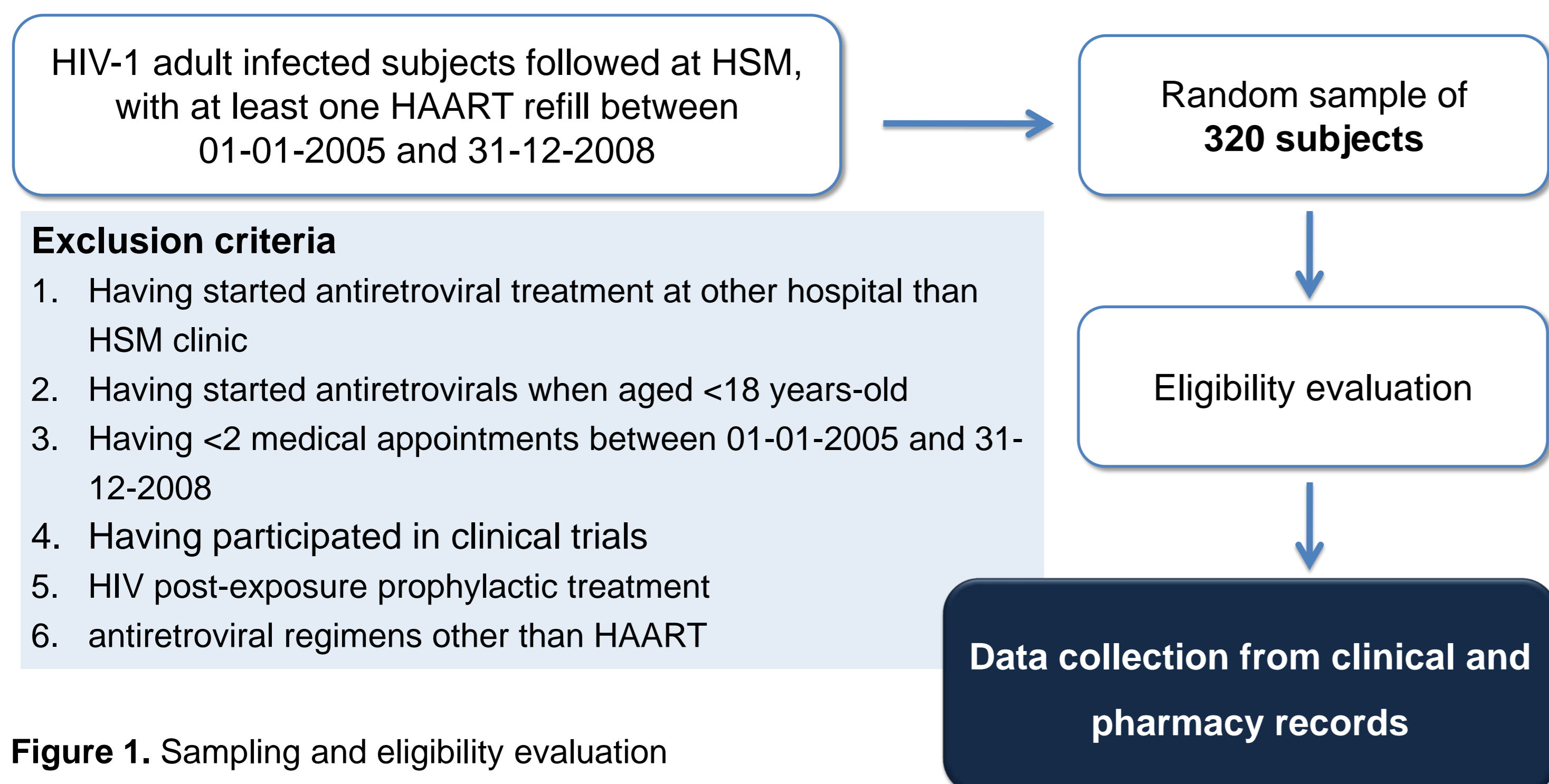


Figure 1. Sampling and eligibility evaluation

Subjects were censored at the date of death or date of being arrested, being in a social institution or dependent of a third person for taking medication. Baseline was the date of the first medical appointment during the study period.

