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Simplification of complex antiretroviral treatment regimens to 2-class therapies in people with HIV

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Introduction

- Complex antiretroviral treatment (ART) regimens with ≥3 drug classes carry a higher risk for toxicity and drug-drug interactions compared to 2-class regimens
- Recent studies with modern integrase strand transfer inhibitors (INSTIs) suggest that ART simplification is safe and effective in people with HIV (PWH) on complex regimens due to prior virological failure or acquired HIV drug resistance mutations

Aims

- to describe the population of PWH who continue to receive ≥3 drug classes since the availability of INSTI-based single tablets
- to assess the proportion who switched to any 2-class regimen
- to explore predictors of switching

Methods

- **Study design:** prospective Swiss HIV Cohort Study
- **Population:** PWH on ART containing ≥3 drug classes and follow-up between 11/2013 and 11/2023
  - Definition of drug classes: NRTI, NNRTI, PI, INSTI, or entry inhibitors
- **Outcome:** ART simplification, defined as switch from a ≥3-class regimen to a regimen containing any 2 drug classes
- **Statistical analysis:**
  - Comparison of characteristics of switchers and non-switchers at the index date
  - Index date: defined as the switching date for individuals who switched to a 2-class regimen, and a random sample of these switching dates was selected and assigned to individuals who remained on ≥3 drug classes
  - Multivariable logistic regression to identify factors associated with switching

Results

- Of 1736 participants with a regimen containing ≥3 drug classes, 963 (55.5%) switched to a 2-class regimen over the study period
- The number of PWH with ≥3 drug classes decreased over time (**Figure 1**), as did the proportion of individuals who switched to a 2-class regimen
- Characteristics of switchers and non-switchers are shown in **Table**
- Switchers had their ART simplified to BIC/FTC/TAF (n=127, 13%), 3TC/ABC/DTG (n=111, 12%), COB/FTC/EVG/TAF (n=108, 11%), DTG/FTC/TAF (n=98, 10%), or other 2-class regimens (n=519, 54%)
- Current viral suppression, time since ART start, a prior AIDS-defining event, a history of virological failure, and availability of a resistance test were associated with a lower likelihood of switching to a 2-class regimen (**Figure 2**)
- There was no association between low adherence to ART, recreational drug use, or hazardous drinking with switching (**Figure 2**)

