ART switch for pro-active, re-active or cost-saving reasons: a real world evaluation of the determinants over the period 2017-2020 in the Veneto Region

Anna Maria Cattelan, Alessandro Cozzi-Lepri, Maria Mazzitelli, Marina Malena, Lolita Sasset, Pierangelo Rovere, Vinicio Manfrin, Roberto Ferretto, Marta Fiscon, Marcello Vincenzi, Giuliana Battagin, Ilaria Coledan, Lucio Da Ros, Massimiliano Lanzafame

Anna Maria Cattelan

Background

- As PLWH are living longer, continual advancements in antiretroviral regimens have been a focus to provide optimal life-long therapy options.
- In recent years, with the advent of simpler and more tolerated regimens an increasing proportion of persons living with HIV (PLWH) undergo treatment switches (TSw)
- TSw occur for **«pro-active reasons»**, such as to prevent long-term toxicity, reduce drug-drug interactions, simplify therapy, and improve adherence, or for **«re-active reasons»** typically driven by ongoing toxicities, drug-drug or drug-food interactions, or treatment failure. In addition, ART may be switched for «**cost saving reasons»** in absence of other triggers

Aim of this study is to investigate and compare patients' profiles more frequently associated with pro-active or re-active switch vs. those due to cost-saving reasons

Methods

- We performed a retrospective analysis in a cohort of HIV-positive pts of 6 outpatient's clinic for HIV care in the Veneto Region who switched their antiretroviral regimen over a period of 4 years (2017-2020)
- TSw were classified as: i) pro-active (TSw-1),
  ii) re-active (TSw-2)
  iii) cost-saving (TSw-3).
- For PLWH who underwent more than one TSw in the same calendar period, only the first of these TSw was included
- We collected the demographics and disease characteristics of the patients as well as viro-immunological parameters and markers of metabolic profile at switching time

- The frequency of TSw according to participants' characteristics at time of switch and their comparison were calculated using a chi-square test. The association between a selected number of participants' characteristics and the probability of switching for pro-active or re-active vs. cost-saving reasons was evaluated using a multinomial logistic regression Separate multivariable models were fitted for each of the characteristics after controlling model-specific confounding variables.

Participants characteristics at time of switch by main reason for switch

Characteristics	Reason for therapy switch				
	Cost-saving	Pro-active	Re-active	p-value*	Total
	N= 93	N= 112	N= 200		N= 405
Age, years				0.093	
Median (IQR)	49 (40, 56)	51 (45, 57)	52 (43, 57)		51 (43, 57)
Gender, n(%)				0.477	
Female	24 (25.8%)	32 (28.6%)	65 (32.5%)		121 (29.9%)
Mode of HIV Transmission, n(%)				0.136	
IDU	11 (11.8%)	14 (12.5%)	46 (23.0%)		71 (17.5%)
Homosexual contacts	42 (45.2%)	46 (41.1%)	60 (30.0%)		148 (36.5%)
Heterosexual contacts	34 (36.6%)	46 (41.1%)	83 (41.5%)		163 (40.2%)
Other/Unknown	6 (6.5%)	6 (5.4%)	11 (5.5%)		23 (5.7%)
Nationality, n(%)				0.402	
Not Italian	20 (21.5%)	22 (19.6%)	52 (26.0%)		94 (23.2%)
AIDS diagnosis, n(%)				0.475	
Yes	18 (19.4%)	23 (20.5%)	50 (25.0%)		91 (22.5%)
Comorbidities, n(%)					
Cardiovascular	14 (15.1%)	23 (20.5%)	40 (20.0%)	0.538	77 (19.0%)
Diabetes	3 (3.2%)	11 (9.8%)	12 (6.0%)	0.151	26 (6.4%)
Dyslipidemia	6 (6.5%)	34 (30.4%)	37 (18.5%)	<.001	77 (19.0%)
Hepatitis	15 (16.1%)	19 (17.0%)	52 (26.0%)	0.599	86 (21.2%)
Neurologic	4 (4.3%)	6 (5.4%)	13 (6.5%)	0.068	23 (5.7%)
Cancer	12 (12.9%)	8 (7.1%)	19 (9.5%)	0.740	39 (9.6%)
Bone	5 (5.4%)	8 (7.1%)	10 (5.0%)	0.379	23 (5.7%)
Renal	3 (3.2%)	9 (8.0%)	5 (2.5%)	0.728	17 (4.2%)
Psychiatric	4 (4.3%)	8 (7.1%)	15 (7.5%)	0.057	27 (6.7%)
Other	9 (9.7%)	21 (18.8%)	33 (16.5%)	0.578	63 (15.6%)
Calendar period of switch				0.179	
2017-2018	33 (35.5%)	66 (58.9%)	98 (49.0%)		197 (48.6%)
2019-2020	60 (64.5%)	46 (41.1%)	102 (51.0%)		208 (51.4%)