Medication possession ratio (MPR) was determined using a fixed 12- or 6-month period (Figure 2). Non-adherence was defined as MPR<95%. **HAART prescription** was analyzed according to regimens, within each antiretroviral class, and regarding fixed-dose combinations, for the first subjects' prescription in each period. **Clinical characterization**, including viral load (VL) and CD4 cell count, was retrieved from clinical records.

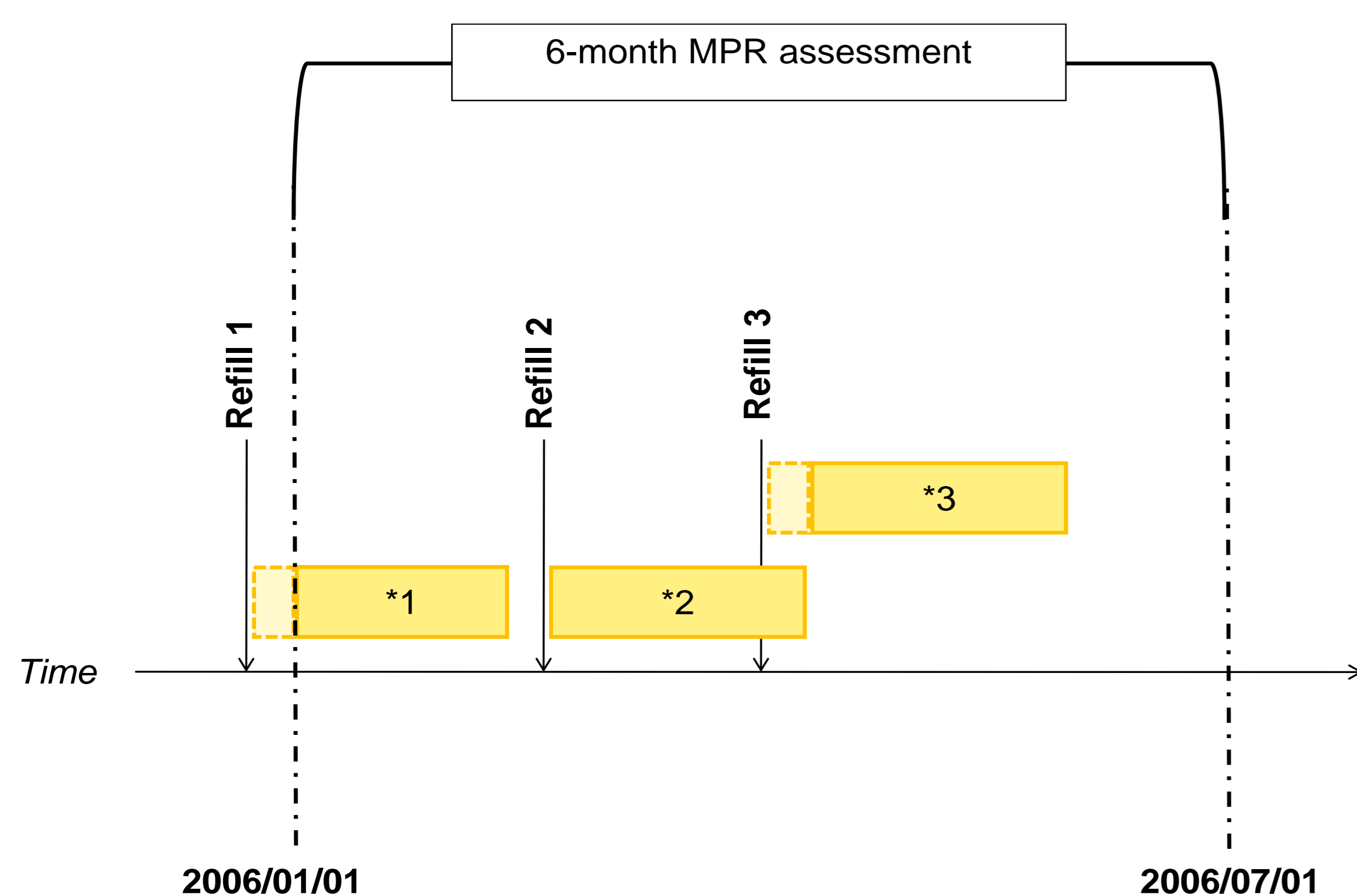


Figure 2. Scheme for the calculation 6-month Medication Possession Ratio. MPR is determined by assessing the total number of days with ART available (*periods) from all refills occurring in each semester, divided by total number of days for the semester

The χ^2 test for linear trend was used to assess temporal differences within each variable, for a 5% significance level. The study was authorized by the Ethics Committee of the HSM, and by the Portuguese Data Protection Authority.

References:

- Ortego C, et al. Adherence to highly active antiretroviral therapy (HAART): a meta-analysis. AIDS Behav 2011
- Introduction to Drug Utilization Research. World Health Organization; 2003.

Acknowledgements

To clinicians and administratives of the HSM outpatient clinic. To the Pharmaceutical Services of the HSM.

Conflict of Interest Statement

The study received a grant from the Merck Sharp & Dohme Foundation (Portugal), with no implications in the study design, research permission, data collection, discussion of results or report publication, which responsibility are attributable to the research team. APM has received honoraria from Merck, Sharp & Dohme (Portugal). The remaining authors declare that they have no competing interests.

Results

Study sample at baseline

