Fondazione Icona
ITALIAN COHORT NAIVE ANTIRETROVIRALS

Quali trattamenti stiamo utilizzando: i dati della Coorte ICONA

Antonella d'Arminio Monforte
Fondazione Icona

Firenze, 28 gennaio 2025

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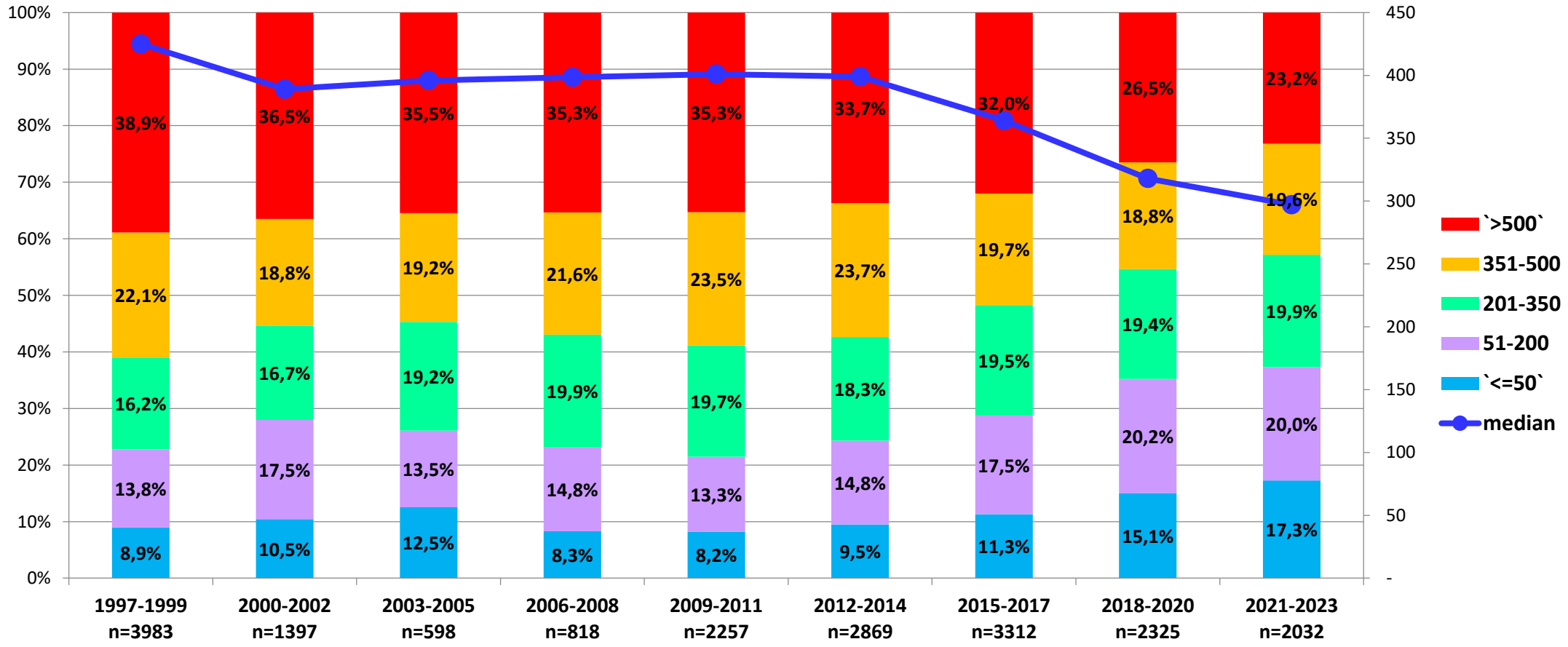
CD4 cells/mmc strata and median values at enrolment according to calendar period



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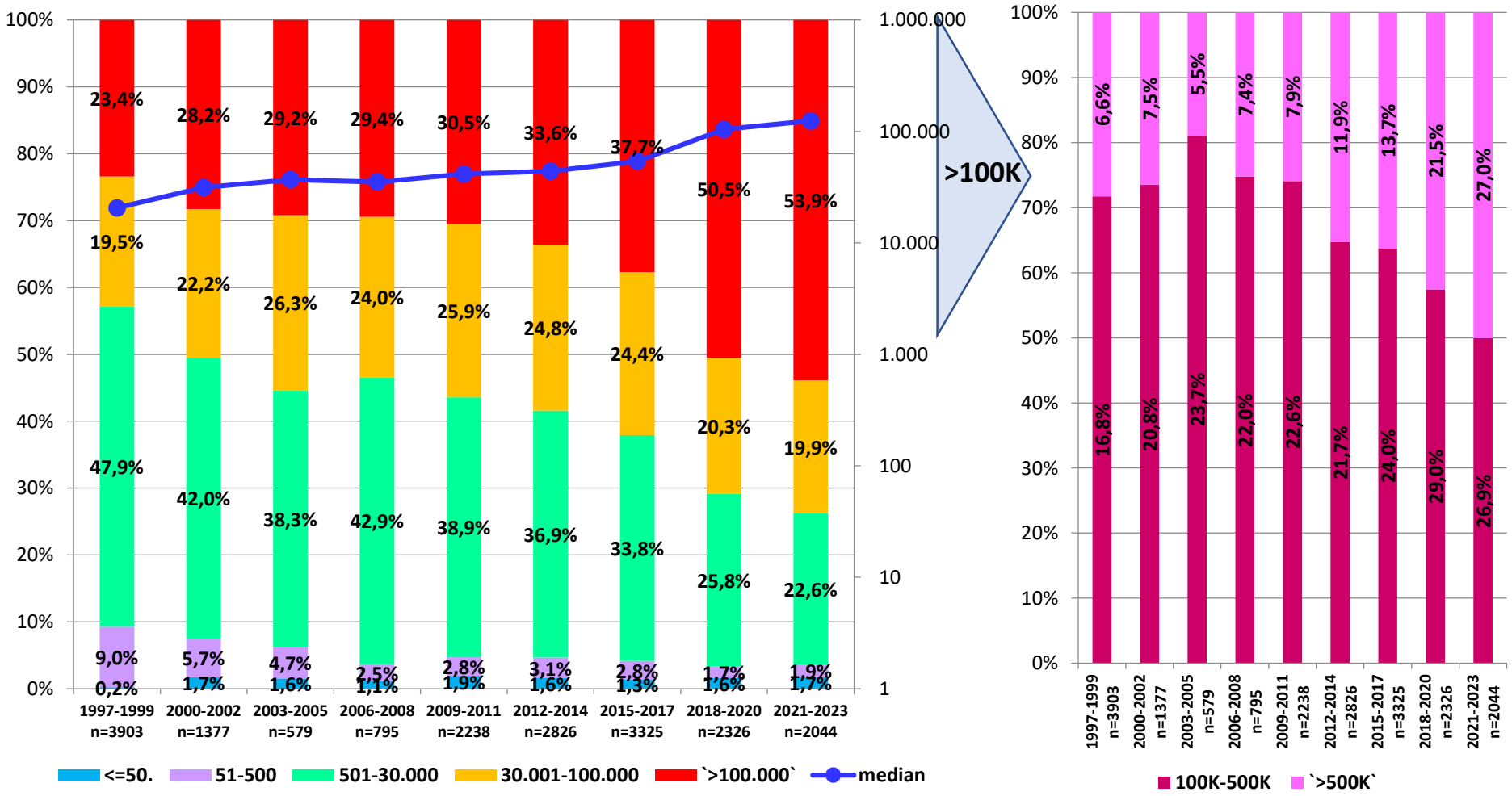
HIV-RNA strata and median values at enrolment according to calendar period



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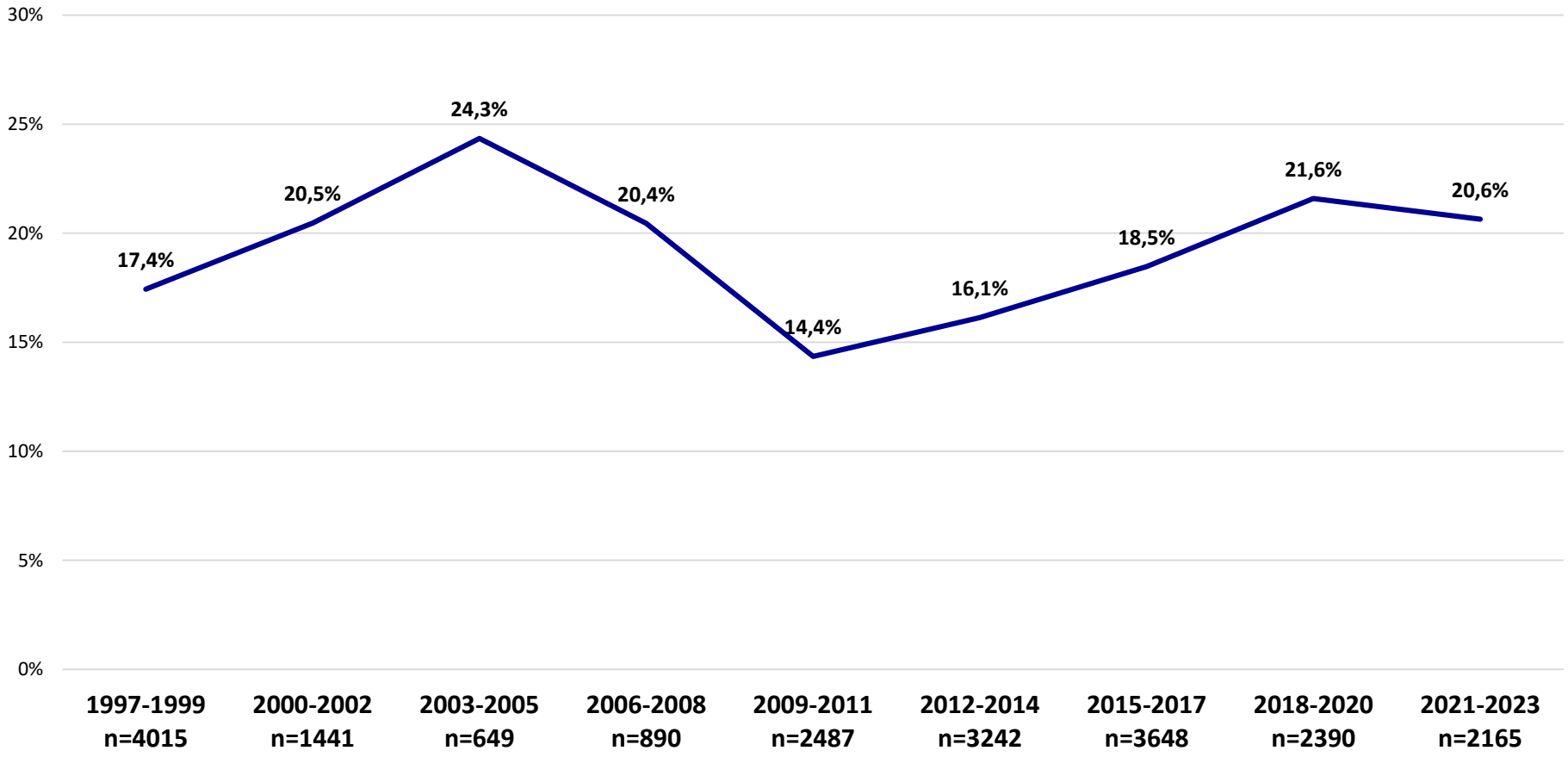
Prevalence of AIDS presenters (n=3847) according to calendar period at enrolment (total patients n=20927)