*Chi-square or Kruskal-Wallis test as appropriate

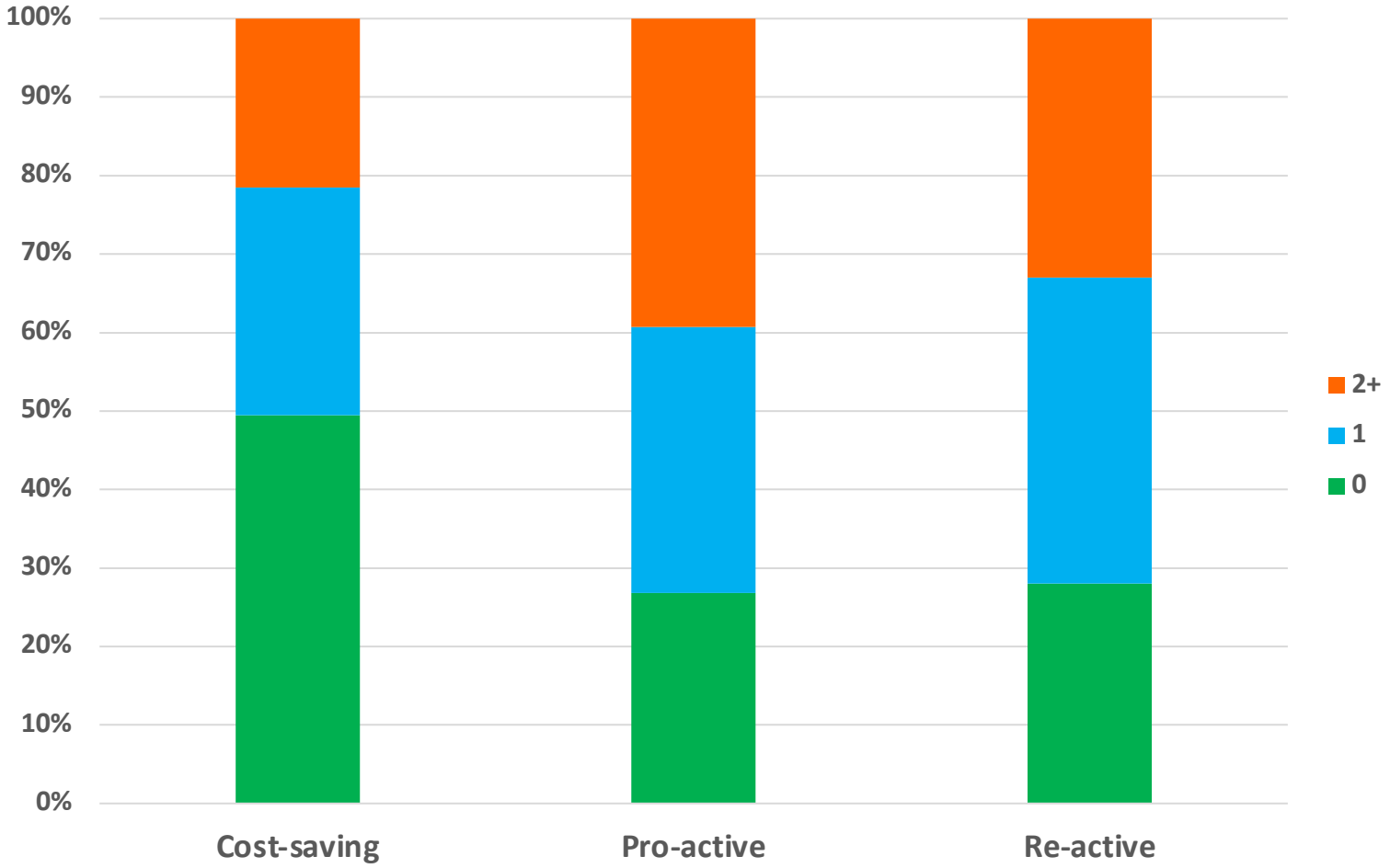
Immuno-virological markers by main reason for switch

