Ospedale San Paolo
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Regione Lombardia
ASST Santi Paolo e Carlo

AdICoNA 2

Fondazione Icona
ITALIAN COHORT NAIVE ANTIRETROVIRALS

Italian Cohort
I. C O.
N A.
Naive Antiretrovirals

UNIVERSITÀ DEGLI STUDI DI MILANO

Non aderenza: i dati ICONA

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Institute of Infectious and Tropical Diseases
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AdICoNA Cosa abbiamo fatto

Correlazione sintomi/eff. collaterali & aderenza

Ammassari A, JAIDS 2001

Correlazione tra aderenza e sviluppo di lipodistrofia

Ammassari A, JAIDS 2002

Valutazione dei determinanti di non-aderenza

Ammassari A, JAIDS 2002

Relazione aderenza, livelli plasmatici di farmaci, efficacia virologica e sviluppo di resistenze

Perno CF, JAIDS 2002;

Antinori A, Antivir Ther 2004

Relazione tra aderenza e depressione

Starace F, JAIDS 2002;

Ammassari A, Neurology 2003;

Ammassari A, Psychosomat 2004

L'aderenza in rapporto ai diversi tipi di trattamento

Trotta MP, JAIDS 2002;

Trotta MP, AIDS 2003

L'aderenza nel rapporto medico/paziente

Murri R, JAIDS 2002

Murri R, JGIM 2004

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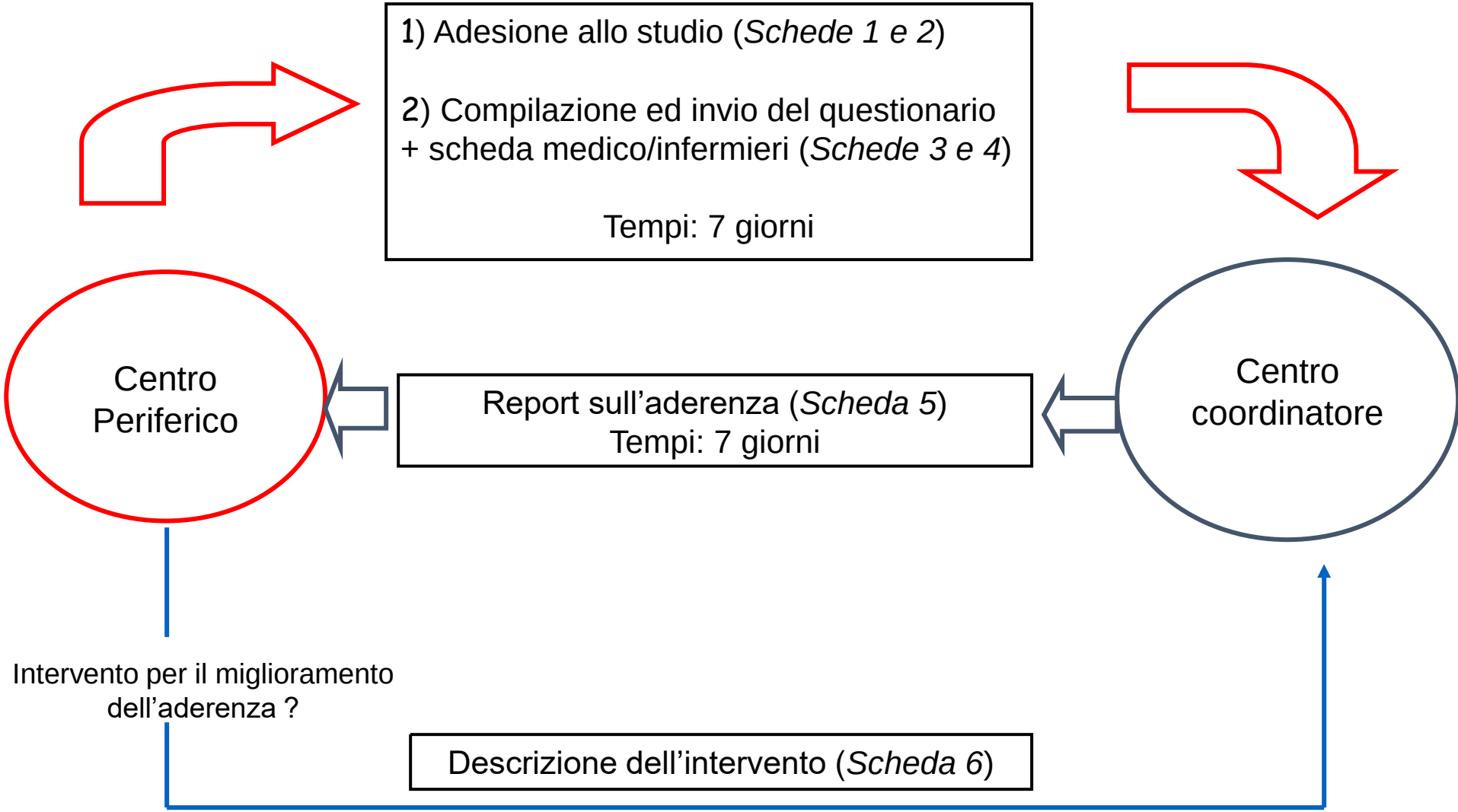
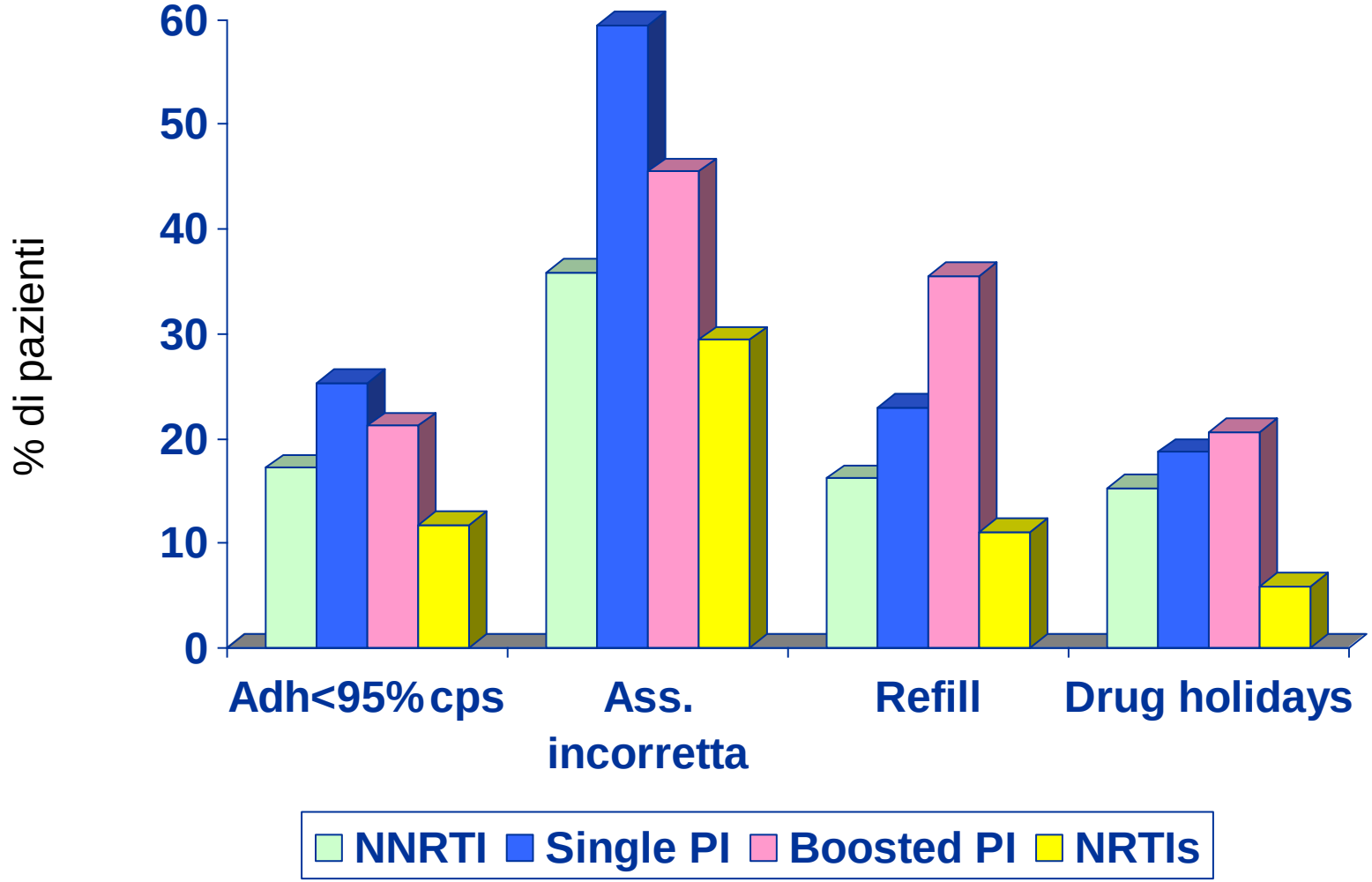
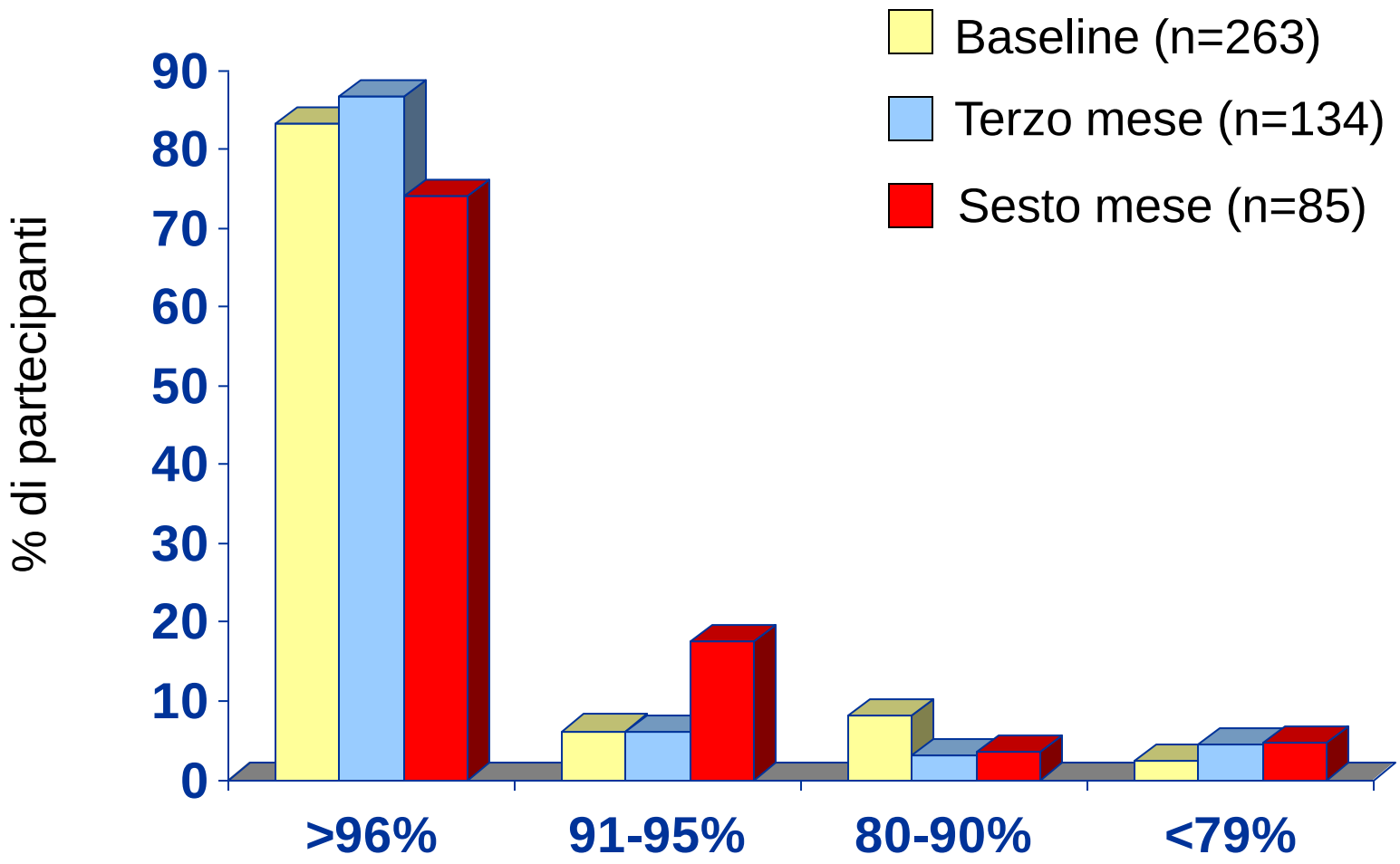
Flusso dei dati