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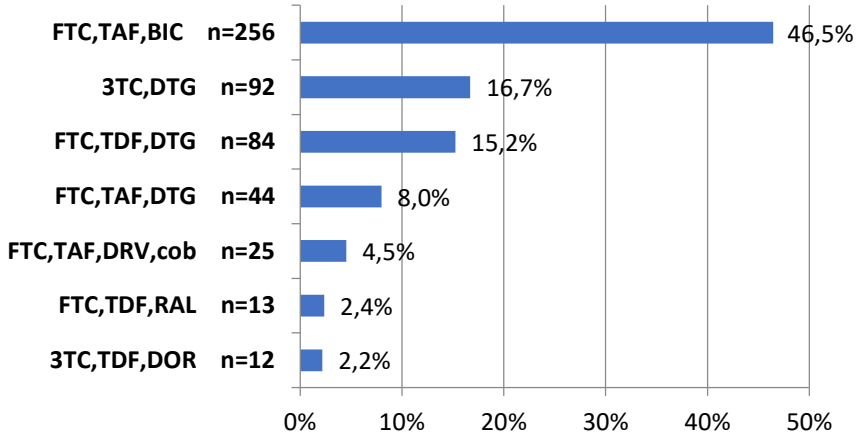
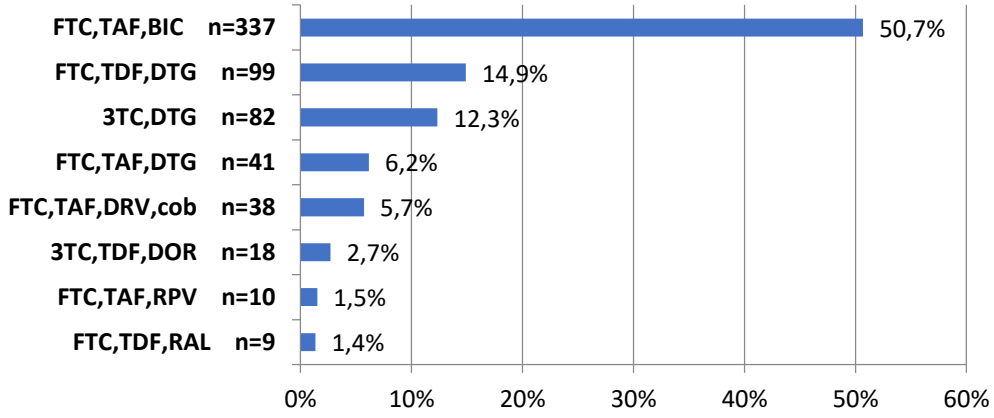
Distribution of most frequent first line regimens in patients starting ART from 2020 to 2023

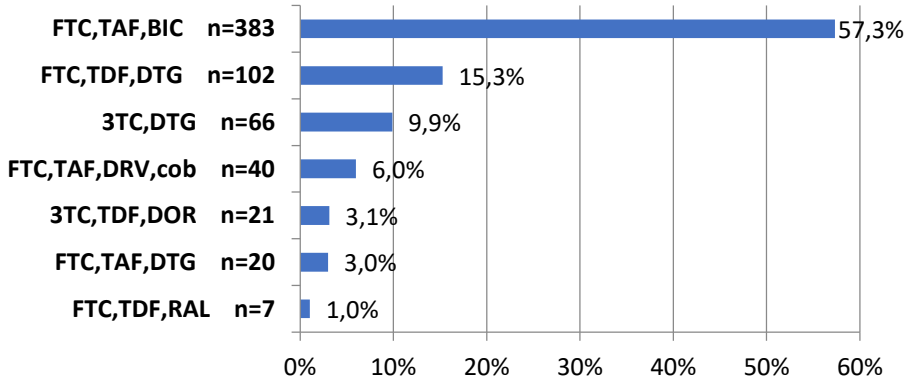
2020=551



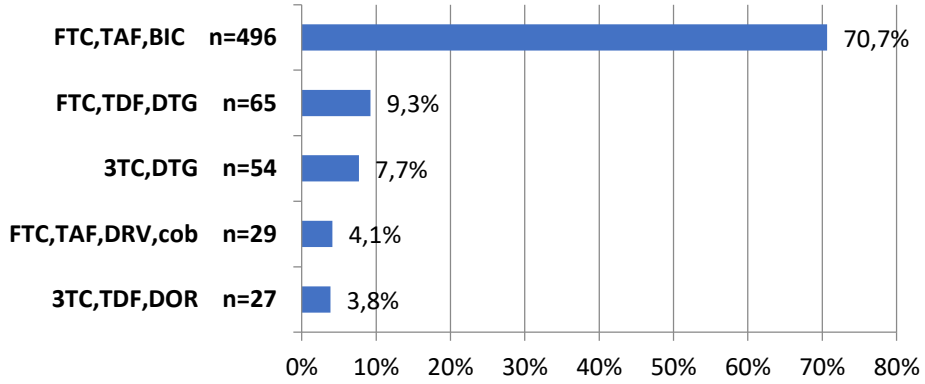
2021=665



2022=668



2023=702



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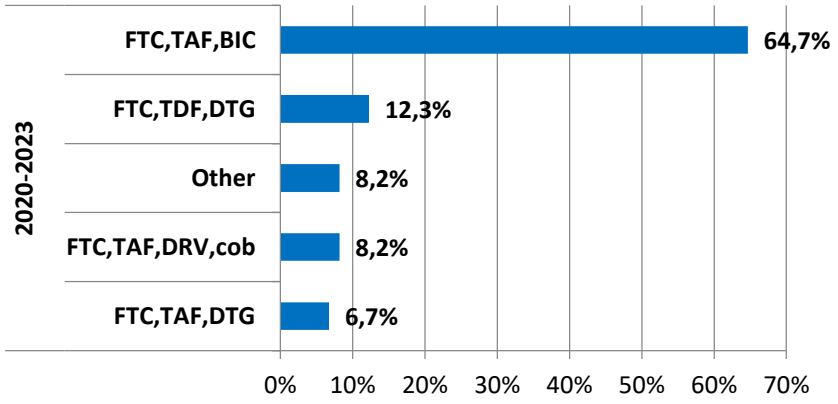
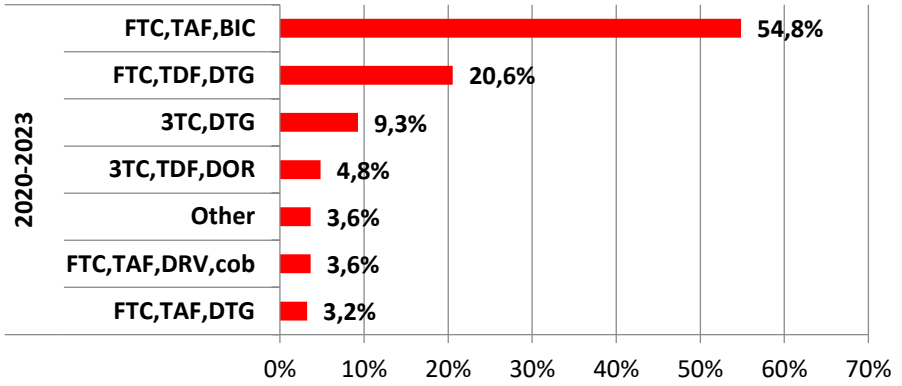
Distribution of first line regimens in patients starting ART according to CD4 count in 2020-2023

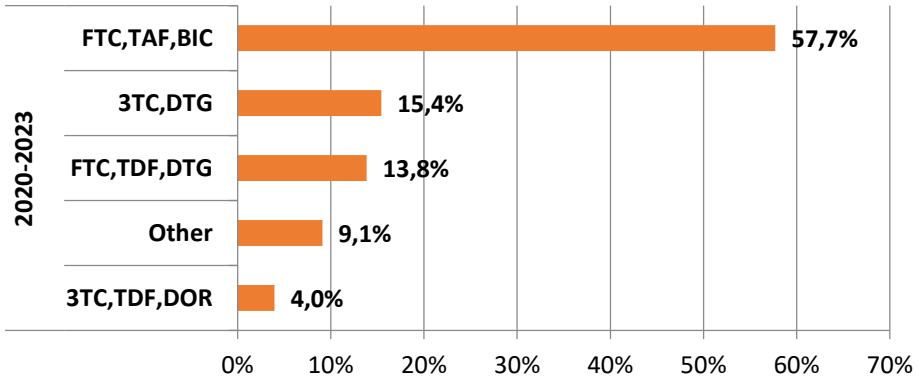
<=200/cmm



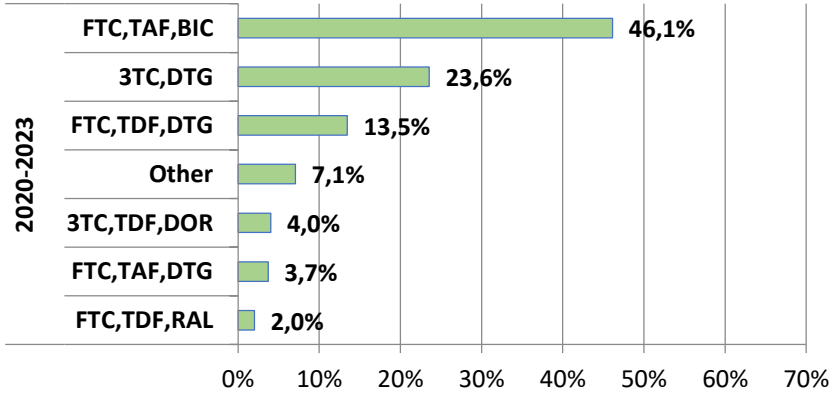
201 to 350/cmm



351 to 500/cmm



>500/cmm



J Antimicrob Chemother 2024; **79**: 1279–1288
https://doi.org/10.1093/jac/dkae081 Advance Access publication 6 April 2024

Journal of Antimicrobial Chemotherapy

Long-term outcomes of bictegravir/emtricitabine/tenofovir alafenamide as first-line therapy and as switch strategy in virologically suppressed persons with HIV: data from the ICONA cohort

Antonella d'Arminio Monforte[1]*†, Alessandro Tavelli[1]†, Antonio Di Biagio [2], Loredana Sarmati [3], Giulia C. Marchetti[4], Francesca Bai[4], Antonella Cingolani[5], Eugenio Quiros Roldan[6], Cristina Mussini[7], Miriam Lichtner[8], Alessandra Vergori [9], Stefania Piconi[10], Giancarlo Orofino[11], Francesco Maria Fusco[12], Alessandra Bandera[13], Silvia Nozza [14], Antonella Castagna[14] and Andrea Antinori[9]; on behalf of the ICONA Foundation Study Group‡

Objectives: To assess the effectiveness of bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) among people poorly represented in clinical trials and potentially at higher risk of suboptimal response to ART.