	Reason for therapy switch				
Characteristics	**Cost-saving**	**Pro-active**	**Re-active**	**p-value***	**Total**
	N= 93	N= 112	N= 200		N= 405
Current HIV-RNA, log_{10} copies/mL				**<.001**	
Median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 1.3)		0.0 (0.0, 0.0)
0-50	85 (91.4%)	105 (95.5%)	160 (80.4%)		350 (87.1%)
50-1000	7 (7.5%)	4 (3.6%)	26 (13.1%)		37 (9.2%)
1000+	1 (1.1%)	1 (0.9%)	13 (6.5%)		15 (3.7%)
Nadir CD4 count, cells/mm^3				0.063	
Median (IQR)	270 (110, 390)	276 (150, 380)	210 (66, 347)		243 (88, 363)
0-200	37 (40.7%)	34 (32.1%)	84 (47.5%)		155 (41.4%)
200-500	43 (47.3%)	60 (56.6%)	75 (42.4%)		178 (47.6%)
500+	11 (12.1%)	12 (11.3%)	18 (10.2%)		41 (11.0%)
Current CD4 count, cells/mm^3				0.101	
Median (IQR)	662 (472, 902)	734 (518, 993)	678 (472, 820)		686 (487, 893)
0-200	3 (3.2%)	3 (2.7%)	8 (4.0%)		14 (3.5%)
200-500	25 (26.9%)	20 (17.9%)	51 (25.5%)		96 (23.7%)
500+	65 (69.9%)	89 (79.5%)	141 (70.5%)		295 (72.8%)

