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*Determinants, pattern and outcomes of
non-adherence to HAART in a Portuguese
cohort of HIV-1 infected subjects*

Milene Fernandes (mccf@fm.ul.pt), Rui Simões, Luís Caldeira, Andreia Leite, José A Freitas, Paulo J Nicola,
Ana P Martins, Vasco AJ Maria



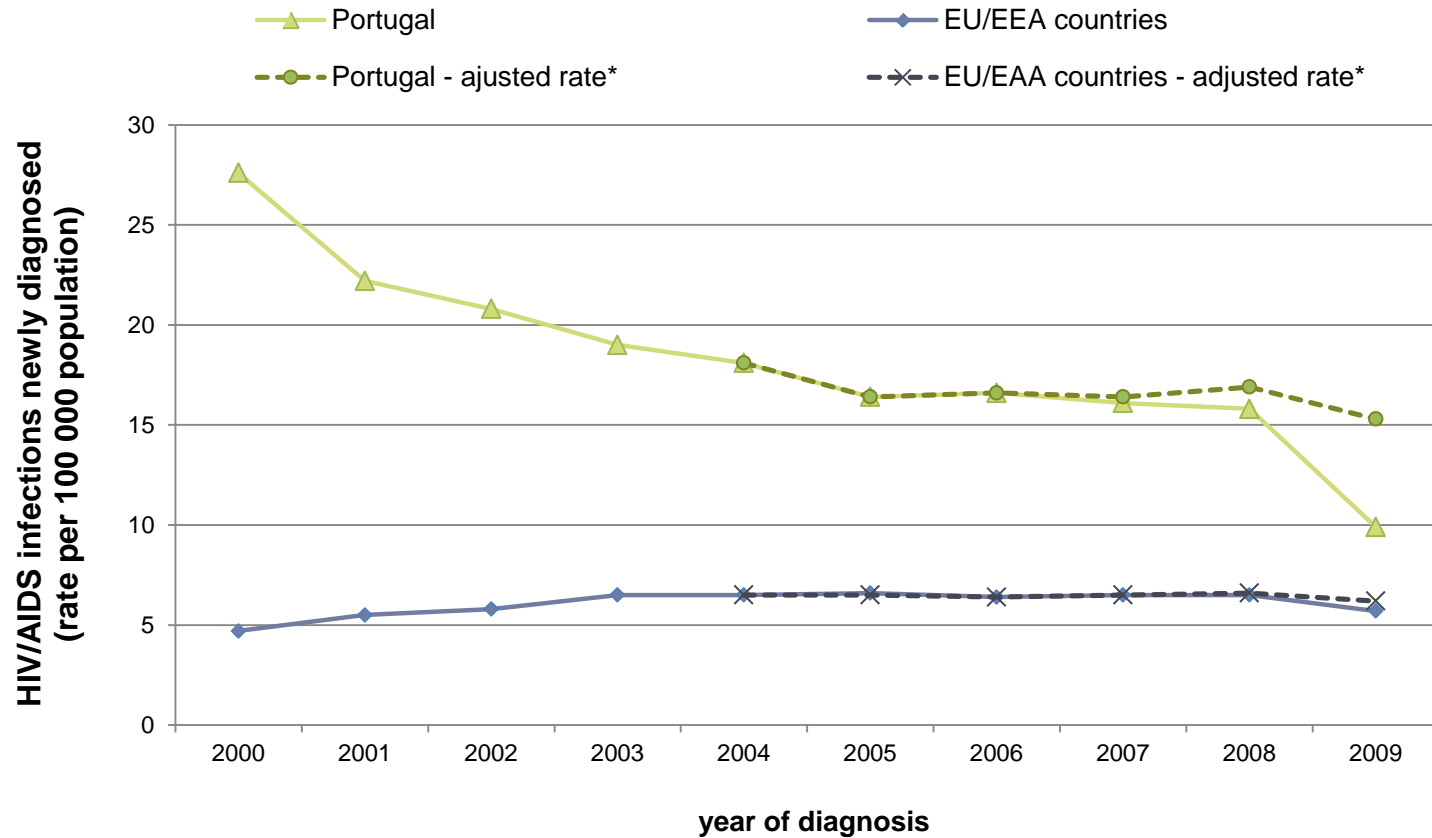
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Disclosures

- The project received an unrestricted 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 were attributable to the research team.
- The following personal or financial relationships relevant to this presentation existed during the conduct of the study:
 - Ana P Martins works in the external affairs department of pharmaceutical company Merck Sharp & Dohme, Portugal.
 - Other research studies conducted by the Institute of Preventive Medicine – Faculty of Medicine of Lisbon are funded by pharmaceutical companies.