Non-aderenza e tipo di HAART



Andamento dell' aderenza nel tempo



Motivazioni di non-aderenza

• Temere futuri effetti collaterali	109 (41.4%)
• Troppe compresse	87 (33.1%)
• Essere visto dagli altri	82 (31.2%)
• Essere fuori casa	79 (30.0%)
• Ricordarsi della malattia	75 (28.5%)
• Essere troppo impegnato	71 (27.0%)
• Precedenti effetti collaterali	55 (20.9%)
• Dover modificare gli orari abituali	55 (20.9%)
• Compresse troppo grandi	48 (18.3%)
• Schema troppo complicato	43 (16.3%)
• Assumere la terapia negli orari di sonno	39 (14.8%)
• Assumere farmaci di sapore sgradevole	38 (14.4%)

Sintomi auto-riportati

• Astenia	40 (15.2%)
• Ansia	36 (13.7%)
• Insonnia	32 (12.2%)
• Mialgia	22 (8.4%)
• Disturbi della vista	21 (8.0%)
• Alterazioni nella sfera sessuale	21 (8.0%)
• Confusione	20 (7.6%)
• Dolore	20 (7.6%)
• Lipodistrofia	17 (6.5%)
• Tosse	16 (6.1%)
• Anoressia	16 (6.1%)
• Diarrea	16 (6.1%)
• Prurito	15 (5.7%)
• Nausea	13 (4.9%)