*Chi-square or Kruskal-Wallis test as appropriate

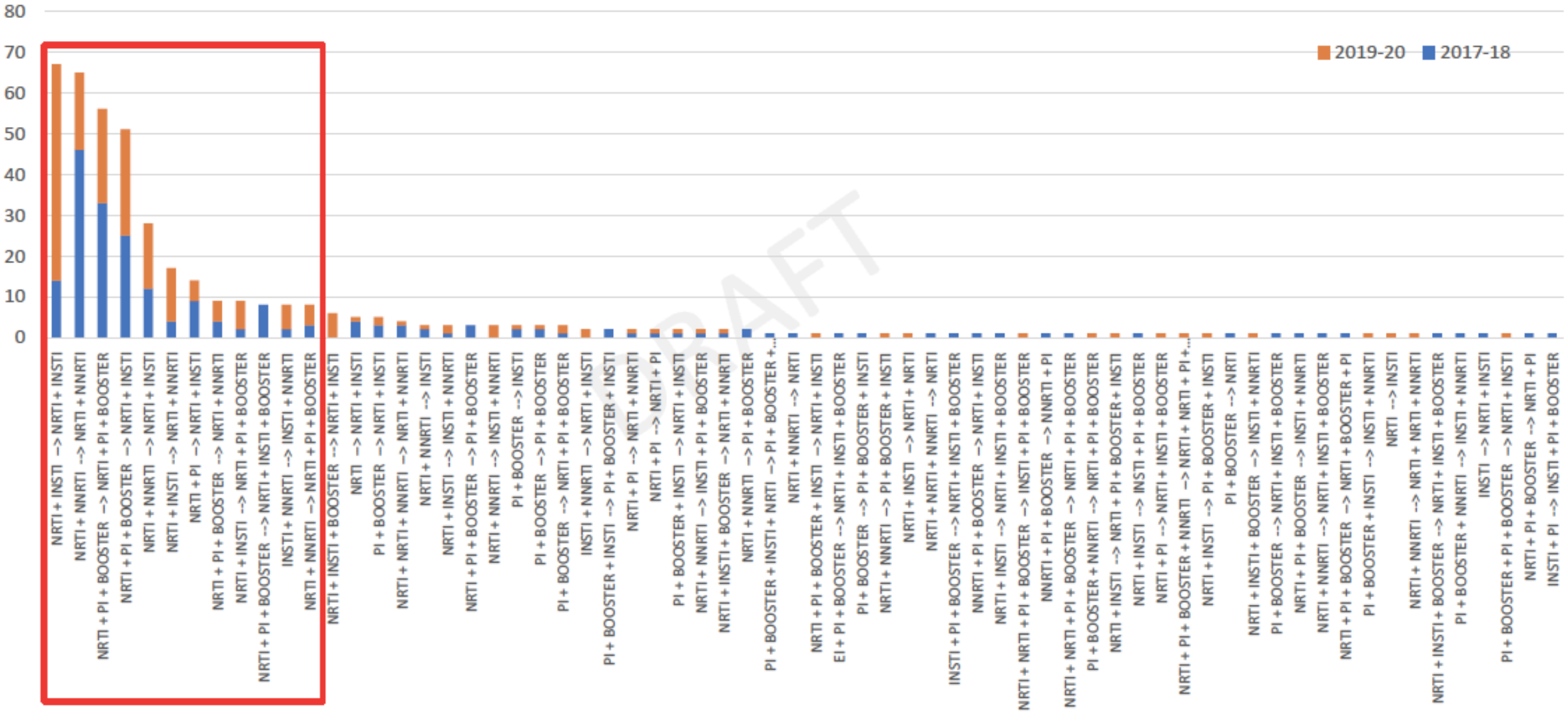
Number of Co-morbidities vs. switches type