Results: Nine hundred and thirty-three ART-naive and 1655 ART-experienced PWH initiated BIC/FTC/TAF. Over a median follow-up of 69.8 weeks, 89 (9.6%) PWH at their first regimen experienced TF. PWH aged >50 years had 1.83-fold (95% CI: 1.19–2.83) higher risk of TF; PWH with advanced HIV disease had 2.21-fold (95% CI: 1.53–3.82) higher risk; there were no differences in TF according to sex.
Over a median follow-up of 146.3 weeks, 109 (6.6%) out of 1655 switching PWH experienced TF; no differences were found in the risk of TF, TDT and VF according to groups of interest.

Table 2. HR and AHR of TF by univariable and multivariable Cox regression models

	HR	95% CI		*P*	AHR[a]	95% CI		*P*
ART-naive PWH initiating BIC/FTC/TAF								
Age ≥50 years (versus <50 years)	1.95	1.29	2.96	0.002	1.83	1.19	2.83	0.006
Sex, female (versus male)	1.05	0.60	1.83	0.857	0.96	0.54	1.68	0.876
Advanced HIV disease (versus non-advanced)	2.52	1.61	3.95	<0.001	2.21	1.40	3.51	0.001
PWH initiating BIC/FTC/TAF while with undetectable viral load								
Age ≥50 years (versus <50 years)	1.28	0.87	1.87	0.21	1.26	0.84	1.9	0.268
Sex, female (versus male)	0.91	0.55	1.52	0.732	0.92	0.55	1.54	0.748
Advanced HIV disease (versus non-advanced)	1.13	0.74	1.71	0.565	1.1	0.72	1.69	0.643

[a]Set of adjustments for ART-naive PWH initiating BIC/FTC/TAF: age adjusted for nationality and mode of HIV transmission; sex adjusted for nationality and age; advanced HIV disease adjusted for sex, mode of HIV transmission, age, HIV-RNA and nationality. Set of adjustments for PWH initiating BIC/FTC/TAF while with undetectable viral load: age adjusted for nationality, year of first combination ART and mode of HIV transmission; sex adjusted for nationality, age and year of first combination ART; advanced HIV disease adjusted for sex, mode of HIV transmission, HIV-RNA, year of first combination ART and nationality.

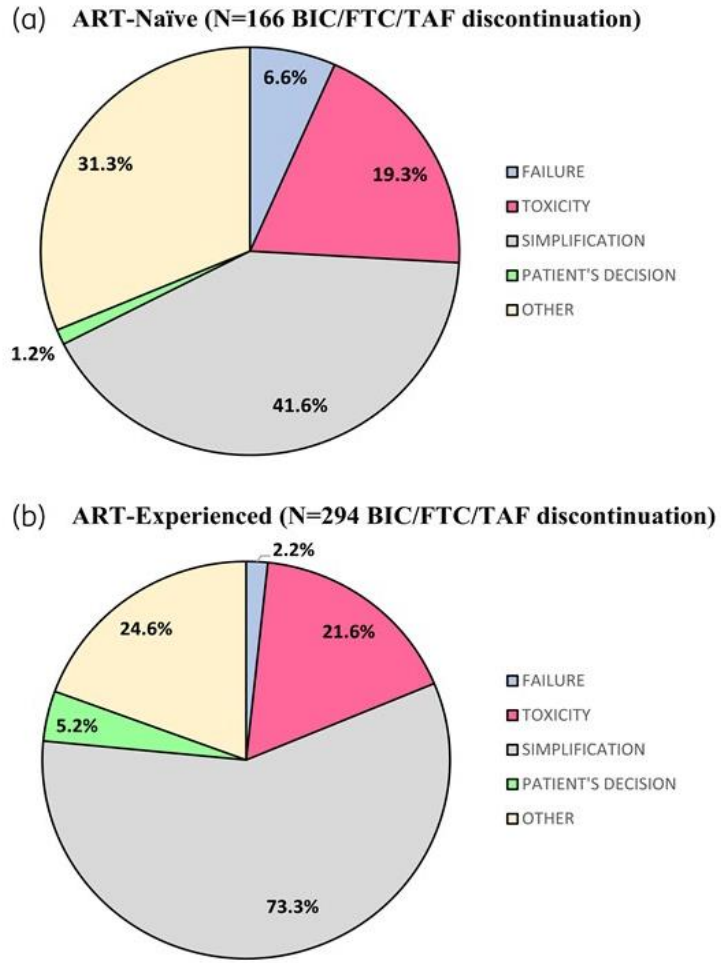


Figure 3. Reasons for BIC/FTC/TAF discontinuation among naive (a) and experienced (b) PWH.

J Antimicrob Chemother 2023; **78**: 933–945
https://doi.org/10.1093/jac/dkad026 Advance Access publication 13 February 2023

Journal of Antimicrobial Chemotherapy

Long-term outcome of dolutegravir-containing regimens according to sex: data from the ICONA study

Antonella D'arminio Monforte[1]*, Alessandro Tavelli[2], Matteo Sala[1], Annalisa Mondi[3], Stefano Rusconi[4], Spinello Antinori[5], Massimo Puoti[6], Benedetto Maurizio Celesia[7], Lucia Taramasso[8], Annalisa Saracino[9], Andrea Antinori[3] and Alessandro Cozzi-Lepri[10]; on behalf of ICONA Foundation Study Group†

Results: A total of 2304 PLWH (15% women) initiated dolutegravir-based therapy from ART-naive, and 1916 (19.8% women) while experienced. After a median follow-up of 2.2 (IQR: 0.9–3.9) years in ART-naive and 2.4 (IQR: 1.1–4.3) years in experienced, the 4-year cumulative probability of treatment failure was 33% (95% CI 30.5–35.1) and 20% (95% CI 17.8–22.3), respectively. In the multivariable analyses, in ART-naive the risk of treatment failure was higher for women, but not different after excluding women discontinuing dolutegravir for pregnancy concerns. We also observed a higher risk of discontinuation for toxicity in women (ART-naives: Adjusted Hazard Ratio (AHR): 1.56%; 95% CI: 1.03–2.37; ART-experienced: AHR: 1.53%; 95% CI: 1.01–2.32), although the absolute 4-year probability was low: 7.7% (95% CI 6.5–9.2) in ART-naive and 8.3% (95% CI 6.9–9.9) in experienced.

Conclusions: In our cohort of PLWH treated with dolutegravir-based regimens and followed up for up to 4 years, we observed a low risk of treatment failure and no evidence for a difference by sex, after excluding discontinuation due to pregnancy concerns. However, we observed a higher risk of dolutegravir discontinuation for toxicity in women.

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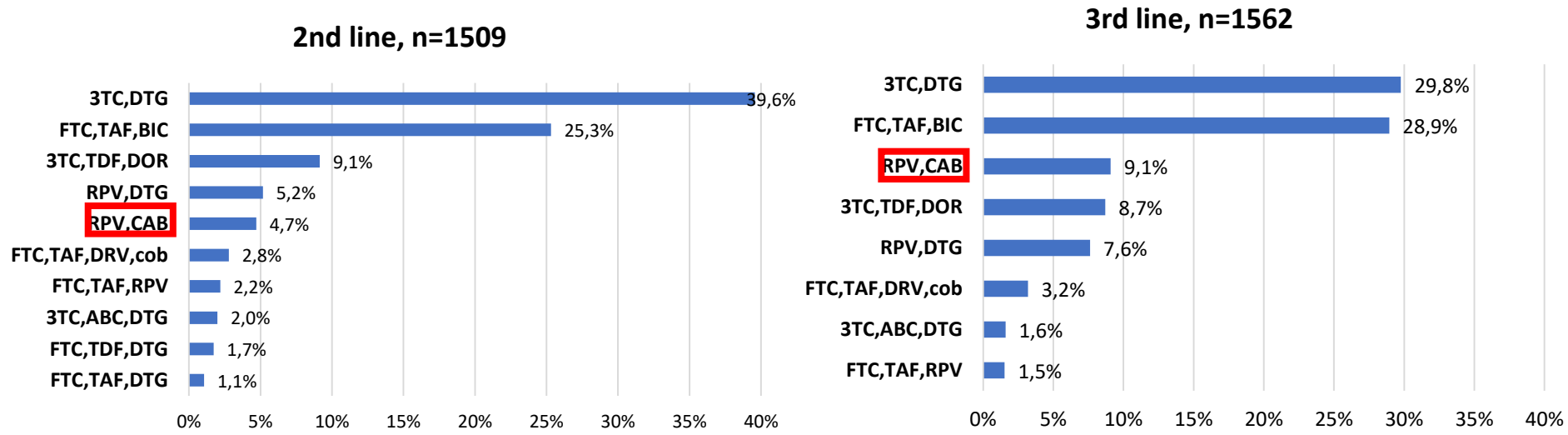
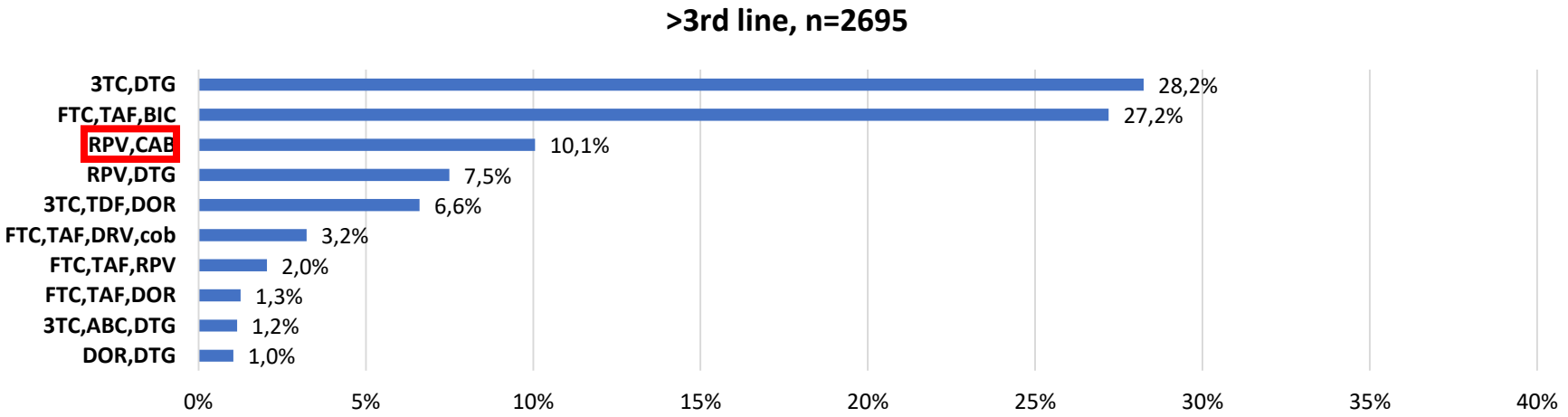
Most frequent regimens used in after the first line therapy in PWH in follow-up in 2020-2023