Interventi proposti dal paziente

• Riduzione n° di cps o somministrazioni	92 (47.2%)
• Gestione degli effetti collaterali	57 (29.2%)
• Materiale informativo	51 (26.0%)
• Sospensione temporanea della terapia	39 (20.0%)
• Più tempo dedicato all’aderenza	35 (17.9%)
• Colloquio psicologico	31 (15.9%)
• Servizio telefonico	30 (15.4%)
• Più facile approvvigionamento di farmaci	29 (14.9%)
• Coinvolgimento di famigliari e amici	26 (13.3%)
• Dispositivo sonoro	26 (13.3%)
• Gruppi di auto-aiuto	16 (8.21%)
• Colloquio con l’assistente sociale	13 (6.67%)
• Incontri con il personale infermieristico	8 (4.10%)
• Trattamento delle dipendenze da alcol o droghe	6 (3.08%)

DOI: 10.1111/j.1468-1293.2009.00750.x
HIV Medicine (2010), 11, 104–113

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Conceived by Professor Mauro Moroni

Insights into reasons for discontinuation according to year of starting first regimen of highly active antiretroviral therapy in a cohort of antiretroviral-naïve patients

P Cicconi,[1] A Cozzi-Lepri,[2] A Castagna,[3] EM Trecarichi,[4] A Antinori,[5] F Gatti,[6] G Cassola,[7] L Sighinolfi,[8] P Castelli[9] and A d'Arminio Monforte[1] for the ICoNA Foundation Study Group*

Aim: The objective was to compare the incidence of discontinuation according to calendar period of HAART initiation:

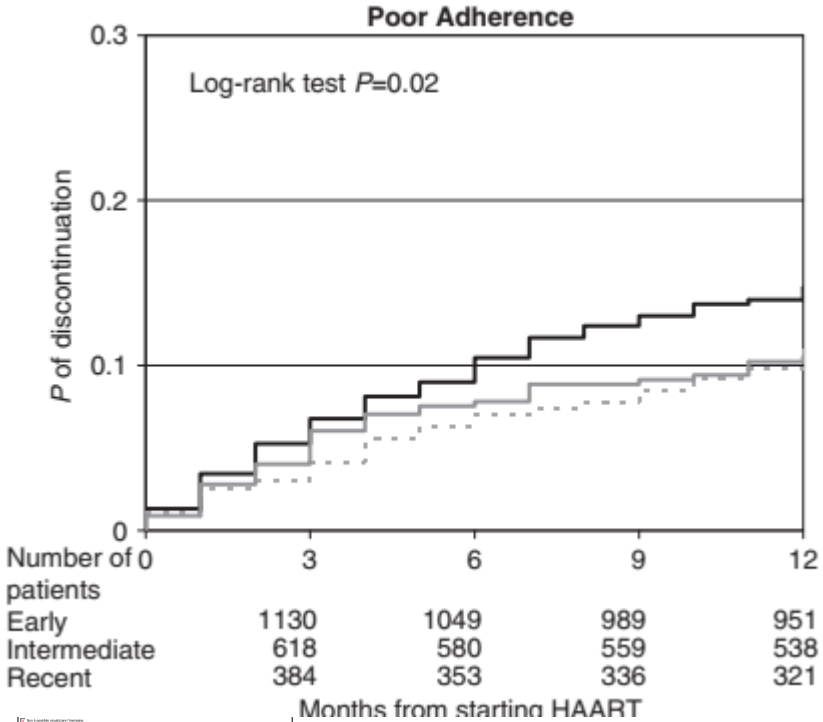
- Early period: 1997–1999;
- Intermediate period: 2000–2002;
- Recent period: 2003–2007,

Study Population: PLWH enrolled in the Icona cohort who started HAART when ART-naive from 1997 to 2007, and with at least one follow-up clinical visit after starting therapy.

Methods: Standard survival analysis employing Kaplan–Meier estimates was used to estimate the probability of discontinuing at least one drug of the HAART regimen by 1-year after starting therapy.

3,273 PLWH included in the analysis:

- N=1713 (1997-1999; Early)
- N=925 (2000-2002; Intermediate)
- N=635 (2003-2007; Recent)



1-year probability of discontinuation by KM for poor adherence (log-rank p=0.02)

- 14.7% (95% CI 12.7–16.8%) early period
- 10.9% (95% CI 8.4–13.4%) intermediate period
- 10.5% (95% CI 7.4–13.6%) recent period

Adjusted Cox Regression model

Variable	Poor adherence ARH (95% CI)	P
Year of first HAART		
1997–1999	1	
2000–2002	0.85 (0.59–1.21)	0.36
2003–2007	1.00 (0.64–1.56)	0.98
Female *vs.* male gender	1.42 (1.07–1.89)	0.01
Age group		
<30 years	1.34 (0.97–1.84)	0.07
30–45 years	1	
>45 years	0.98 (0.63–1.53)	0.94
HIV risk group		
MSM *vs.* heterosexual	0.96 (0.62–1.50)	0.88
IDU *vs.* heterosexual	2.85 (1.89–4.30)	<0.0001
HCV antibody–positive	1.01 (0.69–1.46)	0.95
HIV RNA pre-therapy, per $\log_{10}$ copies/mL higher	1.05 (0.92–1.21)	0.42
CD4 pre-therapy, per 100 cells/μL higher	1.08 (1.02–1.14)	0.002
HAART regimen		
2 NRTIs + 1 NNRTI	1	
2 NRTIs + single PI	1.19 (0.83–1.69)	0.32
2 NRTIs + boosted PI	0.96 (0.55–1.68)	0.90
3 NRTIs	1.84 (1.09–3.12)	0.02
Other regimen	2.98 (1.36–6.54)	0.006

Patient-Reported Outcomes (PROs) evaluation among HIV-infected patients starting EVG/cob/FTC/TDF

I. Mastrorosa et al. (Oral presentation; 10th ICAR 2018, Roma)

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Aim: longitudinal evaluation of PROs in PLWH enrolled in ICONA cohort starting E/C/F/TDF, over 2015-2017, from either ART-naïve or ART-experienced patients

Methods: Patients were asked to complete previously validated self-administered questionnaires at the start of E/C/F/TDF (baseline), after 3 and 6 months.

PROs evaluated were:

- Health-related Quality of Life (EuroQol, EQ-5D-5L)
- Self-reported adherence (visual analogue scale, VAS 0-100)*
- Depression (CES-D-10)
- Health status (VAS 0-100 for general, psychological and physical health)
- 21 symptoms listed on a likert scale (0=never; 4=always).

Stats: *EQ-5D-5L* was calculated considering Italian Population-Based Values. *Stepwise backward multivariable logistic regression* was used to identify independent predictors of having a EQ-5D-5L worse than the ideal score of 1,1,1,1,1 (**MaxScore**) at baseline, from factors including socio-demographic and clinical features, as well as answers to the other *PROs*.