* 32% subjects: no comorbidities
* 68% subjects: 1 o > comorbidities

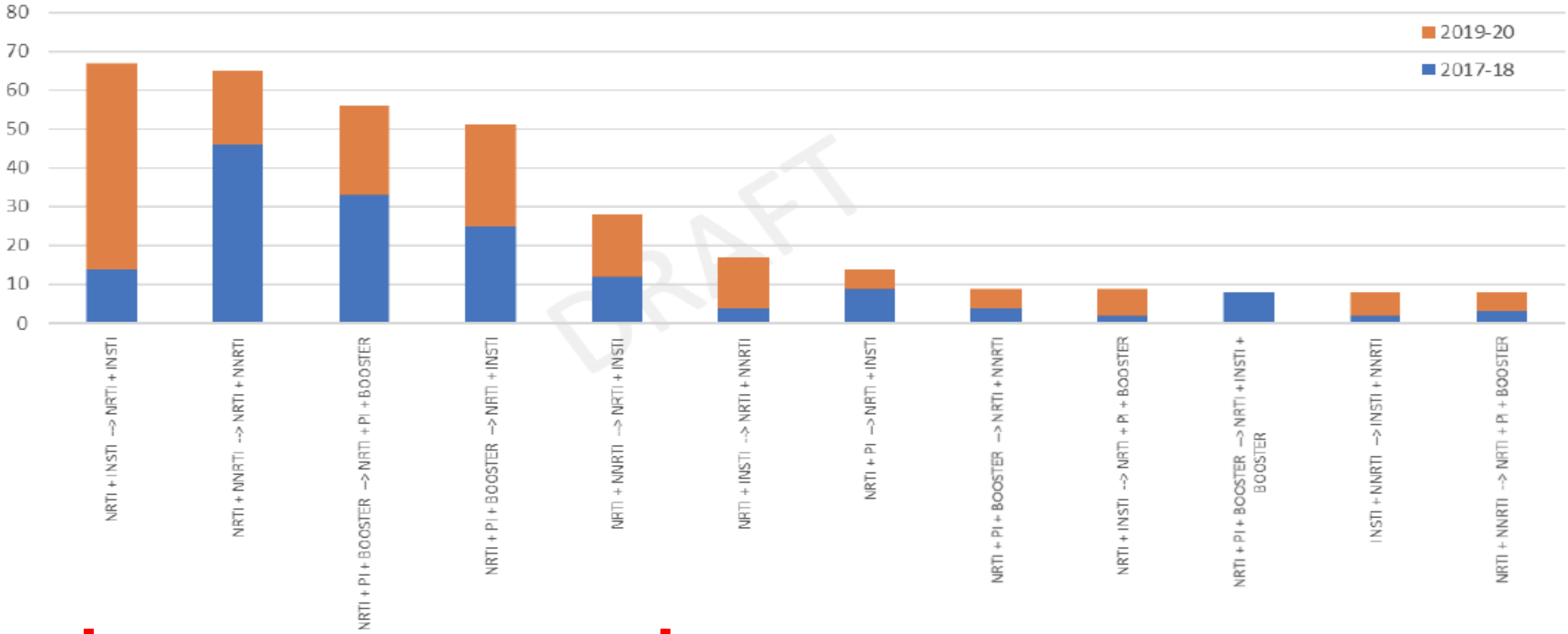


Comorbidities Number -->	0	1	≧2	
Cost-saving	46	27	20	93
Pro-active	30	38	44	112
Re-active	56	78	66	200
Total	**132**	**143**	**79**	**405**