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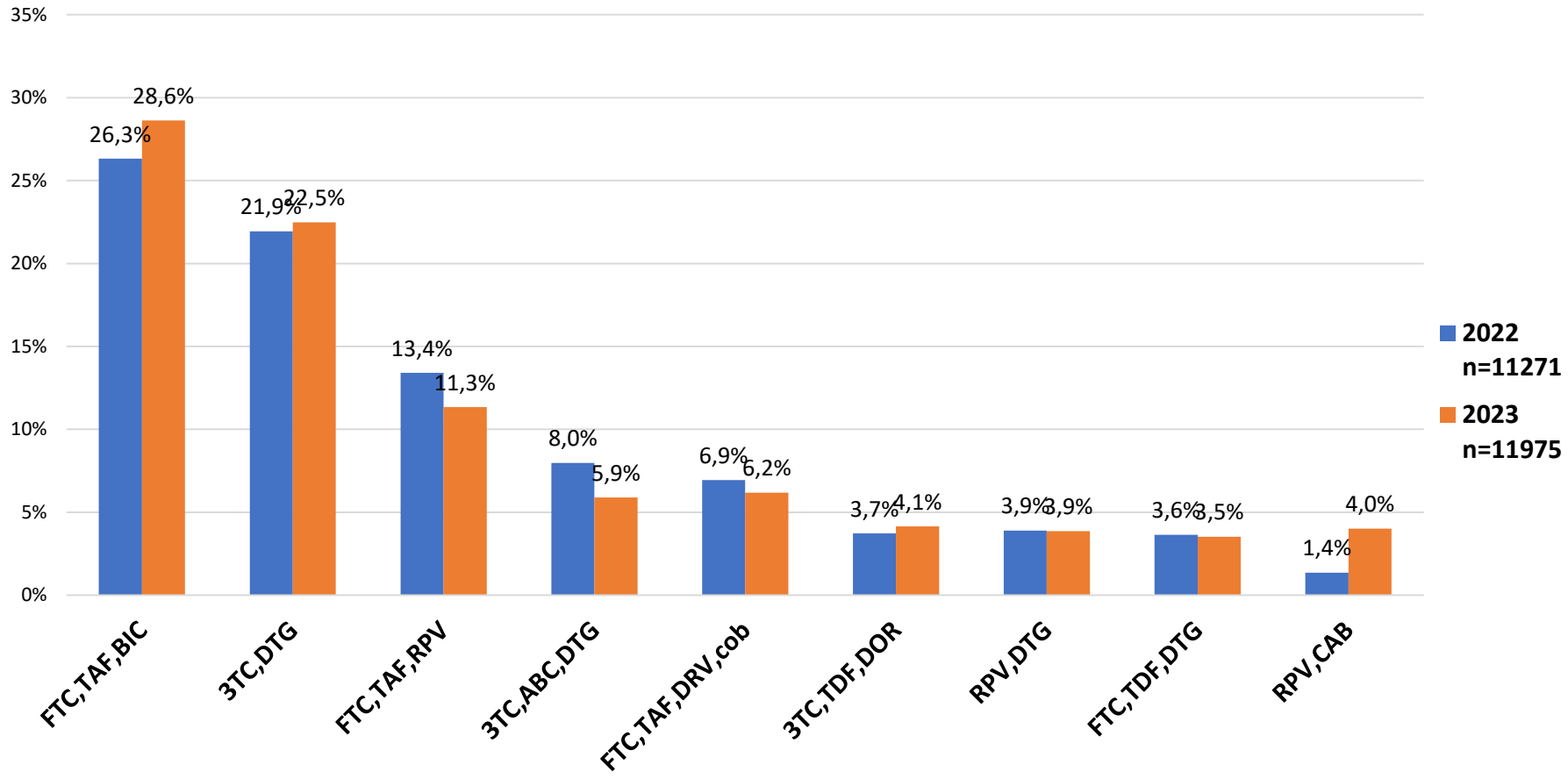
Most used regimens in patients in follow up in 2022-2023



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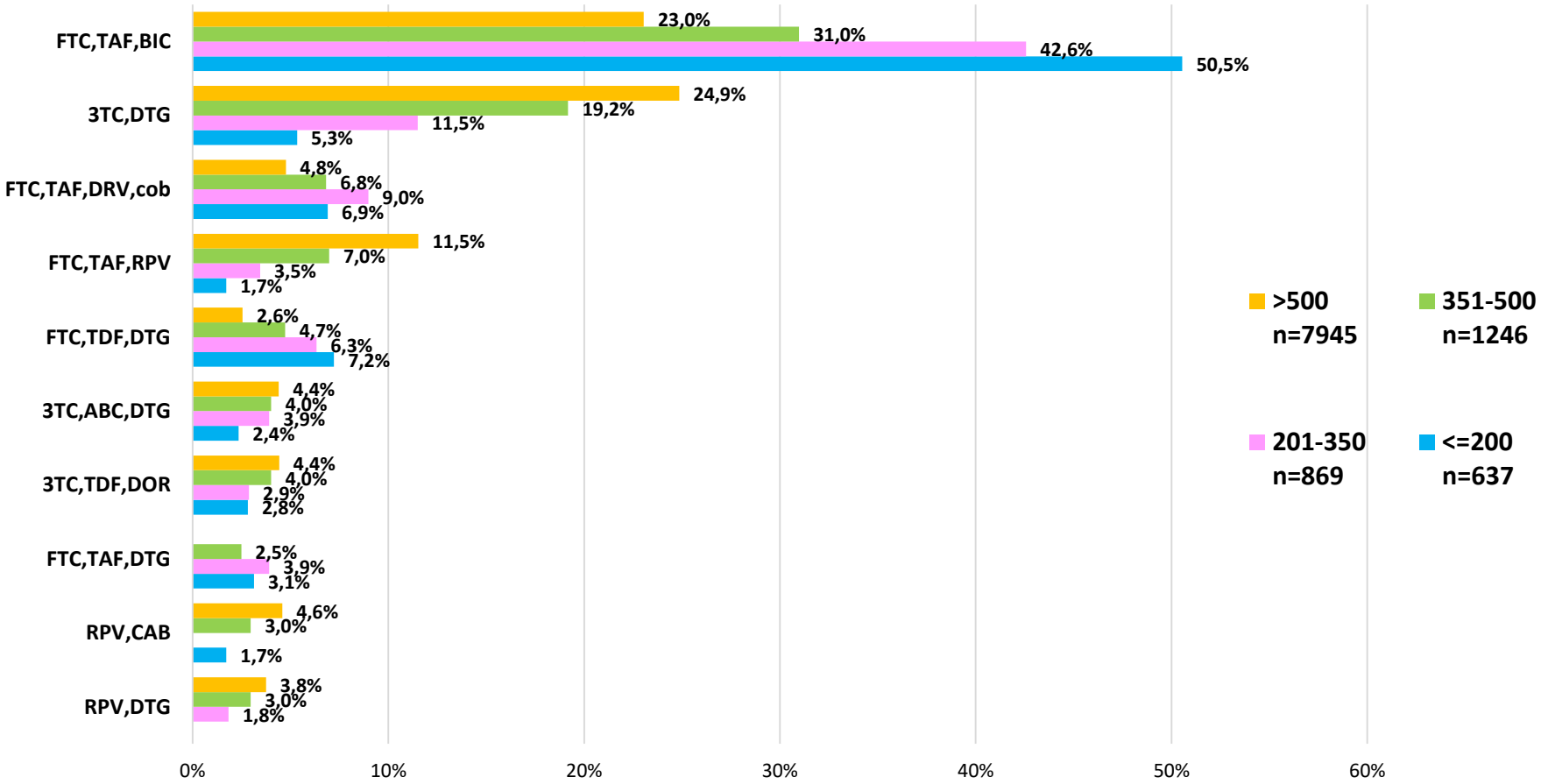
Ongoing regimens of PWH in follow up in 2022-2023 according to CD4 strata (last CD4 available in the last 6 months of follow-up)



Dec 2023 Report

viruses

MDPI

Brief Report

Probability of Starting Two-Drug Regimen (2DR) vs. Three-Drug Regimen (3DR) in ART-Naïve and ART-Experienced Person with HIV (PWH) Across the First Wave of COVID-19 Pandemic

Alessandra Vergori [1,*], Nicola Gianotti [2], Alessandro Tavelli [3,4], Camilla Tincati [5], Andrea Giacomelli [6,7], Elena Matteini [8], Giuseppe Lapadula [9], Lucia Taramasso [10], Loredana Sarmati [11], Antonella D'Arminio Monforte [3,4], Andrea Antinori [1], Alessandro Cozzi-Lepri [12] and on behalf of the ICONA Foundation Study Group [†]

Viruses **2024**, *16*, 1822. https://doi.org/10.3390/v16121822

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Aims

- **To calculate the proportion of PLWH initiating 2DR vs. 3DR by calendar year in the Icona Foundation Study Cohort**

- **To investigate whether there has been a reduction in the propensity to initiate 2DR instead of 3DR because of the COVID-19 pandemic and consequent temporary modification in treatment guidelines**