From a total of 186 included subjects, 78.5% were treatment-experienced at baseline, being on average 39.7±9.5 years old. The majority were male (63.4%) and Caucasian (78.6%). Acquisition of HIV infection was due to heterosexual intercourse for 50.3% of subjects, while injection drug use and men having sex with men were the modes of acquisition for 23.2% and 19.2%, respectively.

Adherence to HAART

Between 2005-2008, there was a significant increase in non-adherence, based on annual MPR estimation (Table 1). In the 6-month analysis (Figure 3), a higher proportion of non-adherent subjects was observed among those with past or current IDU and among those that had depression or anxiety. Subjects that had started treatment previous to HAART regimes usually showed inferior estimates of non-adherence.

Table 1. Annual estimates of non-adherence to HAART

	2005	2006	2007	2008	P*
n	146	157	154	157	
% MPR<95% (CI95%)	12.3 (7.7-19.0)	24.8 (18.4-32.5)	14.9 (9.9-21.8)	25.9 (19.5-33.6)	0.03
% MPR<50%	4.1	8.9	5.2	4.5	0.71
% IDU	23.3	26.1	27.9	26.8	0.70
% MPR<95% IDU	9.8	32.6	25.0	14.0	<0.01
% D/A	34.2	37.6	39.0	38.2	0.60
% MPR<95% D/A	18.3	26.2	18.3	20.0	<0.01
% detectable VL	53.1	41.8	40.8	37.5	0.02
% CD4 < 350 cells/μl	43.6	42.4	38.2	34	0.07
% HAART naïve-subjects	11.0	7.0	3.9	4.5	0.01
% fixed-dose combinations	54.8	62.4	72.1	77.7	<0.01
HAART regimens					
2 NRTIs + NNRTI	50.0	47.8	47.4	47.1	0.63
2 NRTIs + PI	41.1	39.5	39.6	39.5	0.80
3 NNRTIs	3.4	3.2	3.2	3.8	0.84
4 antiretrovirals	0.7	3.8	5.2	3.8	0.11
other regimens	4.8	5.7	4.5	5.7	0.84

* p-value for the χ^2 test for linear trend; MPR, medication possession ratio; CI, confidence interval; IDU, injection drug use; D/A, depression or anxiety; HAART, Highly Active Antiretroviral Therapy