	ART-naïve (N=160)	ART-experienced (N=117)	*p-value*	Total (N=277)
Gender, n. (%)			*0.444*	
Female	36 (22.5%)	31 (26.5%)		67 (24.2%)
Age (years), median (IQR)	38 (30, 47)	44 (38, 50)	***<.001***	41 (34, 48)
Mode of HIV transmission, n. (%)			*0.091*	
PWID	11 (7.0%)	12 (10.3%)		23 (8.4%)
MSM	86 (54.4%)	51 (44.0%)		137 (50.0%)
Heterosex	51 (31.9%)	50 (42.7%)		101 (36.5%)
Other/Unknown	10 (6.3%)	3 (2.6%)		13 (4.7%)
Italian Nationality, n. (%)	114 (71.3%)	94 (80.3%)	*0.085*	208 (75.1%)
Education, n. (%)			***0.001***	
Elementary	6 (3.8%)	4 (3.4%)		10 (3.6%)
Secondary	25 (15.6%)	11 (9.4%)		36 (13.0%)
College	59 (36.9%)	30 (25.6%)		89 (32.1%)
University	31 (19.4%)	15 (12.8%)		46 (16.6%)
Other/Unknown	39 (24.4%)	57 (48.7%)		96 (34.7%)
Year of enrolment, n. (%)			***0.002***	
2015	67 (41.9%)	72 (61.5%)		139 (50.2%)
2016	91 (56.9%)	42 (35.9%)		133 (48.0%)
2017	2 (1.3%)	3 (2.6%)		5 (1.8%)
CD4 count (cells/mm3), n. (%)			***<.001***	
350+	70 (50.0%)	38 (84.4%)		108 (58.4%)
201-350	26 (18.6%)	4 (8.9%)		30 (16.2%)
0-200	44 (31.4%)	3 (6.7%)		47 (25.4%)
HIV-RNA (log10 copies/mL), median (IQR)	4.75 (4.09, 5.21)			3.97 (1.59, 5.01)
Time from HIV diagnosis (years), median (IQR)	0 (0, 1)	7 (3, 14)	***<.001***	1 (0, 7)
CD4 count nadir (cells/mm3), median (IQR)	347 (158, 526)	421 (246, 646)	***0.009***	373 (189, 569)

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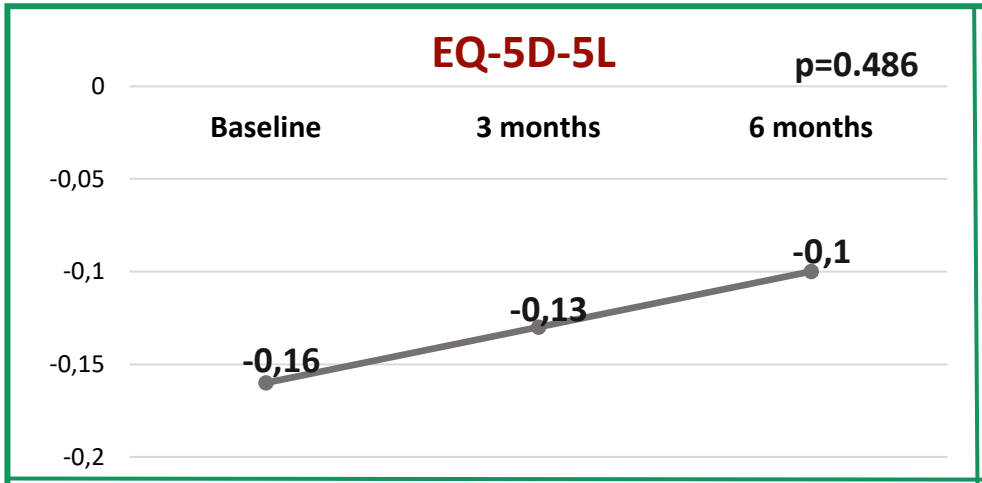
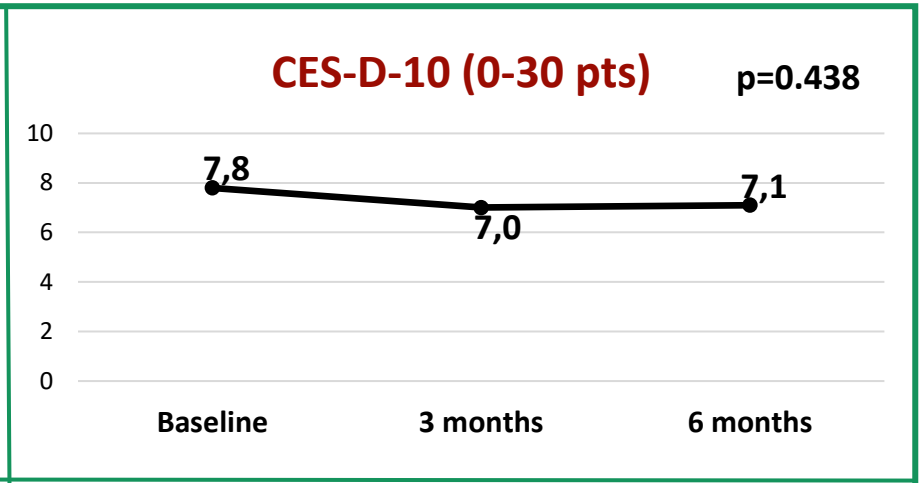
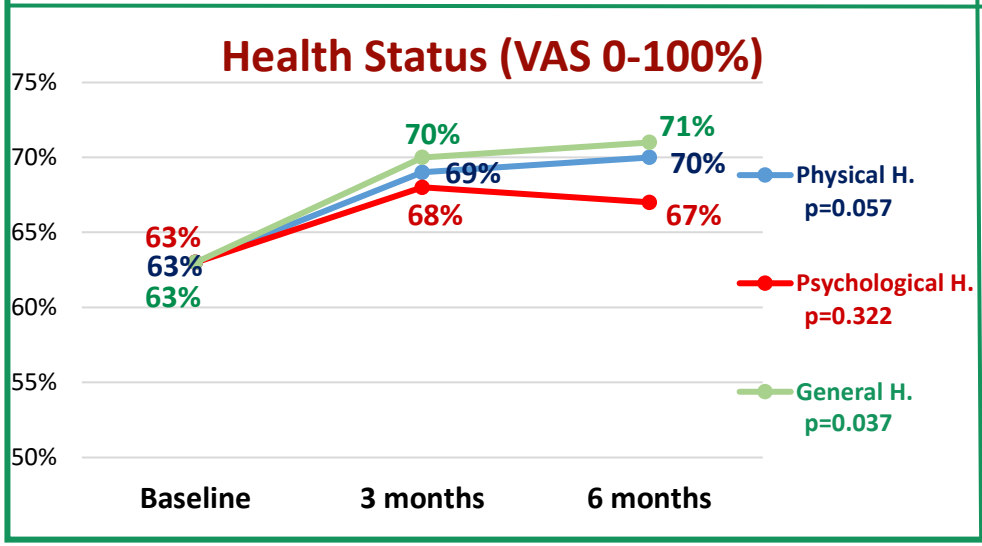
I. Mastrorosa et al.
(10th ICAR 2018, Rome)