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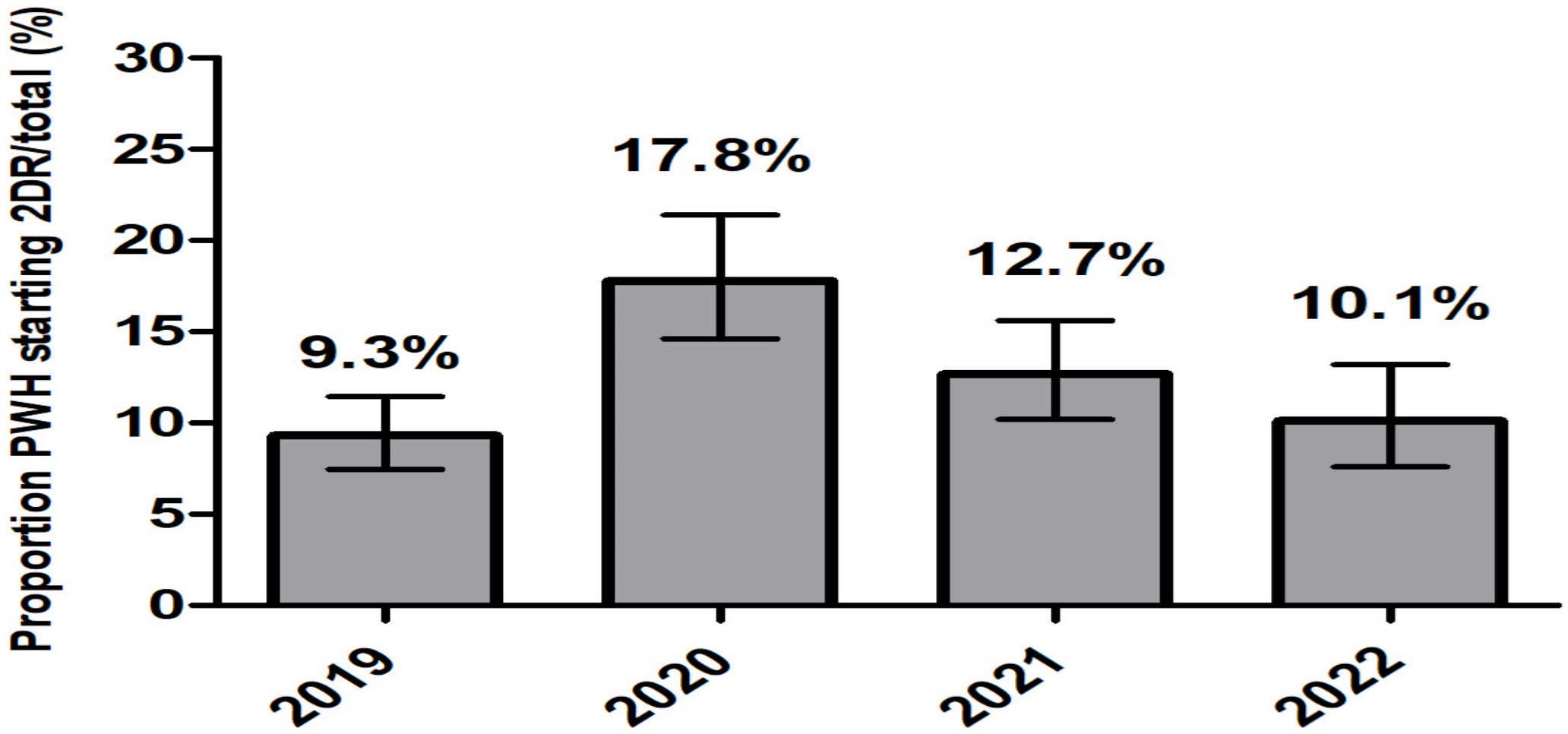
Proportion of PWH starting a two-drug regimen (2DR) (12%) among 2481 ART-naive PWH according to calendar year



ART-naive

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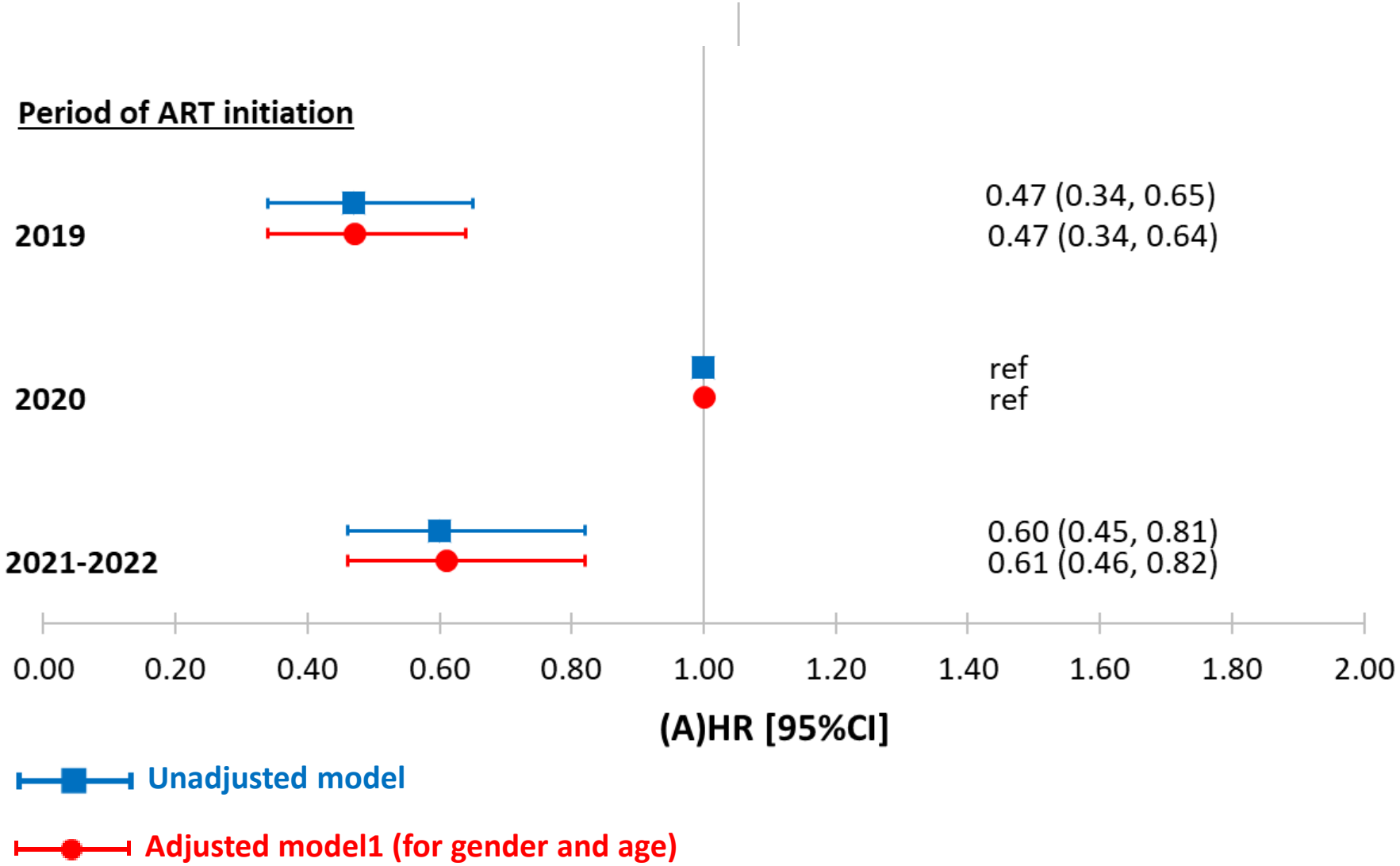
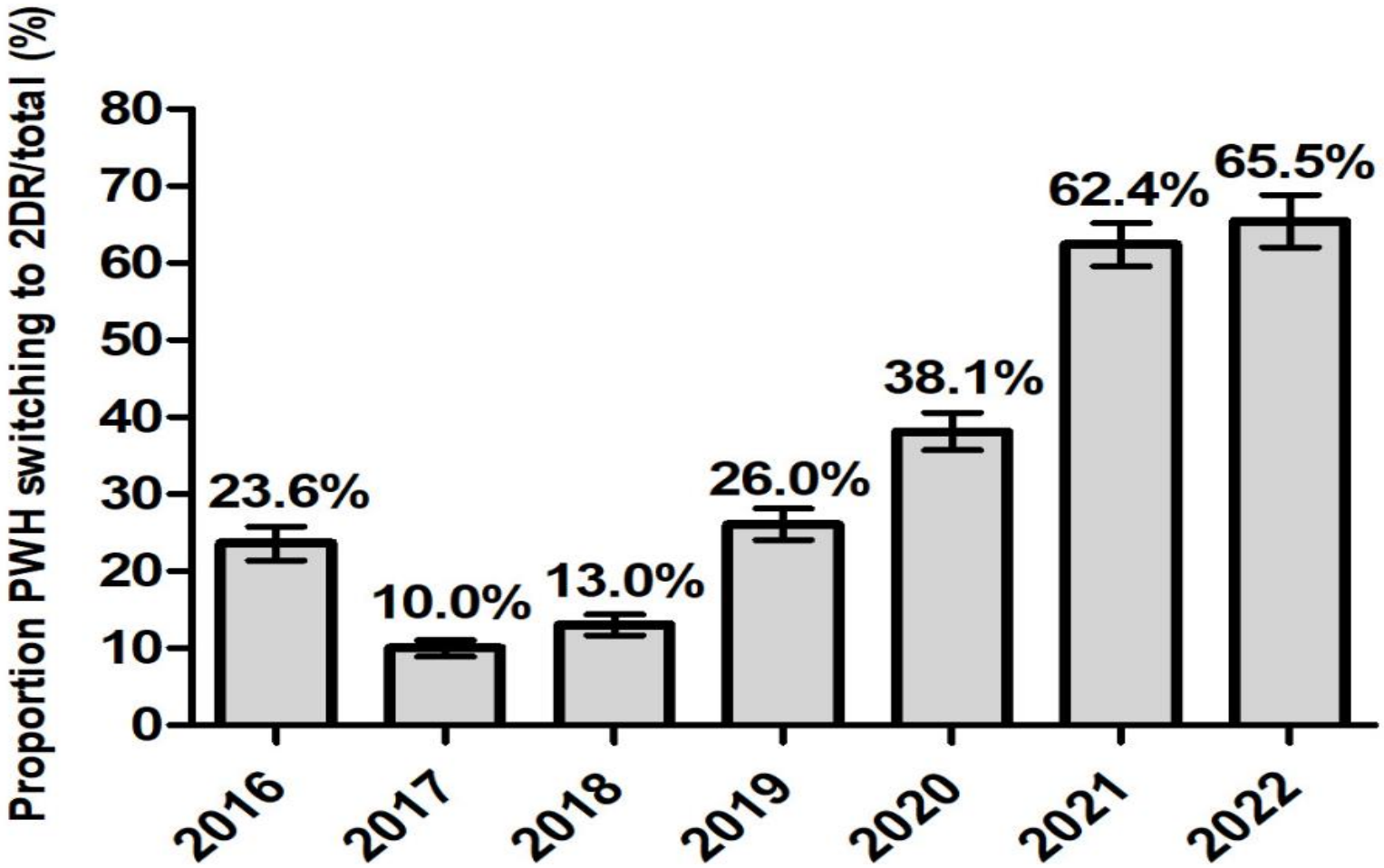
Odds ratios of starting a 2DR vs 3DR regimen from fitting a logistic regression model