Epidemiology of HIV/AIDS infection

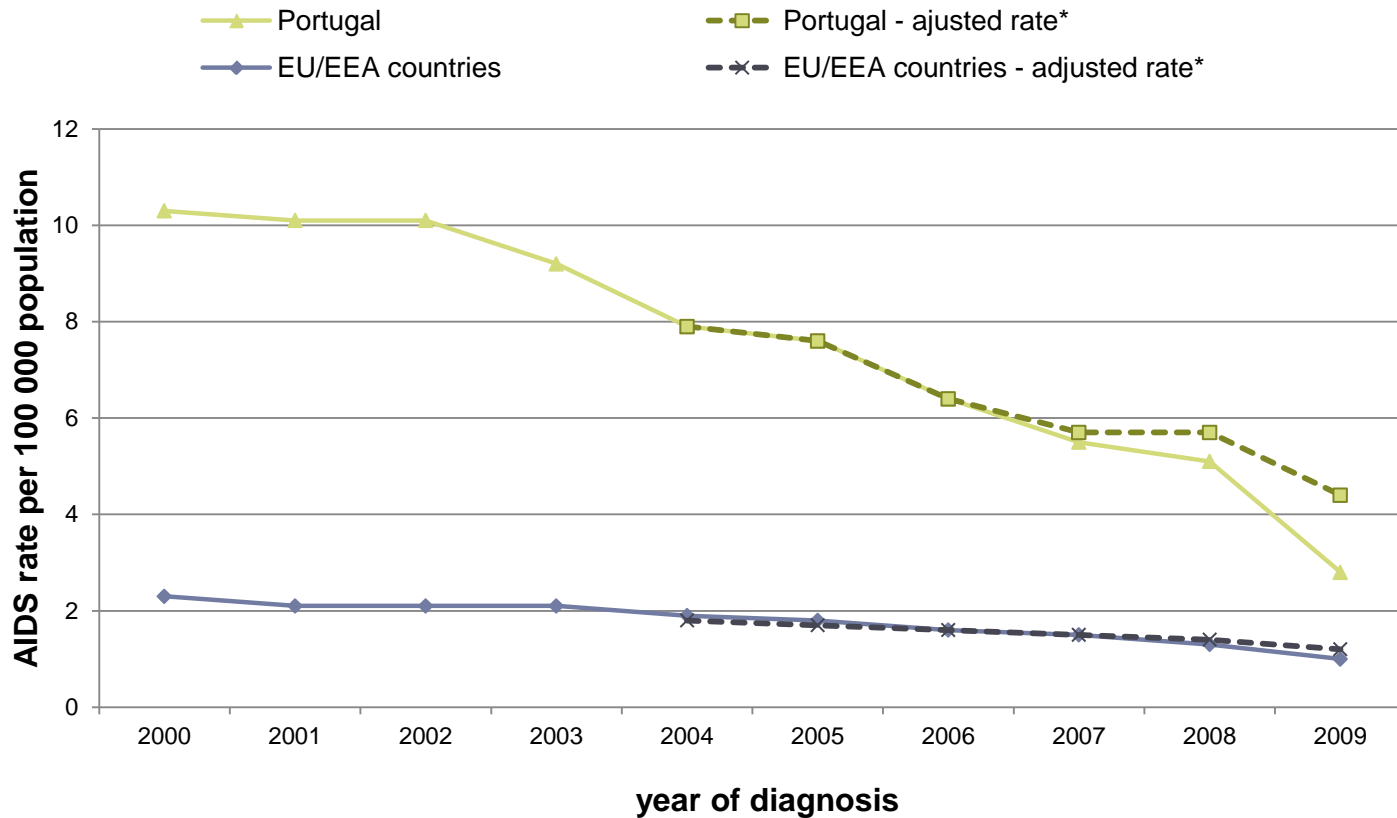


EU/EEA and Portuguese trends of new HIV/AIDS cases diagnosed

(rate per 100 000 population), by year of diagnosis and over the period 2000-2009

[source: HIV surveillance in Europe 2009, ECDC]