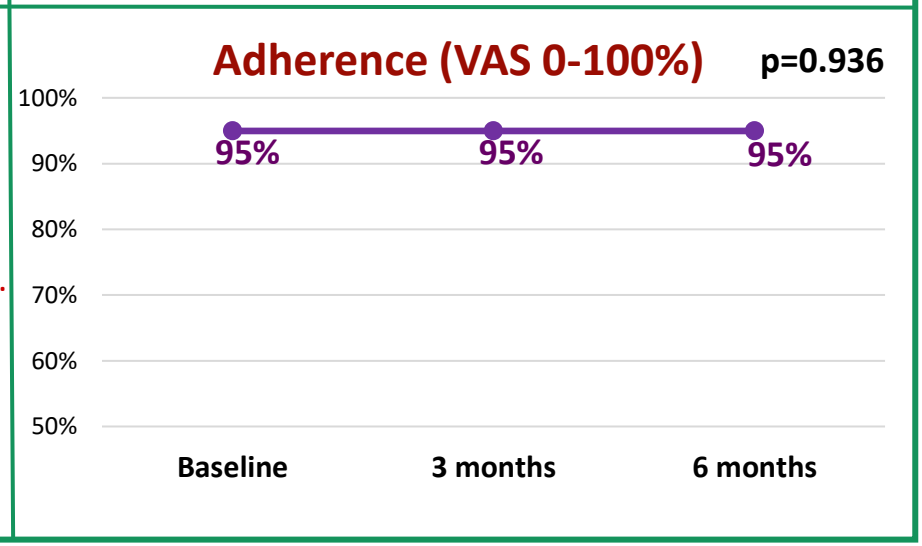
Changes in *PROs** - *ART-experienced*

**considering mean value of each visit questionnaire*









RESULTS
ART-experienced patients: health-related quality of life

	OR of EQ-5D < MaxScore					
	EQ-5D<MaxScore	EQ-5D=MaxScore	Unadjusted* OR (95% CI)	*p-value*	Adjusted* OR (95% CI)	*p-value*
	N= 57	N= 60				
Mental Confusion				*<.001*		***0.007***
No	18 (31.6%)	43 (71.7%)	1.00		1.00	
Yes	39 (68.4%)	17 (28.3%)	5.48 (2.48, 12.10)		3.38 (1.40, 8.16)	
Anxiety				*<.001*		***0.009***
No	15 (26.8%)	39 (65.0%)	1.00		1.00	
Yes	41 (73.2%)	21 (35.0%)	5.08 (2.29,11.24)		3.22 (1.33, 7.77)	
Adherence						
100%	36 (67.9%)	51 (85.0%)	1.00	0.035	1.00	0.065
0-99%	17 (32.1%)	9 (15.0%)	2.68 (1.07, 6.67)		2.61 (0.94, 7.26)	

****stepwise backward multivariable logistic regression, adjusted for all factors included***

Effectiveness of Single- vs Multiple-Tablet Regimens as First-line ART in ICONA Cohort

Mondi A. et al.
(Poster #0511; CROI 2019, Seattle)

Aim: evaluate and compare the effectiveness of first-line STRs versus MTRs, after stratifying MTRs according to the number of pills/daily administrations.

Study Population: PLWH who started a first-line triple ART with recommended or alternative regimens, according to EACS Guidelines 9.0, from Jan 2011 to Dec 2017

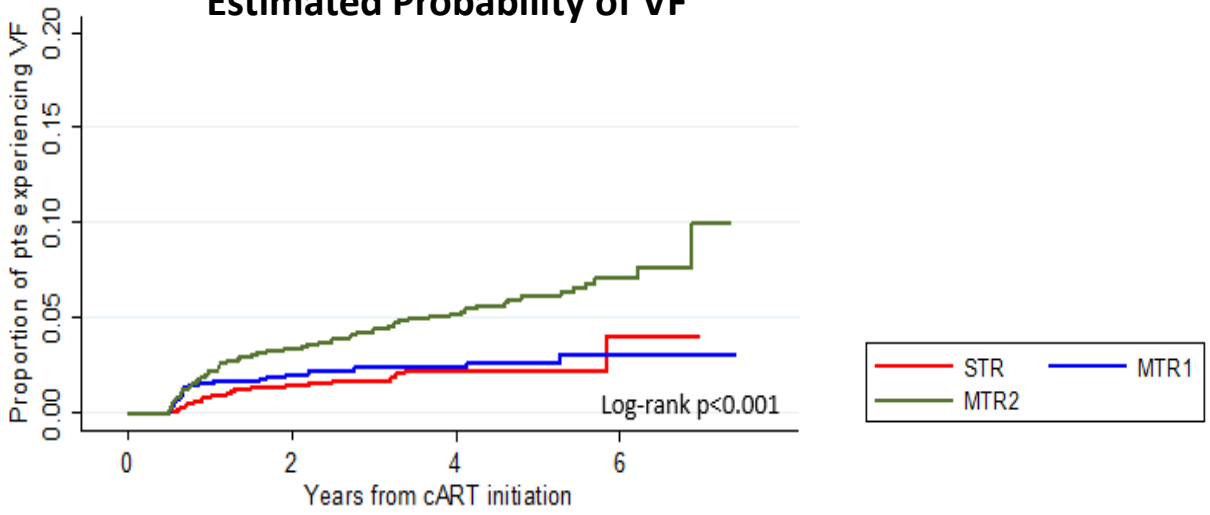
Patients were divided in 3 treatment groups:

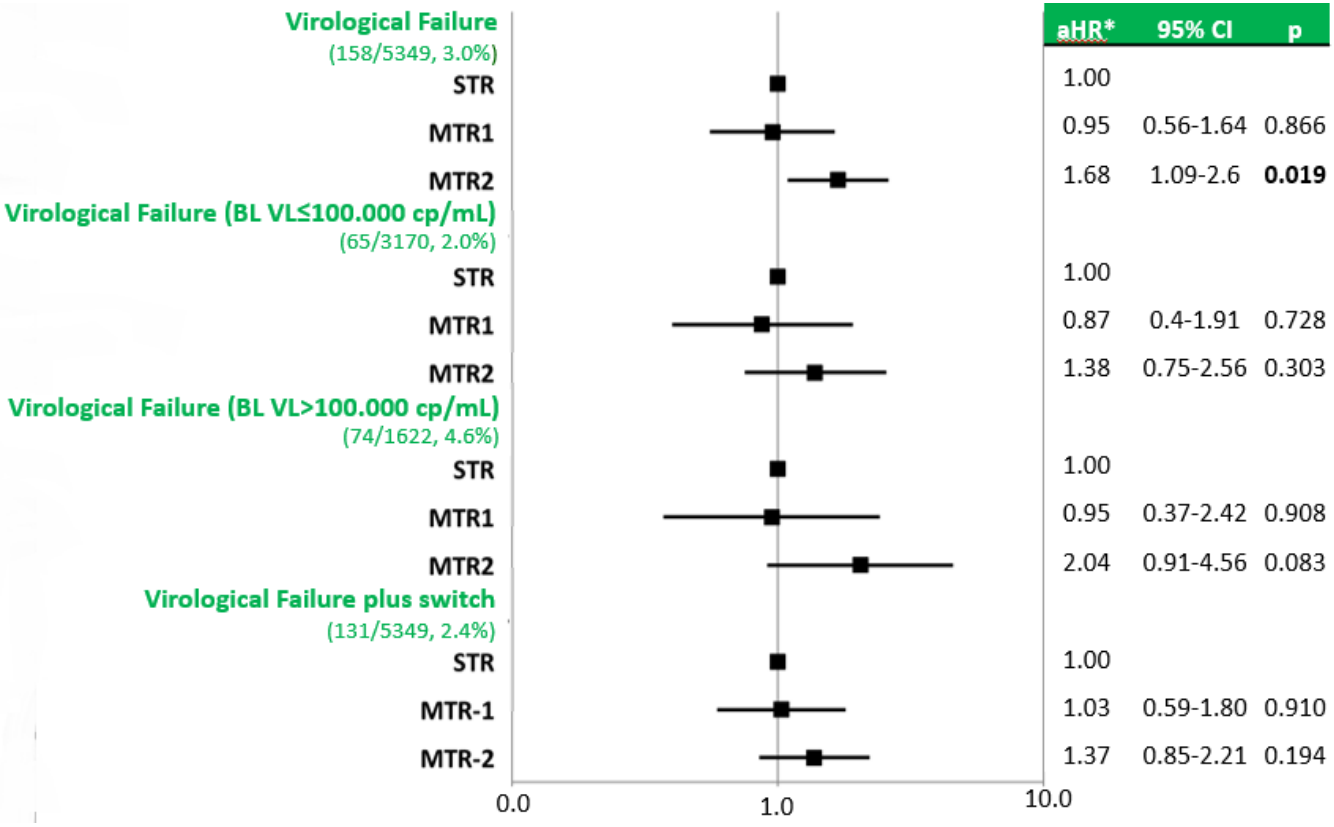
- Single Tablet Regimen (STR) group: 1 pill once daily (QD) regimen
- Multi Tablet Regimen-1 (MTR-1) group: 2 pills QD regimen
- Multi Tablet Regimen-2 (MTR-2) group: 3 pills QD or bis in die (BID) regimen

Primary Outcome: virological failure (VF) in patients starting STRs versus MTRs.
Secondary Outcomes: VF followed by ART switch (VF plus switch) of STRs versus MTRs; virological suppression (VS) of STRs versus MTRs.