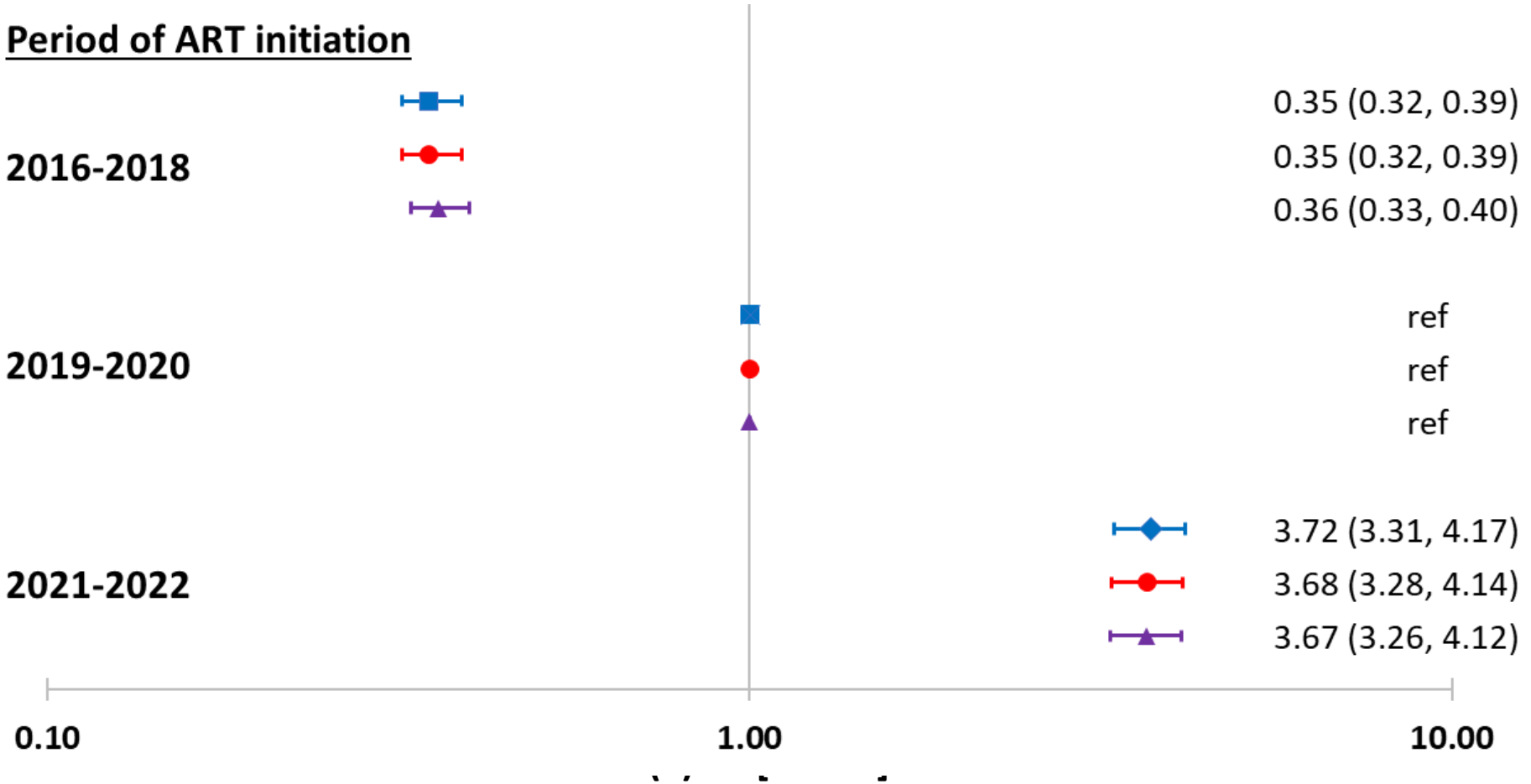


Proportion of PWH starting a two-drug regimen (2DR) (26%) among 12,335 experienced PWH according to calendar year



ART-experienced

Odds ratios of starting a 2DR vs 3DR regimen from fitting a logistic regression model



Unadjusted model

Adjusted* model1 (for gender and age)

Adjusted* model2 (for gender and age and line of therapy)

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Conclusions

- In our cohort of ART-naive PLWH, 10-15% of participants initiated 2DR as first line over 2019-2022 and this proportion remained stable over time

- In contrast, in ART-experienced PLWH, we observed an increasing frequency of 2DR versus 3DR regimens initiation over time, especially in recent years

- Our hypothesis that the COVID-19 pandemic and/or temporary modification of treatment guidelines might have modified the propensity of Italian physicians toward prescribing 2DR over the period 2020-2021 was not confirmed

HIV Medicine / Early View

SHORT COMMUNICATION

Predictors for choosing doravirine-based versus INSTI-based regimen in ART-naïve and ART-experienced people with HIV in real-world setting: Data from the Icona cohort

Antonella d'Arminio Monforte, Alessandro Tavelli ✉, Eugenia Quiros-Roldan, Massimiliano Fabbiani, Micol Ferrara, Sergio Lo Caputo, Nicola Squillace, Stefano Rusconi, Marta Ponzano **... See all authors**

First published: 02 December 2024
https://doi.org/10.1111/hiv.13740

Rationale

Doravirine (DOR) is an attractive new option both for ART-naïve people with HIV (PWH) and those with suppressed HIV-RNA who seek treatment simplification. We used real-world data to examine the pattern of use of DOR-containing regimens in these settings.

Background

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- **Doravirine (DOR)** is a **next-generation NNRTI,** currently available in two formulations:
  - ✓ single-tablet regimen (STR) in fixed dose combination with 3TC and TDF (*Delstrigo™*)
  - ✓ single stand-alone drug (*Pifeltro™*)
- Approved for treatment of PLWH in combination with other antiretroviral agents, as:
  - ✓ **first line therapy for ART-naïve** (*recommended by the EACS guidelines*)
  - ✓ **switch strategy for virologically suppressed** (HIV-RNA < 50 copies/mL) on stable ART

DOR was **designed to address and overcome limitations of previous NNRTIs**:

- drug resistance
- CNS toxicity
- food requirement
- baseline HIV-RNA threshold
- tolerability
- drug-drug interactions
- metabolic changes
- costs

ART naive

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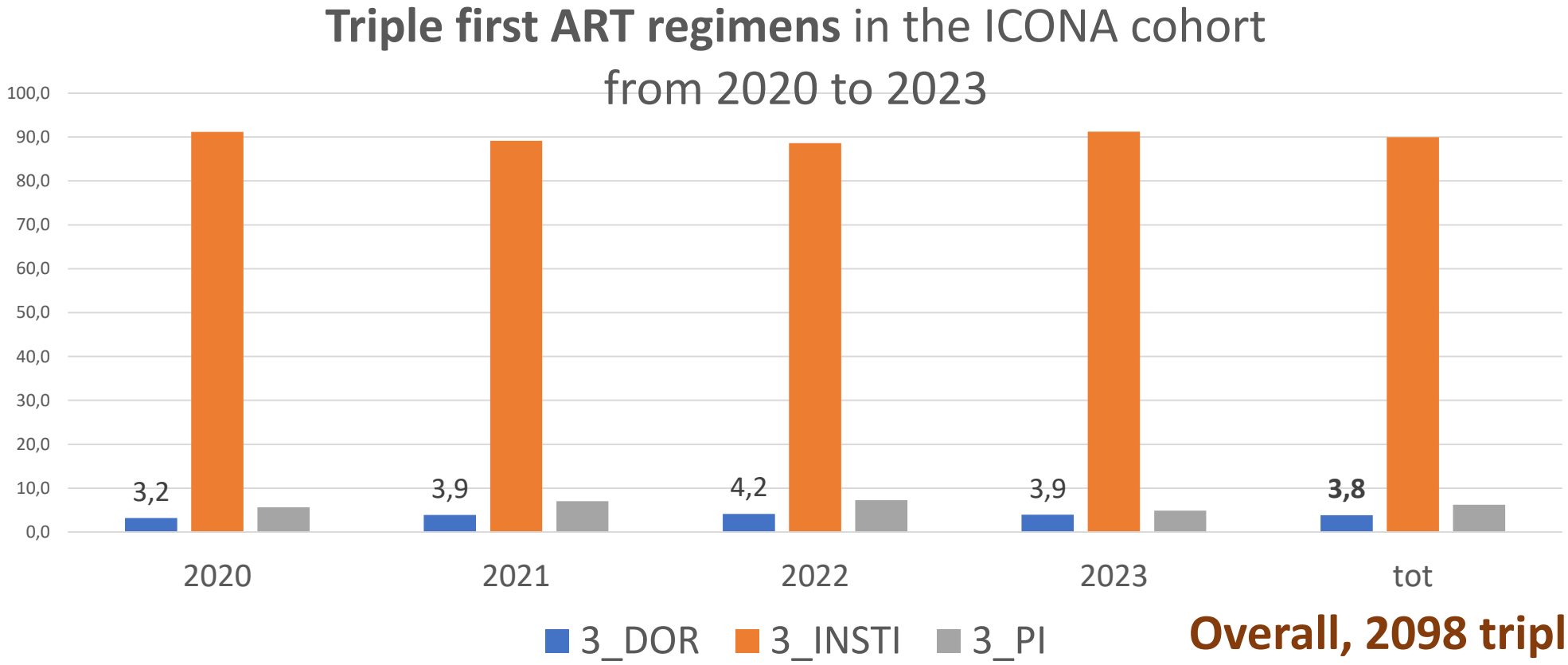

Overall, 2098 triple ART (80 with DOR)