Epidemiology of HIV/AIDS infection



EU/EEA and Portuguese trends of AIDS rates at the time of HIV/AIDS diagnosis (rate per 100 000 population), by year of diagnosis and over the period 2000-2009

[source: HIV surveillance in Europe 2009, ECDC]

Treatment of HIV/AIDS infection

- ▶ Highly Active Antiretroviral Therapy (HAART)

- ▶ Increase of survival
- ▶ Decrease of risk of progression to AIDS

However clinical follow-up is still complex

- ▶ Assessment and prevention of co-infections and comorbidities, drug resistances, toxicity / adverse drug reactions, and **poor adherence to treatment**

- ▶ Patient adherence to HAART is a major determinant of clinical success, with impact at healthcare utilization.
- ▶ Effective interventions require local assessment of adherence determinants and patterns.

Study Aims

- ▶ To identify factors associated to patient non-adherence to HAART, during 2008 year,
- ▶ To characterize frequency and duration of medication gaps, and
- ▶ To verify the association of non-adherence with immunological and virological outcomes, among HIV-1 infected adults.

Methods

HIV-1 adult infected subjects followed at Hospital Santa Maria (Lisbon, Portugal), with at least one antiretroviral refill between 01/01/2005 and 31/12/2008



Random sample of **320 subjects**



Eligibility evaluation



Data collection from clinical and pharmacy records from baseline until 31/12/2008 or death, or when HAART intake is dependent on 3rd persons / institutions

Inclusion criteria

1. Started antiretroviral treatment in HSM clinic
2. Started antiretroviral drugs when aged ≥ 18 years-old
3. ≥ 2 medical appointments from 01/01/2008 to 31/12/2008
4. No participation on clinical trials
5. No HIV post-exposure prophylactic treatment
6. Only HAART regimens
7. Non-dependent on third persons/institutions (e.g. prisional establishments) to take HAART medication