Stats: Probabilities of VF and VS were estimated by Kaplan-Meier analysis. Cox multivariable analysis were fitted to evaluate the independent risk of VF, VF plus switch and VS for STRs versus MTRs, after adjusting for main confounding factors.

Estimated Probability of VF



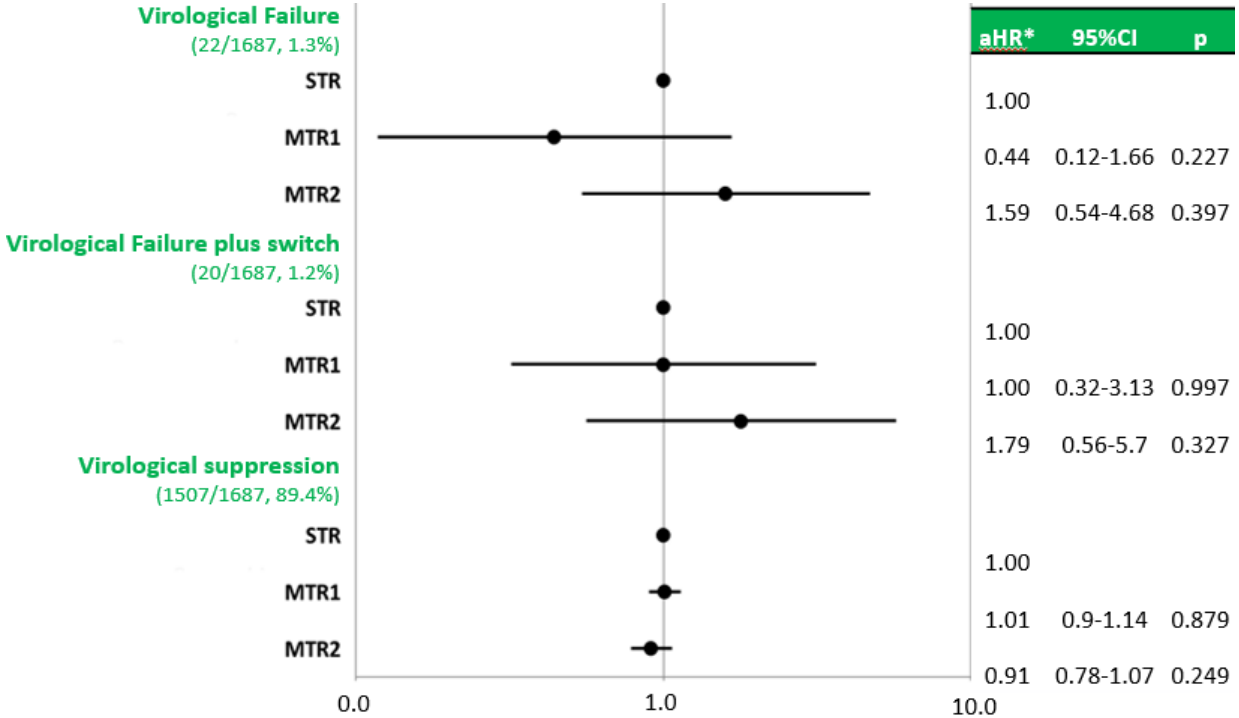


Total Population (n=5,349):

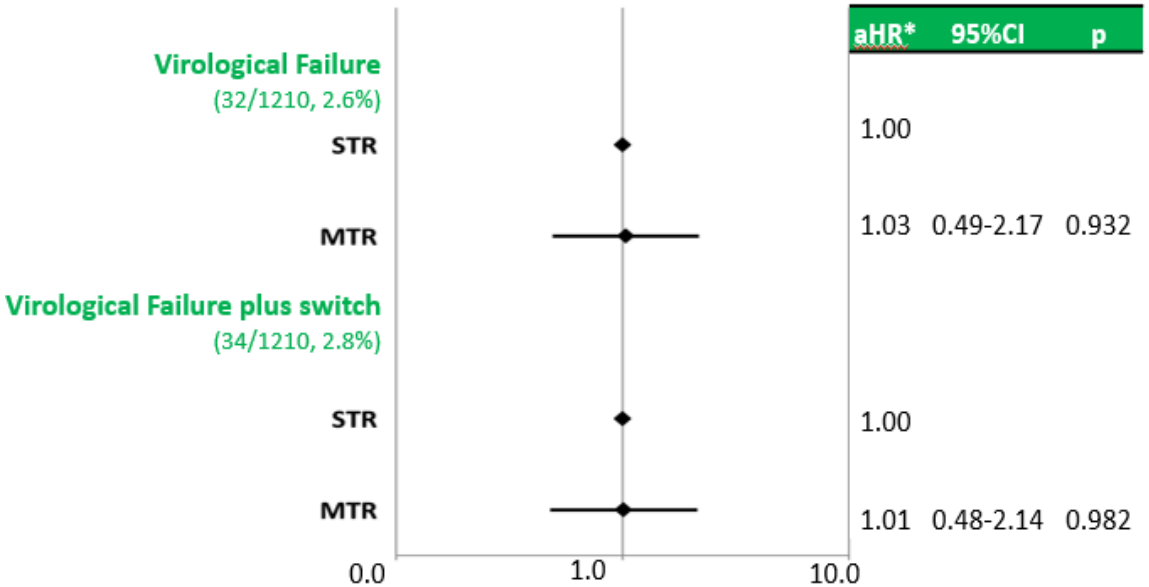
STR (2,240)

MTR-1 (1,128)

MTR-2 (1,981)



INSTI-based regimens (n=1687)



Regimens available as both MTR and STR [TDF,FTC,EFV (n=802) or ABC,3TC,DTG (n=408)]

Conclusions:

- Among currently recommended or alternative first-line antiretroviral regimens, STRs and 2-pills QD MTRs showed a similar impact on virological failure. Conversely, 3-pills containing MTRs were associated to a higher risk of virological failure compared to STRs.
- In the sensitive analyses, restricted to INSTI-based first-line ART and to regimens available as both MTR and STR, the probability of virological failure was not influenced by the number of pills/administrations. Moreover, in patients receiving an INSTI-based regimen, time-to-virological suppression, a possible proxy of patients' adherence, was not different by pill burden of the regimen.
- Even though these results have the limitation of a non-randomized design, the large study population and the reproducibility across different end points and subgroups confirmed the consistency of these findings.
- These data may add important information to guide the choice of first-line ART in every-day clinical practice, particularly in the light of the current availability of generic antiretroviral drugs.