66 different types of switch-regimens

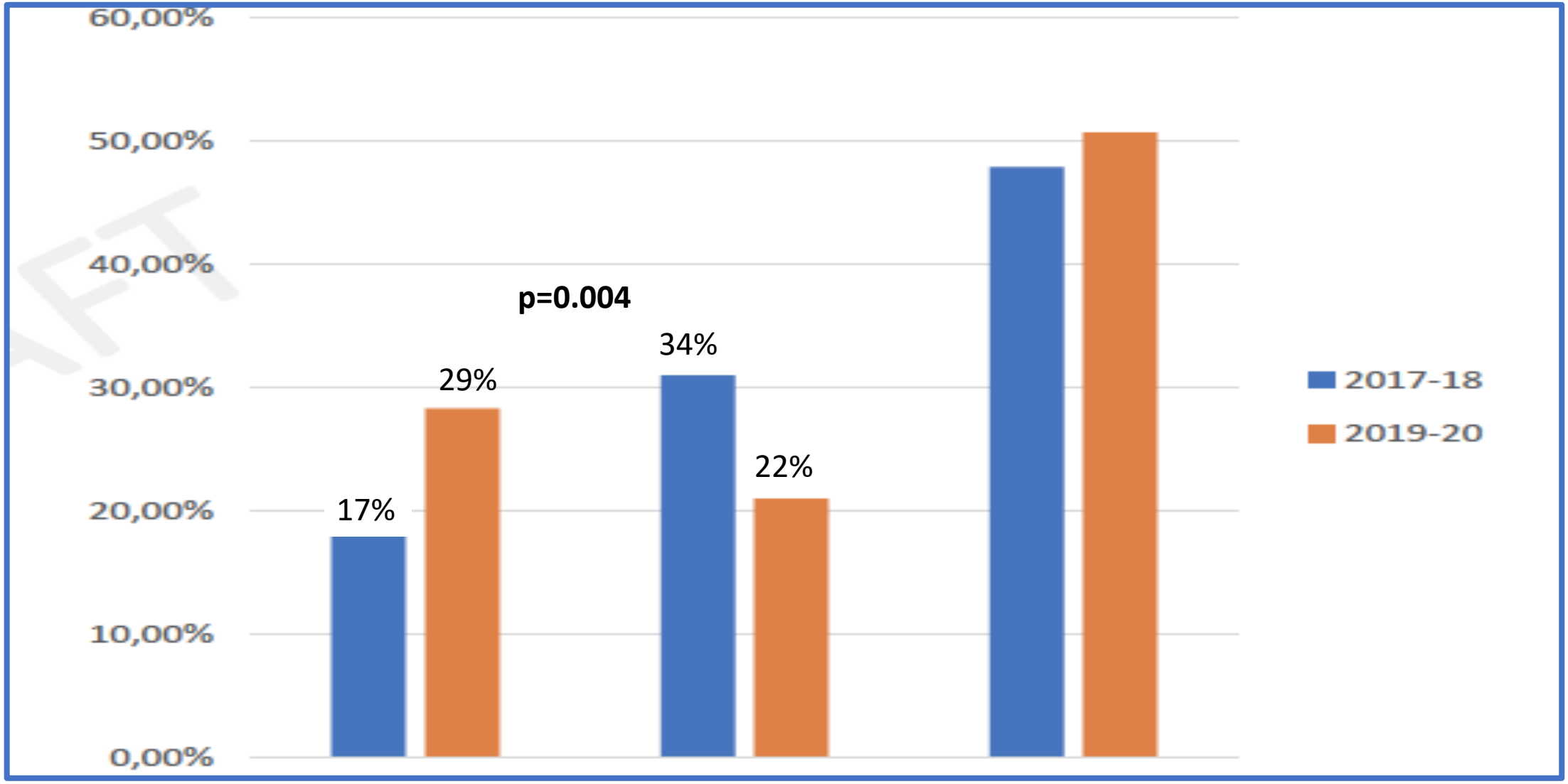


Top 12 types account for 79% of switches



Top 5 for 42%

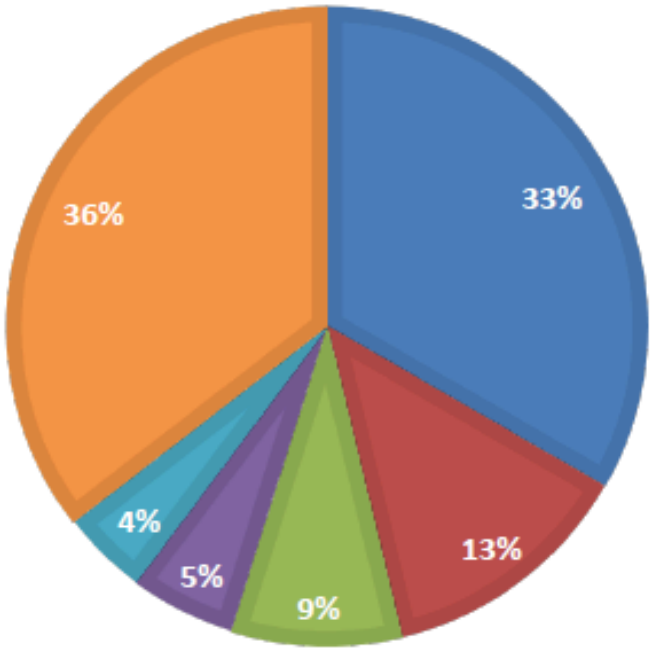
Type of switches by calendar period



Top 5 new regimens after switches by switch reason

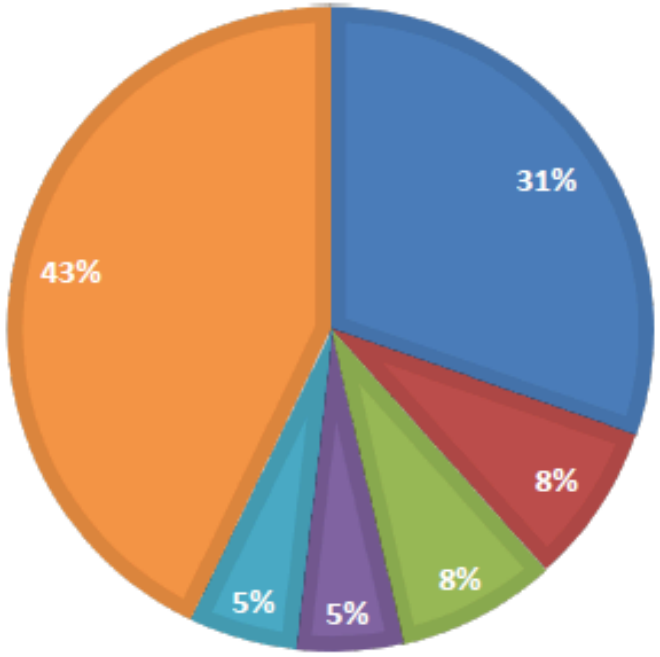
COST SAVING

- lamivudina + dolutegravir
- TAF/emtricitabina/rilpivirina
- darunavir/cobicistat/TAF/emtricitabina
- abacavir/lamivudina/dolutegravir