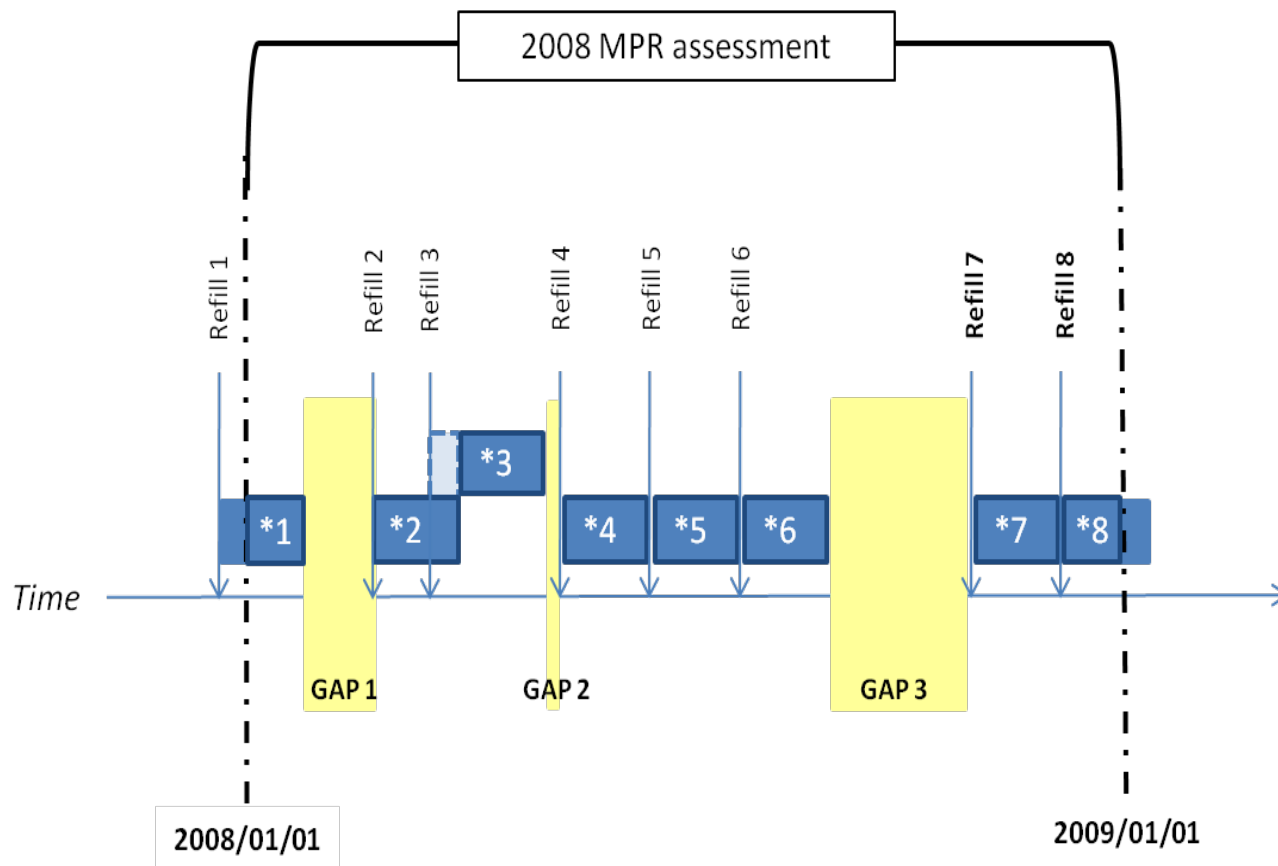
Adherence

- ▶ Assessed through a pharmacy-refill based measure
 - ▶ Annual Medication Possession Ratio (MPR)

- ▶ For one *index* drug of the HAART regimen
 1. Protease Inhibitor (PI) *or*
 2. Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) *or*
 3. Abacavir / Tenofovir

Adherence

- ▶ annual MPR = $\sum \text{days with available medication} / 365 \text{ days}$
- ▶ MPR < 95% → non-adherent subject



Other Variables

1

Patient-related

- age, sex
- mode of acquisition for HIV infection
- depression or anxiety
- injection drug use (IDU)
- comorbidities

2

Healthcare utilization

- no. medical appointments
- hospitalizations
- skipped medical appointments for >12 months

3

Treatment and Infection

- time since diagnosis
- time on HAART
- no. of HAART regimens
- baseline HAART regimen
- CD4 count
- viral load (VL)
- drug resistances
- opportunistic infections
- AIDS classification