Figure 1: PWH switching from a ≥3 to a 2 class regimen over time

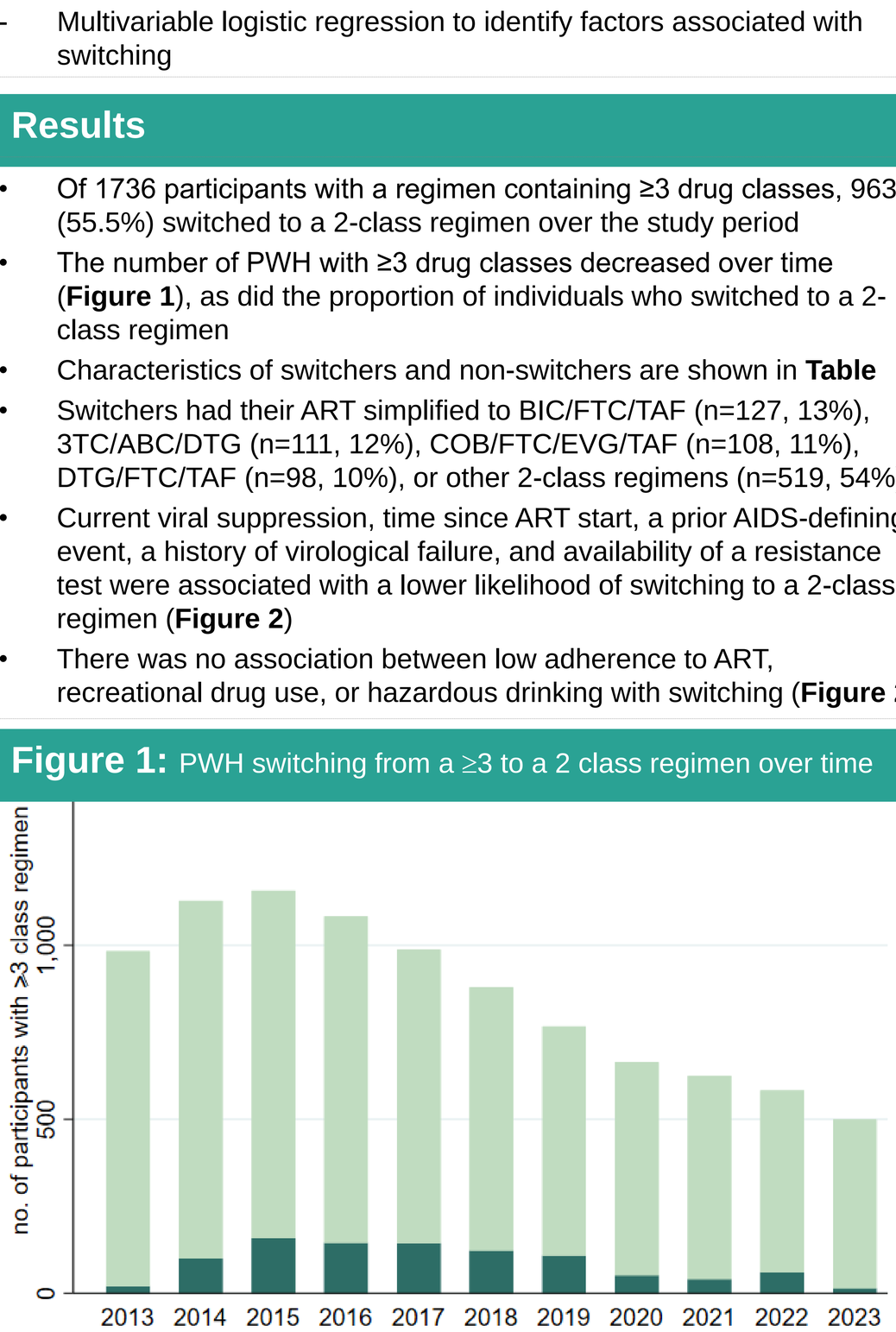


Table: Characteristics of the study population at the index date

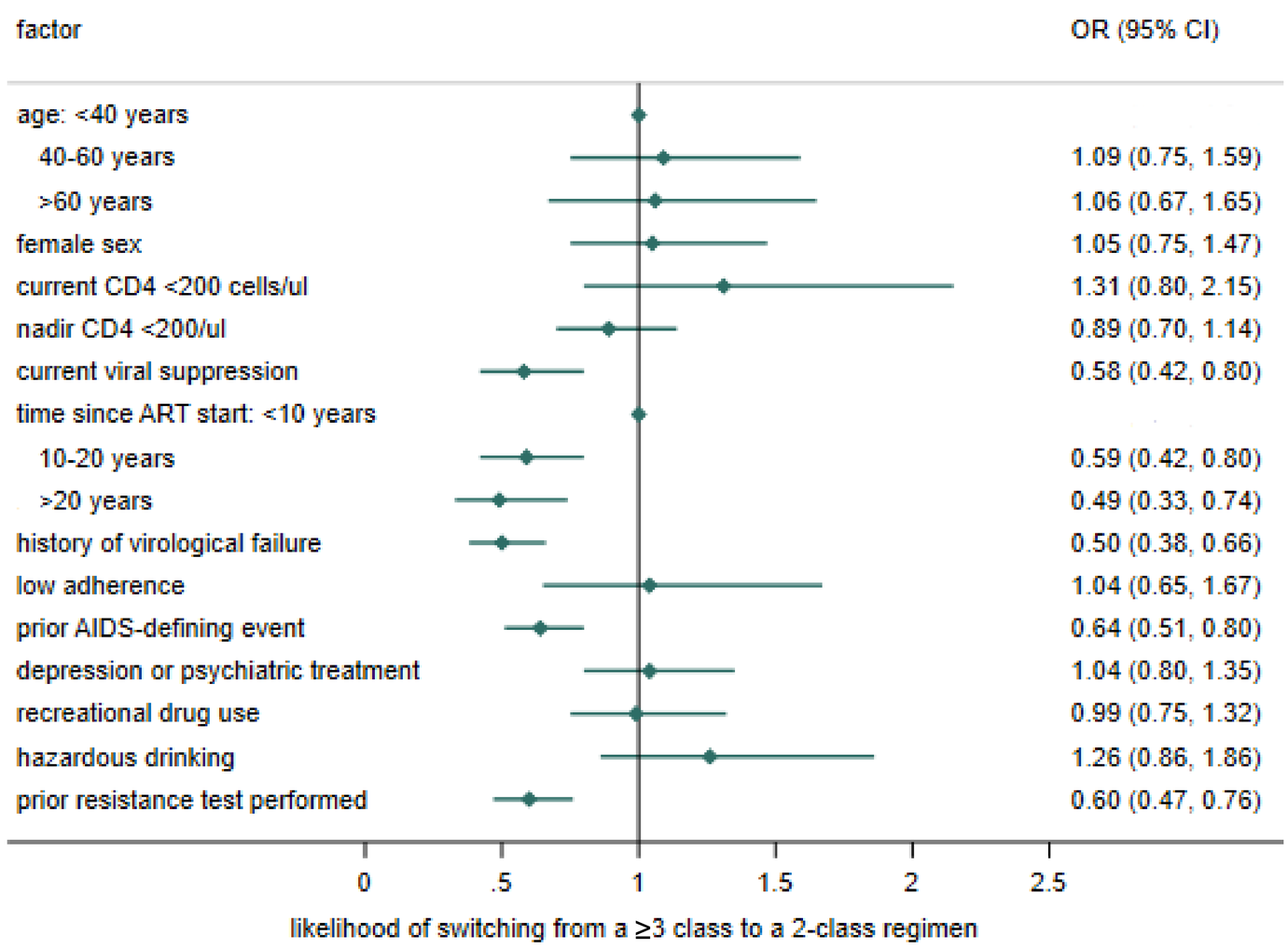
Characteristics	Total (n=1736)	Non-switchers (n=773)	Switchers (n=963)	p-value
Age in years, mean (SD)	53 (12)	54 (11)	52 (12)	0.003
Female sex	28 %	27 %	29 %	0.35
Current CD4 count in cells/ul, median (IQR)	575 (404-776)	573 (406-754)	587 (400-791)	0.55
Nadir CD4 count in cells/ul, median (IQR)	132 (50-250)	109 (40-216)	159 (57-288)	<0.001
Current viral suppression	86 %	91 %	83 %	<0.001
Treatment history				
Time since ART start in years, median (IQR)	18 (9-22)	20 (14-23)	16 (6-21)	<0.001
Ever received NRTI monotherapy	51 %	60 %	44 %	<0.001
History of virological failure*	62 %	76 %	51 %	<0.001
Low adherence §	5 %	5 %	5 %	0.54
Prior resistance test performed	75 %	79 %	71 %	<0.001
Comorbidities				
Prior AIDS-defining event	34 %	42 %	28 %	<0.001
HBs-Ag ever positive	5 %	5 %	6 %	0.41
Depression or psychiatric treatment	20 %	20 %	20 %	0.87
Recent recreational drug use	17 %	17 %	17 %	0.67
Current hazardous drinking	14 %	12 %	15 %	0.09

Abbreviations: ART, antiretroviral therapy; IQR, interquartile range; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; SD, standard deviation

* Documented history of virological failure, defined as 2 consecutive viral loads >200 cp/mL or 1 viral load >200 cp/mL followed by a treatment change if the patient had experienced ≥180 days of continuous ART or ≥90 days of ART if viral suppression was reached

§ defined as a missed ART more than once every two weeks, or more than one dose in a row

Figure 2: Factors associated with ART simplification in multivariable analysis*



*in addition to the variables shown, following predictors were included in the model: ethnicity, mode of HIV acquisition, history of treatment interruption >30d, prior nucleoside/nucleotide reverse transcriptase monotherapy, current boosted regimen, HBs-Ag ever positive, Anti-HBc-alone positive, cardiovascular disease, liver disease, diabetes mellitus, osteoporosis, estimate glomerular filtration rate<60ml/min

Conclusion

- In this real world cohort, more than half of participants with complex treatment regimens were switched to a 2-class regimen within the last decade.
- A prior virological failure, AIDS-defining events, and a long treatment history were barriers to switching, while low ART adherence and substance use were not.

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