- abacavir/lamivudina + dolutegravir
- Other



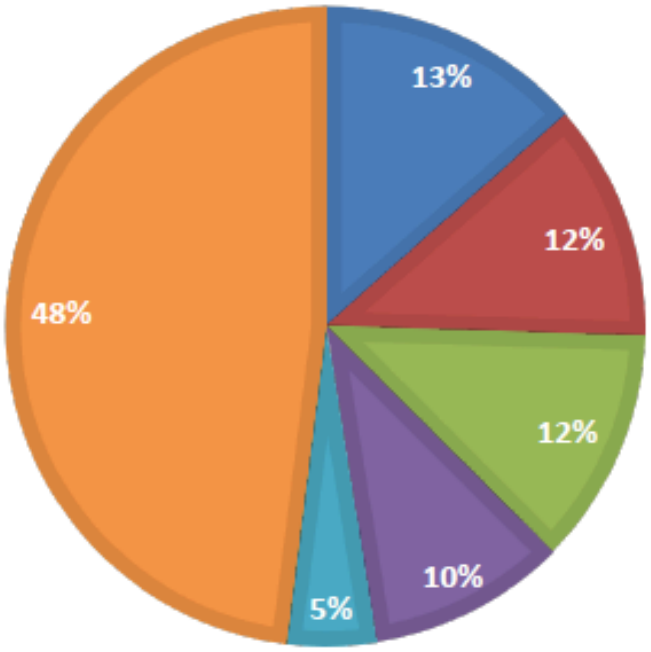
PRO-ACTIVE

- lamivudina + dolutegravir
- TAF/emtricitabina+dolutegravir
- TAF/emtricitabina/rilpivirina
- TAF/emtricitabina+darunavir/cobicistat
- TAF/emtricitabina + nevirapina
- Other



RE-ACTIVE

- TAF/emtricitabina/rilpivirina
- abacavir/lamivudina/dolutegravir
- lamivudina + dolutegravir
- darunavir/cobicistat/TAF/emtricitabina
- abacavir/lamivudina+nevirapina 400mg
- Other