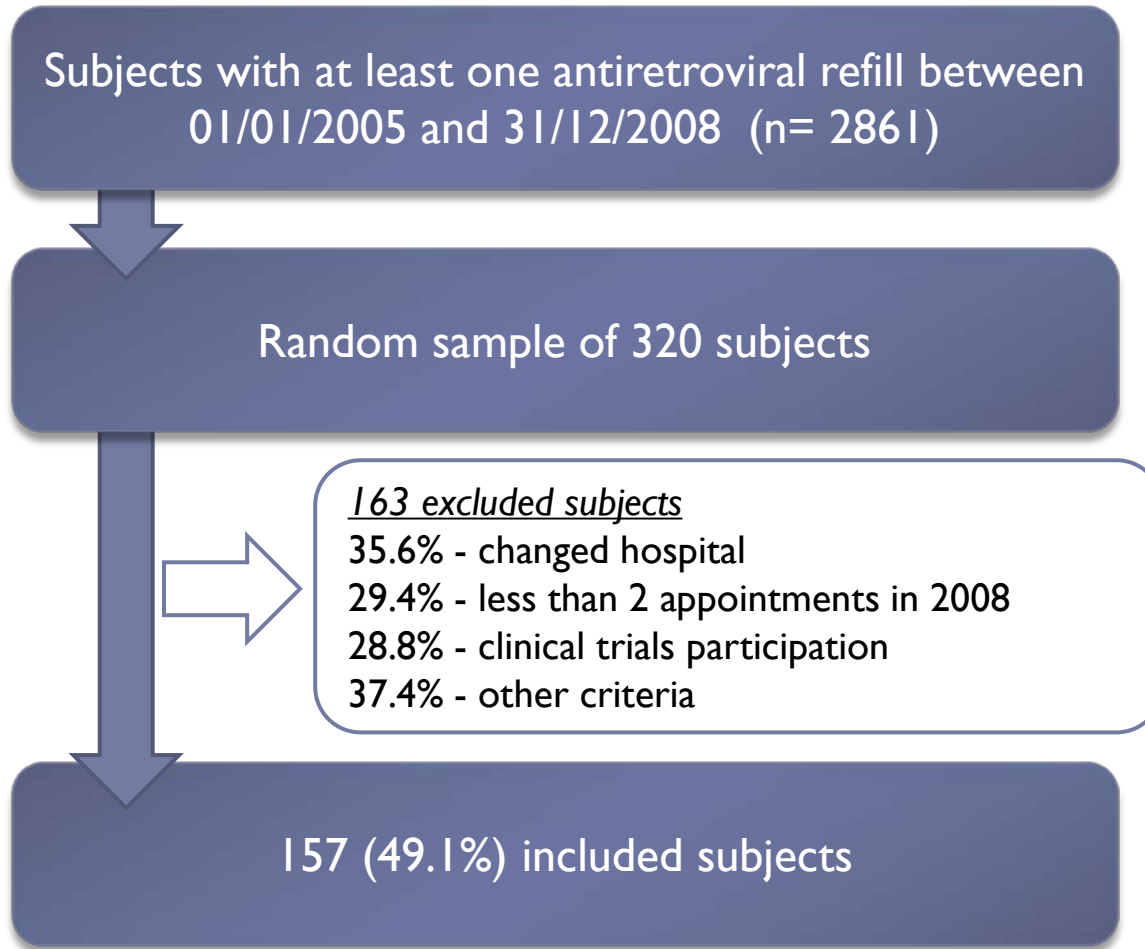
Statistical Analysis

- ▶ *Multivariate logistic regression model*
 - To assess baseline factors associated to 2008 non-adherence

- ▶ *Bivariate analyses*
 - To compare the proportion of subjects with VL >40copies/ml and CD4 <350 cells/ μ l, during 2008 year assuming non-adherence as a dichotomized variable ($\alpha=0.05$)

- ▶ *The study was approved by the Ethics Committee of the HSM and the Portuguese Data Protection Authority*

Study sample



Study participants at baseline*

n	157
Age (years, mean±sd)	42.3 ± 9.2
% male	63.7
% caucasian	77.4
% past or current Injection Drug Use (IDU)	26.8
% past or current Depression or Anxiety	38.2
Mode of acquisition for HIV infection (%)	
- heterosexual intercourse	47.8
- IDU	21.6
- Men having Sex with Men	18.5
- other	7.6
Time since diagnosis of HIV infection (months, median)	84.0
Time on HAART (months, median)	65.6
% HAART-naïve subjects	4.5
% AIDS at baseline	37.9
% at least one record of VL<40 copies/ml previous to baseline	24.2
% at least one record of CD4 <350cells/μl previous to baseline	26.8
* Baseline corresponds to the first medical appointment in 2008	