ART naive

logistic regression

IVDU
High CD4
Low HIV-RNA
BMI>30
High Chol
High HDL

Table 3 OR of initiating ART with Doravirine from fitting a logistic regression analysis

Logistic regression estimates of factors associated with startingfirst line with Doravinine- vs. INSTI-based ART

Factor	Unadjusted Odds ratio (95% CI)	p-value	Adjusted* Odds ratio (95% CI)	p-value	Adjusted** Odds ratio (95% CI)	p-value
Age						
per 10 years older	0.88 (0.73, 1.07)	0.197	0.88 (0.73, 1.06)	0.187	0.89 (0.74, 1.08)	0.228
Gender						
Male	1		1			
Female	1.47 (0.87, 2.49)	0.153	1.48 (0.87, 2.52)	0.145	1.48 (0.87, 2.53)	0.147
Mode of HIV Transmission						
Heterosexual	1		1			
PWID	4.50 (2.38, 8.50)	<.001	4.41 (2.33, 8.35)	<.001	4.03 (2.10, 7.73)	<.001
MSM	0.76 (0.48, 1.21)	0.246	0.78 (0.46, 1.31)	0.341	0.73 (0.43, 1.23)	0.234
HIV-RNA						
per log10 copies/mL lower	1.53 (1.30, 1.81)	<.001	1.07 (1.03, 1.12)	0.001	1.07 (1.03, 1.12)	0.002
CD4 count						
per 100 cells/mmc higher	1.07 (1.03, 1.12)	0.001	1.52 (1.29, 1.80)	<.001	1.52 (1.28, 1.80)	<.001
CD4/CD8 ratio						
per 1 unit higher	1.00 (0.89, 1.13)	0.964	1.00 (0.88, 1.14)	0.964	1.01 (0.88, 1.15)	0.938
Time from HIV diagnosis						
per 3 years longer	1.27 (0.67, 2.42)	0.465	1.23 (0.64, 2.38)	0.540	1.15 (0.60, 2.20)	0.675
Smoker, n(%)						
No	1		1			
Yes	1.52 (0.92, 2.51)	0.100	1.56 (0.94, 2.60)	0.084	1.56 (0.94, 2.61)	0.088
BMI						
20-25	1		1			
25-29	1.43 (0.64, 3.20)	0.382	1.50 (0.67, 3.37)	0.325	1.58 (0.70, 3.57)	0.270
30+	3.82 (1.38, 10.61)	0.010	3.96 (1.41, 11.14)	0.009	4.00 (1.40, 11.43)	0.010
Total cholesterol						
per 100 mg/dl higher	1.21 (1.05, 1.40)	0.009	1.21 (1.05, 1.40)	0.008	1.22 (1.05, 1.41)	0.008
LDL cholesterol						
per 10 mg/dl higher	1.11 (1.03, 1.21)	0.009	1.12 (1.03, 1.21)	0.009	1.12 (1.03, 1.21)	0.011
Haemoglobin						
per 10 g/dl higher	1.48 (0.92, 2.39)	0.108	1.47 (0.91, 2.37)	0.112	1.59 (0.98, 2.57)	0.059
AST						
per 10 UI/mL higher	0.98 (0.90, 1.06)	0.554	0.98 (0.91, 1.06)	0.585	0.99 (0.92, 1.06)	0.751
Nation of birth, n(%)						
Italian vs. Foreign	0.99 (0.61, 1.61)	0.967	1.14 (0.69, 1.90)	0.612	0.96 (0.57, 1.63)	0.891

*adjusted for gender and age

**adjusted for gender, age, calendar year of initiation and geographical region

ART exp DOR vs 2DR *logistic regression*

Older age
Females
No MSM
Longer time from diagnosis
BMI>25

Table 7 OR of switching to Doravirine vs 2DR INSTI from fitting a logistic regression analysis

Logistic regression estimates of factors associated with switchingto Doravinine- vs. a 2DR INSTI-based ART

Factor	Unadjusted Odds ratio (95% CI)	p-value	Adjusted* Odds ratio (95% CI)	p-value	Adjusted** Odds ratio (95% CI)	p-value
Age						
per 10 years older	1.13 (1.04, 1.22)	0.004	1.12 (1.03, 1.22)	0.006	1.15 (1.06, 1.25)	0.001
Gender						
Male	1		1			
Female	1.31 (1.03, 1.66)	0.027	1.28 (1.00, 1.62)	0.046	1.24 (0.97, 1.58)	0.087
Mode of HIV Transmission						
Heterosexual	1		1			
PWID	1.07 (0.74, 1.57)	0.712	1.00 (0.68, 1.46)	0.993	0.92 (0.62, 1.36)	0.681
MSM	0.69 (0.57, 0.84)	<.001	0.75 (0.60, 0.94)	0.013	0.75 (0.60, 0.94)	0.013
HIV-RNA						
per log10 copies/mL lower	0.97 (0.88, 1.08)	0.597	0.97 (0.94, 1.00)	0.048	0.98 (0.95, 1.01)	0.227
CD4 count						
per 100 cells/mmc higher	0.97 (0.94, 1.00)	0.025	0.97 (0.88, 1.07)	0.581	0.98 (0.89, 1.09)	0.753
CD4/CD8 ratio						
per 1 unit higher	0.99 (0.87, 1.12)	0.883	0.98 (0.85, 1.12)	0.749	0.97 (0.83, 1.13)	0.699
Time from HIV diagnosis						
per 3 years longer	1.09 (1.05, 1.13)	<.001	1.07 (1.03, 1.12)	<.001	1.08 (1.04, 1.12)	<.001
Smoker, n(%)						
No	1		1			
Yes	1.10 (0.90, 1.35)	0.334	1.12 (0.92, 1.37)	0.265	1.12 (0.91, 1.38)	0.268
BMI						
20-25	1		1			
25-29	1.37 (1.09, 1.72)	0.006	1.36 (1.08, 1.71)	0.009	1.40 (1.11, 1.78)	0.005
30+	1.31 (0.91, 1.87)	0.143	1.25 (0.87, 1.80)	0.219	1.24 (0.86, 1.79)	0.256
Total cholesterol						
per 100 mg/dl higher	1.23 (1.01, 1.49)	0.039	1.18 (0.98, 1.41)	0.080	1.22 (0.99, 1.50)	0.056
LDL cholesterol						
per 10 mg/dl higher	1.04 (1.01, 1.07)	0.004	1.04 (1.01, 1.07)	0.007	1.04 (1.01, 1.07)	0.005
Haemoglobin						
per 10 g/dl higher	0.84 (0.51, 1.40)	0.509	0.97 (0.69, 1.36)	0.861	0.99 (0.68, 1.44)	0.965
AST						
per 10 UI/mL higher	1.08 (1.02, 1.15)	0.010	1.09 (1.03, 1.15)	0.004	1.09 (1.03, 1.16)	0.003
Tryglicerides						
per 10 mg/dl higher	1.02 (1.01, 1.03)	0.001	1.02 (1.01, 1.03)	0.001	1.02 (1.01, 1.03)	<.001
Number of previously used regimens						
per 3 more	1.10 (0.95, 1.26)	0.209	1.01 (0.87, 1.18)	0.870	1.10 (0.94, 1.28)	0.250
Nation of birth, n(%)						
Italian vs. Foreign	0.99 (0.75, 1.31)	0.952	0.97 (0.73, 1.29)	0.826	0.94 (0.70, 1.27)	0.705

*adjusted for gender and age

**adjusted for gender, age, year of switch and geographical region

ART exp – DOR vs 3DR

logistic regression

Table 9 OR of switching to Doravirine vs 3DR INSTI from fitting a logistic regression analysis

Logistic regression estimates of factors associated with switchingto Doravinine- vs. a 3DR INSTI-based ART

Factor	Unadjusted Odds ratio (95% CI)	p-value	Adjusted* Odds ratio (95% CI)	p-value	Adjusted** Odds ratio (95% CI)	p-value
Age						
per 10 years older	1.13 (1.04, 1.22)	0.004	1.12 (1.03, 1.22)	0.006	1.15 (1.06, 1.25)	0.001
Gender						
Male	1		1			
Female	1.31 (1.03, 1.66)	0.027	1.28 (1.00, 1.62)	0.046	1.24 (0.97, 1.58)	0.087
Mode of HIV Transmission						
Heterosexual	1		1			
PWID	1.07 (0.74, 1.57)	0.712	1.00 (0.68, 1.46)	0.993	0.92 (0.62, 1.36)	0.681
MSM	0.69 (0.57, 0.84)	<.001	0.75 (0.60, 0.94)	0.013	0.78 (0.62, 0.98)	0.035
HIV-RNA						
per log10 copies/mL lower	0.97 (0.88, 1.08)	0.597	0.97 (0.94, 1.00)	0.048	0.98 (0.95, 1.01)	0.227
CD4 count						
per 100 cells/mmc higher	0.97 (0.94, 1.00)	0.025	0.97 (0.88, 1.07)	0.581	0.98 (0.89, 1.09)	0.753
CD4/CD8 ratio						
per 1 unit higher	0.99 (0.87, 1.12)	0.883	0.98 (0.85, 1.12)	0.749	0.97 (0.83, 1.13)	0.699
Time from HIV diagnosis						
per 3 years longer	1.09 (1.05, 1.13)	<.001	1.07 (1.03, 1.12)	<.001	1.08 (1.04, 1.12)	<.001
Smoker, n(%)						
No	1		1			
Yes	1.10 (0.90, 1.35)	0.334	1.12 (0.92, 1.37)	0.265	1.12 (0.91, 1.38)	0.268
BMI						
20-25	1		1			
25-29	1.37 (1.09, 1.72)	0.006	1.36 (1.08, 1.71)	0.009	1.40 (1.11, 1.78)	0.005
30+	1.31 (0.91, 1.87)	0.143	1.25 (0.87, 1.80)	0.219	1.24 (0.86, 1.79)	0.256
Total cholesterol						
per 100 mg/dl higher	1.23 (1.01, 1.49)	0.039	1.18 (0.98, 1.41)	0.080	1.22 (0.99, 1.50)	0.056
LDL cholesterol						
per 10 mg/dl higher	1.04 (1.01, 1.07)	0.004	1.04 (1.01, 1.07)	0.007	1.04 (1.01, 1.07)	0.005
Haemoglobin						
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AST						
per 10 UI/mL higher	1.08 (1.02, 1.15)	0.010	1.09 (1.03, 1.15)	0.004	1.09 (1.03, 1.16)	0.003
Tryglicerides						
per 10 mg/dl higher	1.02 (1.01, 1.03)	0.001	1.02 (1.01, 1.03)	0.001	1.02 (1.01, 1.03)	<.001
Number of previously used regimens						
per 3 more	1.10 (0.95, 1.26)	0.209	1.01 (0.87, 1.18)	0.870	1.10 (0.94, 1.28)	0.250
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Italian vs. Foreign	0.99 (0.75, 1.31)	0.952	0.97 (0.73, 1.29)	0.826	0.94 (0.70, 1.27)	0.705