Unadjusted OR from fitting a multinomial logistic regression model

	Reason for therapy switch			
Factors	**Cost-saving**	**Pro-active**	**Re-active**	**p-value**
	Comparator	**Unadjusted OR 95% CI**	**Unadjusted OR 95% CI**	
Age, >65 years	**1**	**4.46 (0.95, 20.90)**	**3.69 (0.83, 16.48)**	**0.077**
Dyslipidemia	**1**	**6.32 (2.52, 15.85)**	**3.29 (1.34, 8.09)**	**<.001**
Hepatitis	**1**	**1.06 (0.51, 2.23)**	**1.83 (0.97, 3.45)**	**0.067**
Current VL, >50 copies/mL	**1**	**0.51 (0.16, 1.60)**	**2.59 (1.16, 5.79)**	**<.001**
Nadir CD4 count, below 200 cells/mm^3	**1**	**0.69 (0.38, 1.24)**	**1.32 (0.79, 2.20)**	**0.037**
Time from last therapy change, >24 months	**1**	**2.11 (1.20, 3.71)**	**1.37 (0.84, 2.26)**	**0.030**
No. previous regimens, >2	**1**	**0.87 (0.47, 1.62)**	**1.58 (0.92, 2.73)**	**0.050**
No. tablets previous regimen, >1	**1**	**2.08 (1.19, 3.66)**	**3.63 (2.15, 6.11)**	**<.001**
TDF in previous regimen	**1**	**3.00 (1.57, 5.74)**	**1.49 (0.81, 2.76)**	**0.001**
Abacavir in previous regimen	**1**	**0.53 (0.30, 0.95)**	**0.40 (0.23, 0.67)**	**0.003**
DTG in previous regimen	**1**	**0.34 (0.19, 0.63)**	**0.19 (0.11, 0.34)**	**<.001**
PI/r in previous regimen	**1**	**1.14 (0.64, 2.03)**	**1.66 (0.99, 2.76)**	**0.093**
Calendar period, 2019-2020	**1**	**0.38 (0.22, 0.68)**	**0.57 (0.34, 0.95)**	**0.003**
>=1 co-morbidities	**1**	**2.68 (1.49, 4.79)**	**2.52 (1.51, 4.19)**	**<.001**

Adjusted OR of impact of selected exposure variables from fitting a multinomial logistic regression model

	Reason for therapy switch				
Factors	Cost-saving	Pro-active		Re-active	
	Comparator	Adjusted OR 95% CI	p-value	Adjusted OR 95% CI	p-value
Dyslipidemia[1]	1	5.43 (2.14, 13.79)	<.001	3.08 (1.24, 7.67)	0.015
Nadir CD4 count[2], below 200 cells/mm[3]	1	0.60 (0.28, 1.29)	0.190	1.34 (0.70, 2.56)	0.370
No. tablets previous regimen[3], >1	1	2.07 (1.11, 3.87)	0.022	4.40 (2.46, 7.87)	<.001
TDF in previous regimen[4]	1	3.36 (1.75, 6.47)	<.001	1.58 (0.85, 2.94)	0.148
Abacavir in previous regimen[4]	1	0.48 (0.26, 0.86)	0.014	0.36 (0.21, 0.62)	<.001
DTG in previous regimen[4]	1	0.32 (0.17, 0.60)	<.001	0.18 (0.10, 0.33)	<.001
PI/r in previous regimen[4]	1	1.16 (0.65, 2.07)	0.613	1.66 (0.99, 2.77)	0.055
>=1 comorbidities[4]	1	2.58 (1.43, 4.63)	0.002	2.45 (1.47, 4.10)	<.001
[1]adjusted for age, gender, hepatitis, time from last therapy change and PI/r or TAF in previous regimen					
[2]adjusted for age, AIDS diagnosis, no. previous regimens used					
[3]adjusted for age, AIDS diagnosis, no. previous regimens used,>=2 comorbidities					
[4]adjusted for age, gender					

Conclusions

- In our analysis, «cost-saving» Treatment Switch appeared to be most prevalent in recent years
- Dolutegravir and Lamivudine was the most prevalent treatment switch regimen both in the «cost-saving» and «pro-active» switch
- «pro-active» Treatment Switch appeared to be mainly driven by detection of dyslipidaemia and previous use of TDF (53% were switched to TAF)
- The presence of >= 1 comorbidities is more frequently associated with a «pro-active» switch

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