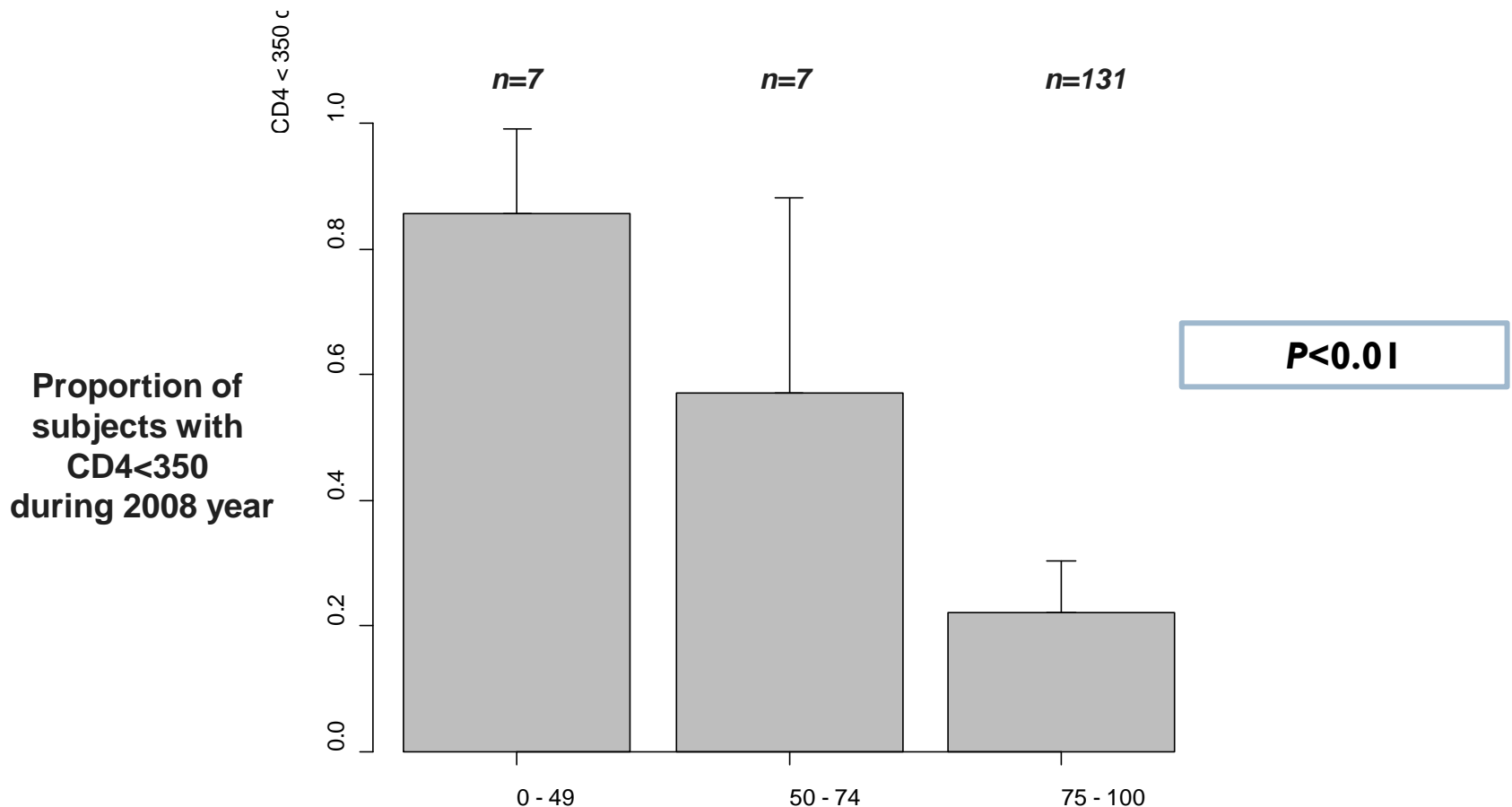
Adherence evaluation

- ▶ Annual MPR estimates ranged from 0.1% to 100%
(median 100%, IQR: 94.4-100%)
- ▶ MPR < 95% → 25.9% of the subjects
 - ▶ from which 81.6% had more than one medication gap < 30 days