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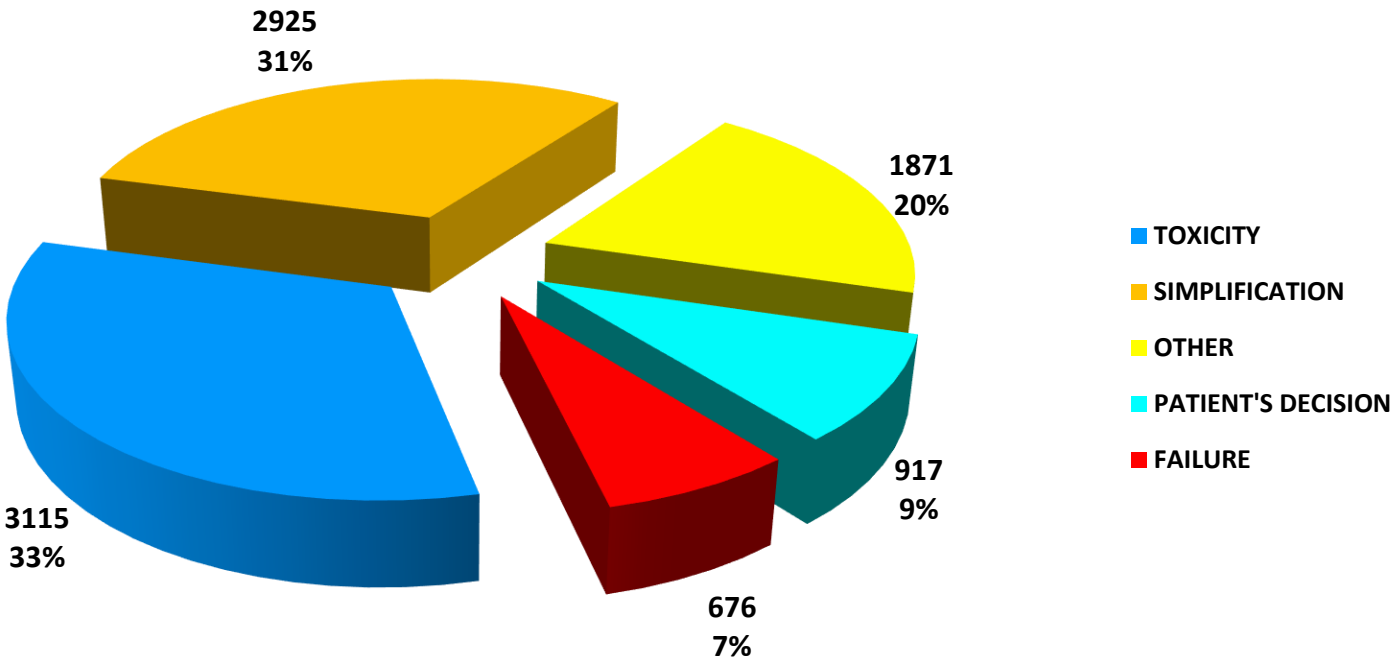
Distribution of reasons for stopping at least one drug included in the first regimen N=9504



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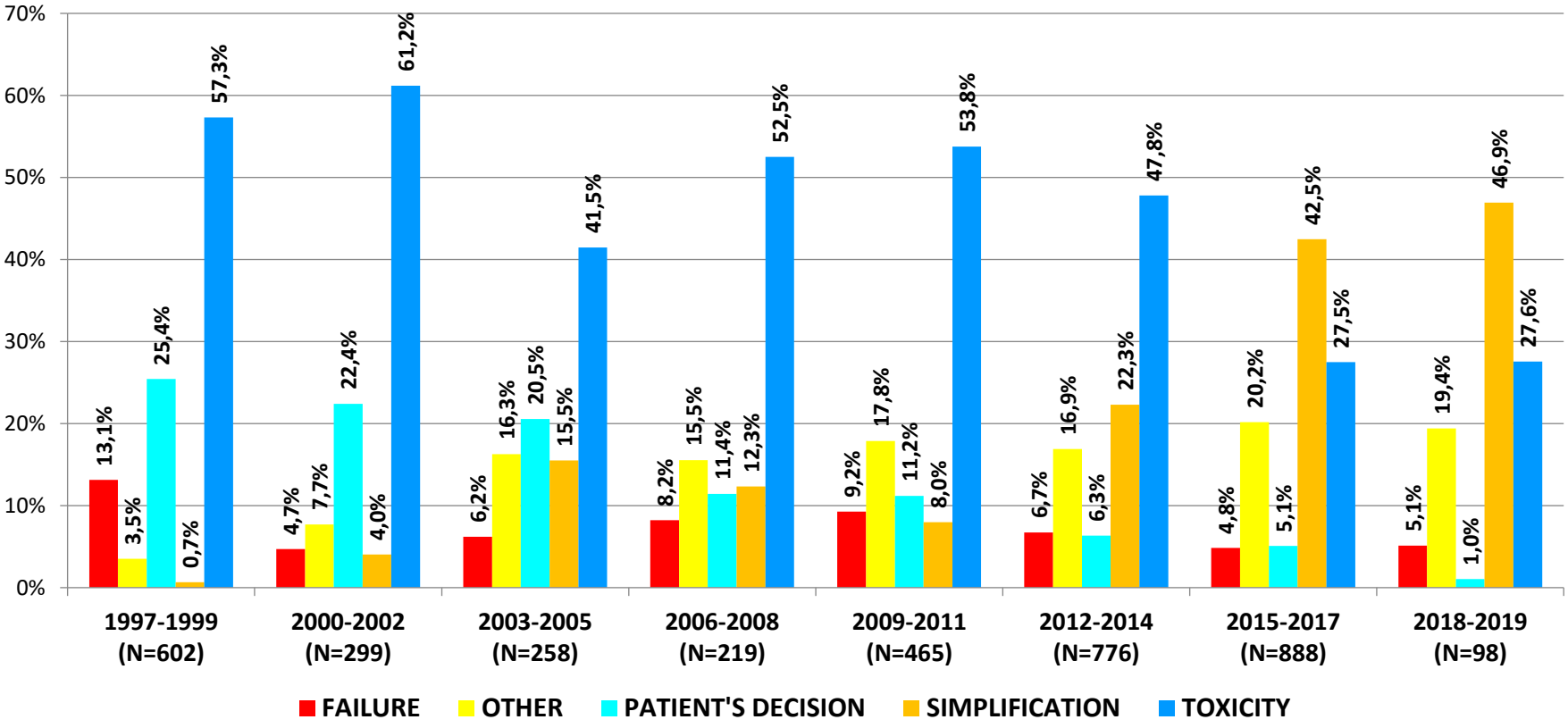
Italian Cohort I. C O. N A. Naive Antiretrovirals

Reasons for stopping at least one drug of the first ART regimen within 1 year, according to calendar period of starting
N = therapy interruptions per period