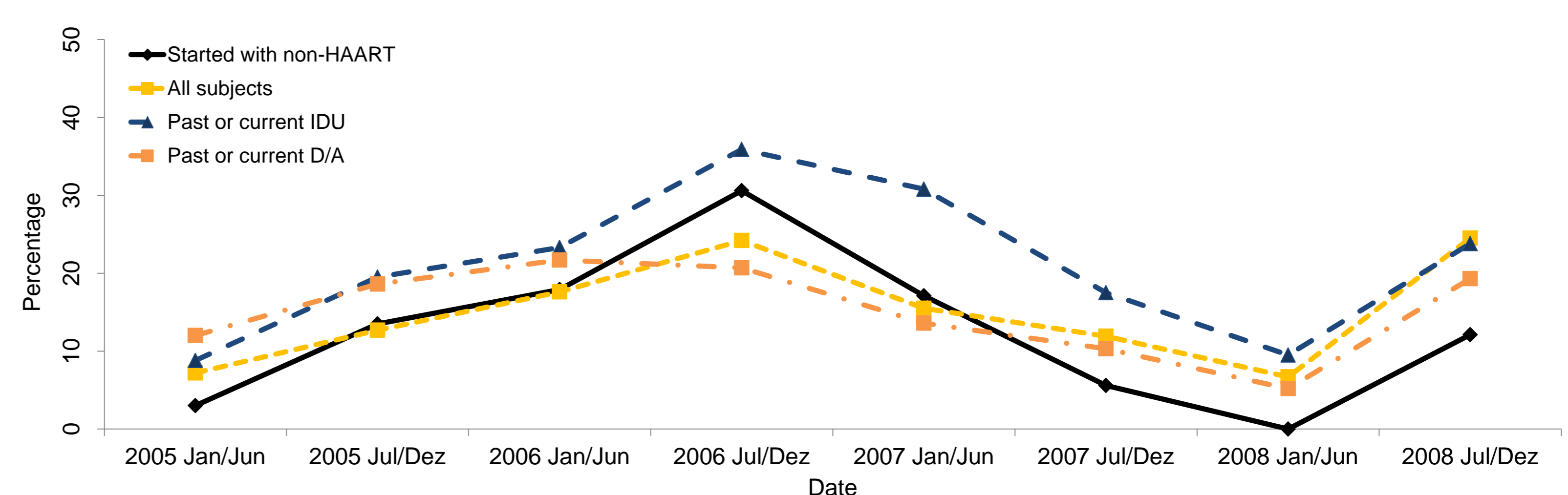


Figure 2. Prevalence of non-adherence, defined as MPR<95%, for each semester from 2005-2008 period. In all cases, p-values for linear trend were >0.05. IDU, Injection Drug Use. D/A, depression/anxiety. Started with non-HAART, when the first antiretroviral treatment was with mono or dual antiretroviral therapy.

HAART prescription pattern

The two most usual HAART regimens were two NRTIs and a NNRTI or a PI. The use of fixed-dose combinations had significantly increased from 54.8 to 77.7% ($P<0.001$), mainly due to emtricitabine/tenofovir association. When considering individual antiretroviral agents, there was an increase in the number of subjects using atazanavir ($P=0.03$) and fosamprenavir ($P=0.04$) among the NRTIs and abacavir ($P>0.05$) among NNRTIs.

Conclusions

- Non-adherence increased** 13.6% over the period 2005-2008, although a better control of virological and immunological outcomes was observed in the same period.
- The proportion of non-adherent subjects was higher among those who had past or current IDU or had depression / anxiety disorders. Physicians should continue to promote adherence among these subgroups.
- The **prescription pattern** seemed to be in accordance with guidelines for the HIV treatment. The increase of fixed-dose combinations reflect the simplification of the HAART regimens, a strong recommendation for adherence improvement.
- Study limitations** were 1) that adherence and antiretroviral prescription were presented as aggregate data, and 2) the fact that MPR assumes that all refilled medication will be actually taken by the subjects.
- Further studies** should assess the relationship between adherence and HIV clinical outcomes, and the identification of adherence determinants in nowadays practice.