Factors Associated to Non-Adherence

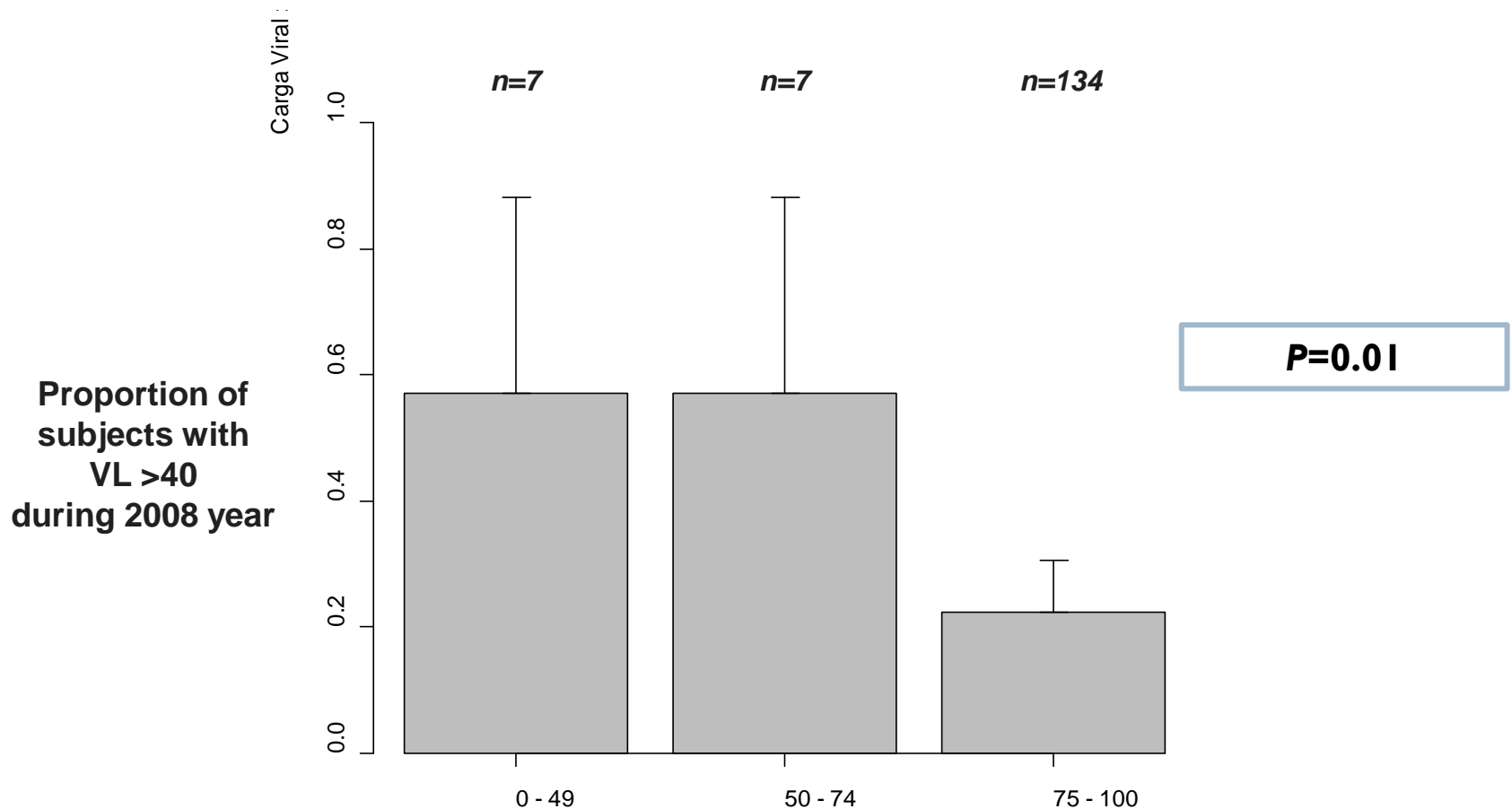
Variable	OR	95% CI	p-value
<i>At least one comorbidity</i>			
Yes	1.95	(0.76-4.89)	0.15
<i>Mean number of medical appointments per subject's year of HAART experience</i>			
more than 3 appointments	1.00		
3 or less appointments	2.37	(0.68-8.24)	0.17
<i>Previous medical appointment abandon periods > 12 months</i>			
Yes	7.14	(1.71-29.78)	0.01
<i>Time on HAART</i>			
more than 7 years	1.00		
4 to 7 years	1.55	(0.45-5.30)	0.48
less than 4 years	8.26	(1.89-36.08)	0.01
<i>Age</i>			
more than 45 years-old			
36 to 45 years-old	0.31	(0.10-0.99)	0.05
less than 36 years-old	1.67	(0.54-5.15)	0.37
<i>Number of HAART regimen experienced</i>			
more than one regimen	1.00		
only one regimen	1.65	(0.55-4.95)	0.37
OR, odds ratio estimation by logistic regression analysis; CI, confidence interval; HAART, Highly Active Antiretroviral Treatment (ROC curve: AUC=0.80, sensitivity=0.80, specificity=0.74)			

Adherence vs. CD4 count <350 cells/ μ l



Having <3years of HAART experience and AIDS classification at diagnosis were also associated to immunological ($P=0.05$ and $P=0.01$) outcomes.

Adherence *vs.* Viral Load >40 copies/ml



Having <3years of HAART experience and AIDS classification at diagnosis were also associated to virological ($P<0.01$ and $P=0.02$) outcomes.

Limitations

- ▶ to evaluate associations between adherence and other determinants or outcomes:
 - ▶ Lack of statistical power
 - ▶ Missing information on clinical records regarding other variables described as associated to non-adherence
- ▶ Pharmacy-based measures assume that subjects take their medication once available after a refill → *overestimation of adherence*.
- ▶ Adherence was not assessed as a time-dependent variable.
- ▶ ...

Conclusions

- ▶ Subjects with **less time on HAART** and those that had already **abandoned medical appointments for a period >12 months** seem to have higher chance of being non-adherents.
- ▶ **Lower to moderate average adherence** levels and **shorter HAART gaps** are frequent among HIV-1 infected adults.
- ▶ **Pharmacy-based measures** may be useful to **identify subjects with poor adherence levels**, enabling the design of interventions to prevent it.

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- ▶ To the HSM Infectious Diseases Outpatient Clinic for the collaboration on the study and providing the consultation of clinical records,
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Obrigada!