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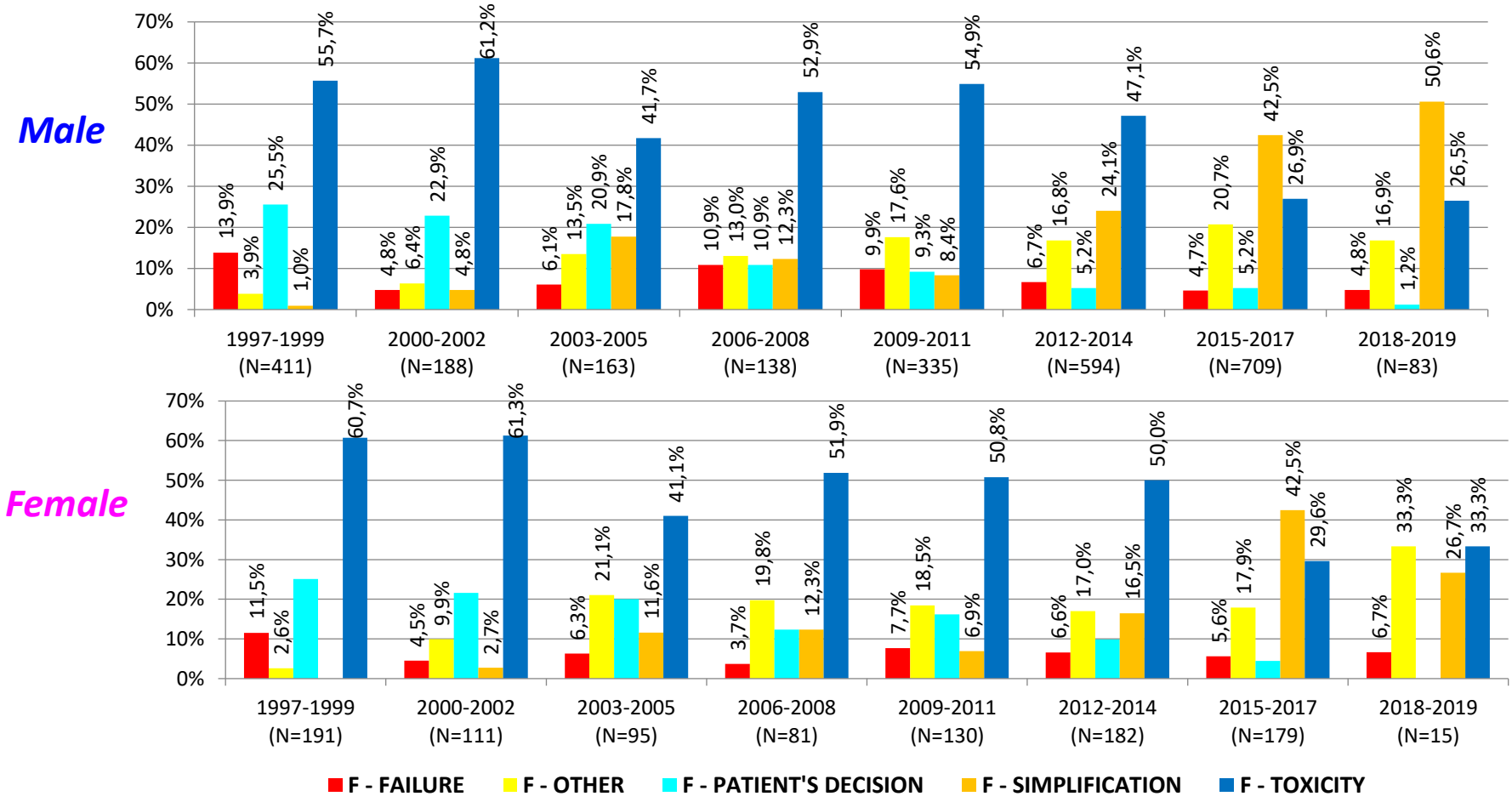
Italian Cohort I. C O. N A. Naive Antiretrovirals

Reasons for stopping at least one drug of first ART regimen within 1 year, according to calendar period of starting



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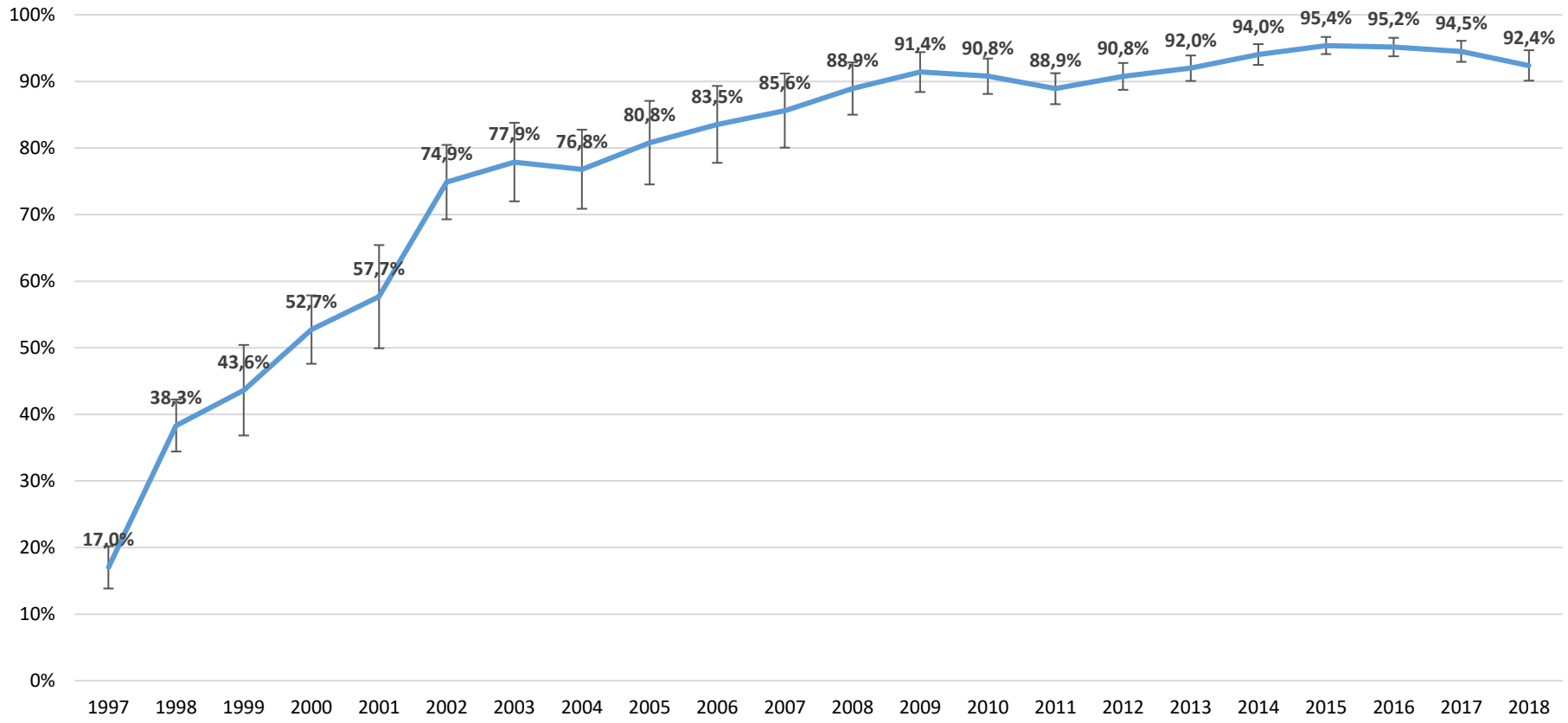
Proportion of patients with a VL<=80 copies/mL at 12 months from starting their first ART regimen by calendar year of initiation



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