*adjusted for gender and age

**adjusted for gender age, year of switch and geographical region

Older age
No MSM
Longer time from diagnosis
High LDL
High tryglerides
High AST

Conclusions

- A **DOR-based regimen** was preferred in about **4% of naïve** among triple regimens and in the **10% of experienced PWH** at their first switch, respectively.
- **Intravenous drug use, lower HIV-RNA, higher CD4 count, BMI>30, higher total and LDL cholesterol** are the major drivers of a DOR-based regimen choice in ***naïve PLWH*** in the cohort
- At the first switch in ***experienced PWH***, reasons for choosing DOR compared to INSTI included **older age**, **female gender, no MSM, higher BMI, higher total and LDL cholesterol, higher tryglicerides**, **higher AST**, and a **longer disease duration**
- In conclusion, DOR is preferentially used by clinicians for ART-naïve PLWH with less advanced HIV disease, and in comorbid PLWH. Overall, clinicians' choices were in agreements with guidelines and were in line with the lower toxicity of doravirine-regimen

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

Demographic characteristics of 11.519 patients at last follow up in 2021-2023

	n (%)
Gender M	9206 (79.9%)
Median age	49
Age>60	2055 (17.8%)
Italians	9261 (80.3%)
Risk: Heterosexual contacts	4572 (39.6%)
Risk: Homo/Bisexual contacts	5193 (45%)
Risk: IDU/ex IDU	723 (6.2%)
Risk: Other/Unknown/not compiled	1031 (8.9%)
CD4<200	695 (6%)
CD4<350	1612 (13.9%)
Line: Naïve	193 (1.6%)
Line: 1	2938 (25.5%)
Line: 2	2435 (21.1%)
Line: >=3	5953 (51.6%)
INSTI	8242 (71.5%)

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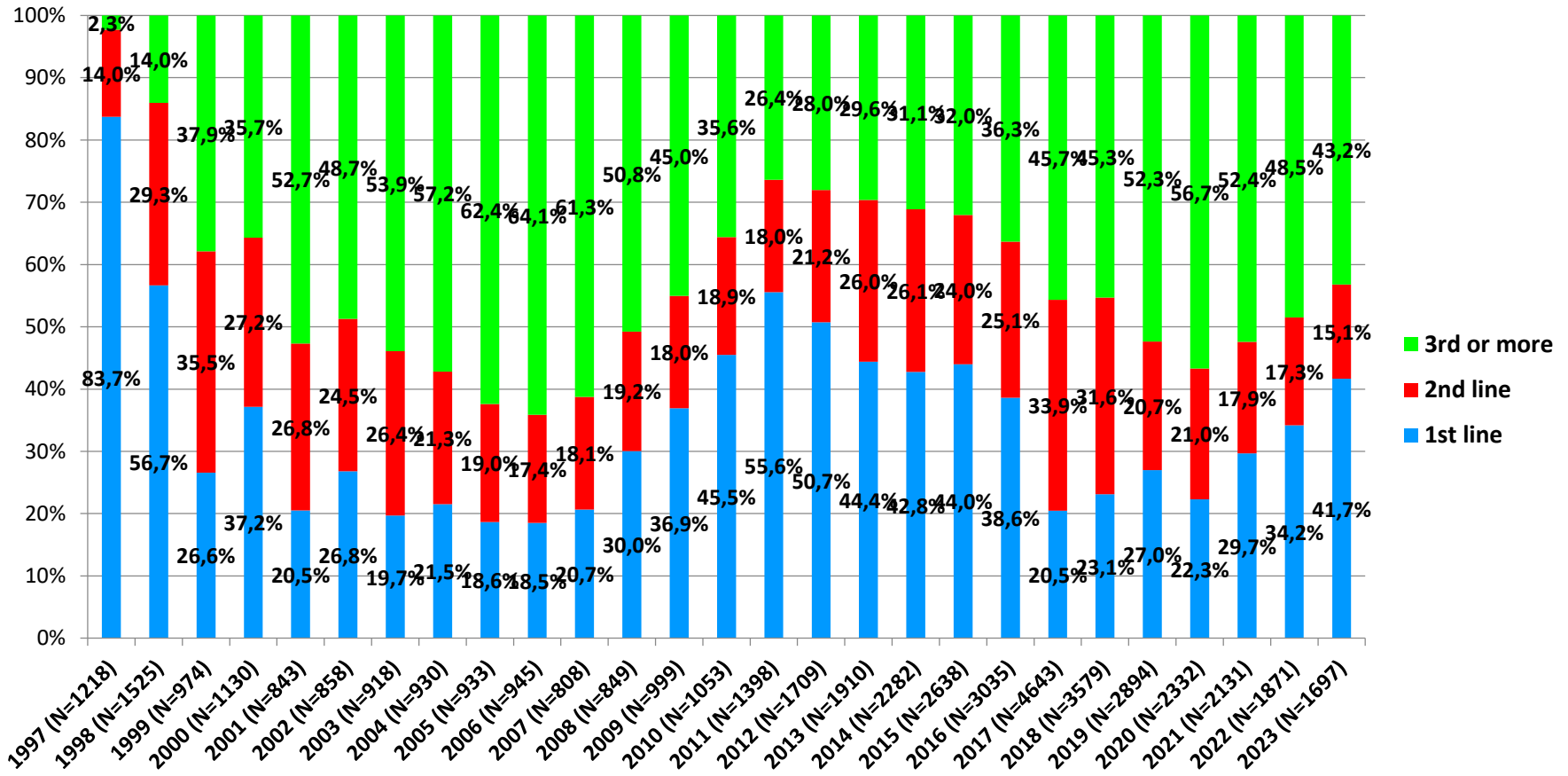
Italian Cohort Naive Antiretrovirals

Proportion of patients under different ART regimen lines according to calendar year



Dec 2023 Report

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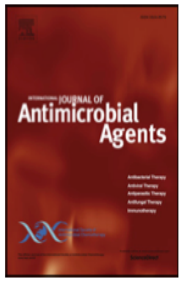

Characterization and outcomes of difficult-to-treat patients starting modern first-line ART regimens: Data from the ICONA cohort

Roberta Gagliardini[a,*], Alessandro Tavelli[b], Stefano Rusconi[c], Sergio Lo Caputo[d], Vincenzo Spagnuolo[e], Maria Mercedes Santoro[f], Andrea Costantini[g], Alessandra Vergori[a], Franco Maggiolo[h], Andrea Giacomelli[i], Giulia Burastero[j], Giordano Madeddu[k], Eugenia Quiros Roldan[l], Antonella d'Arminio Monforte[m], Andrea Antinori[a], Alessandro Cozzi-Lepri[n], ICONA Foundation Study Group

PWH were classified as 'difficult-to-treat' (DTT) if, after starting modern regimen ART, they experienced at least one of the following events (whichever occurred first):

I) At least two VF (VF defined as two consecutive HIV-RNA >200 copies/mL or a single HIV-RNA >1000 copies/mL after at least 6 months from the initiation of ART) with or without subsequent ART change;
II) At least two treatment discontinuations due to toxicity/intolerance/failure on two different regimens;
III) At least one VF (VF defined as two consecutive HIV-RNA >200 copies/mL or a single HIV-RNA >1000 copies/mL after >6 months from the initiation of ART) followed by ART change plus at least one treatment discontinuation due to toxicity/intolerance/failure.

Results: Among 806[illegible] PWH, 320 (4%) became DTT. Estimates of becoming DTT was 6.5% (95% CI: 5.8–7.4%) by 6 years. DTT PWH were significantly older, with a higher prevalence of AIDS and lower CD4+ at nadir than the non-DTT. In the prospective analysis, DTT demonstrated a higher unadjusted risk for all the outcomes. Once controlled for confounders, significant associations were confirmed for VF (aHR 2.23, 1.33–3.73), treatment failure (aHR 1.70, 1.03–2.78), and SNAE/death (aHR 2.79, 1.18–6.61).

Conclusion: A total of 6.5% of PWH satisfied our definition of DTT by 6 years from ART starting. This appears to be a more fragile group who may have higher risk of failure.

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ISID INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

Heavily treatment-experienced persons living with HIV currently in care in Italy: characteristics, risk factors, and therapeutic options—the ICONA Foundation cohort study

Sergio Lo Caputo[1,§], Mariacristina Poliseno[2,§,*], Alessandro Tavelli[3], Roberta Gagliardini[4], Stefano Rusconi[5], Giuseppe Lapadula[6], Andrea Antinori[4], Daniela Francisci[7], Loredana Sarmati[8], Andrea Gori[9], Vincenzo Spagnuolo[10], Francesca Ceccherini-Silberstein[11], Antonella d'Arminio Monforte[12], Alessandro Cozzi-Lepri[13], the ICONA Foundation Study Group

Patients and Methods

Def1) A composite of 2 or more of the below will define those HTE adults living with HIV-1 infection:

1A) Current regimen indicative of HTE

Regimen includes ≥3 drugs, including one or more of the following: DTG BID or DRV BID or T20; ETV + DTG BID or MVC or boosted DRV BID or T20

1B) At least 3 core ARV classes prior to current regimen

last drug regimen included ≥3 drugs

1C) Individuals who had at least 4 anchor agent switches at any previous time

with the 4th or subsequent regimen including one of the following: DTG BID or DRV BID or T20; ETV + DTG BID or MVC or boosted DRV BID or T20; ≥2 core agents + any other ARV;

1D) Virologic failure prior to class switch

Pts have recorded history of ≥3 virologic failure followed by a treatment switch (within 90 days)

Def2) fall within the proportion of this population, that are:

2A) unstable unsuppressed

• confirmed virological failure (HIV RNA levels of ≥200 copies/mL, at ≥2 consecutive determinations ≤6 months apart)

OR

2B) stable but compromised

• persistent low-level viremia (HIV RNA levels of ≥50, <200 copies/mL, at ≥2 consecutive determinations ≤6 months apart); or

• persistent low CD4 counts (<200 cells/mmc, at ≥2 consecutive determinations ≤6 months); and/or <15% improvement in CD4, following initiation of a new ARV treatment; or

• ≥4 switches in ARV treatment with significant DDI, comorbidities or safety/ tolerability/ toxicity challenges on current ARV treatment.

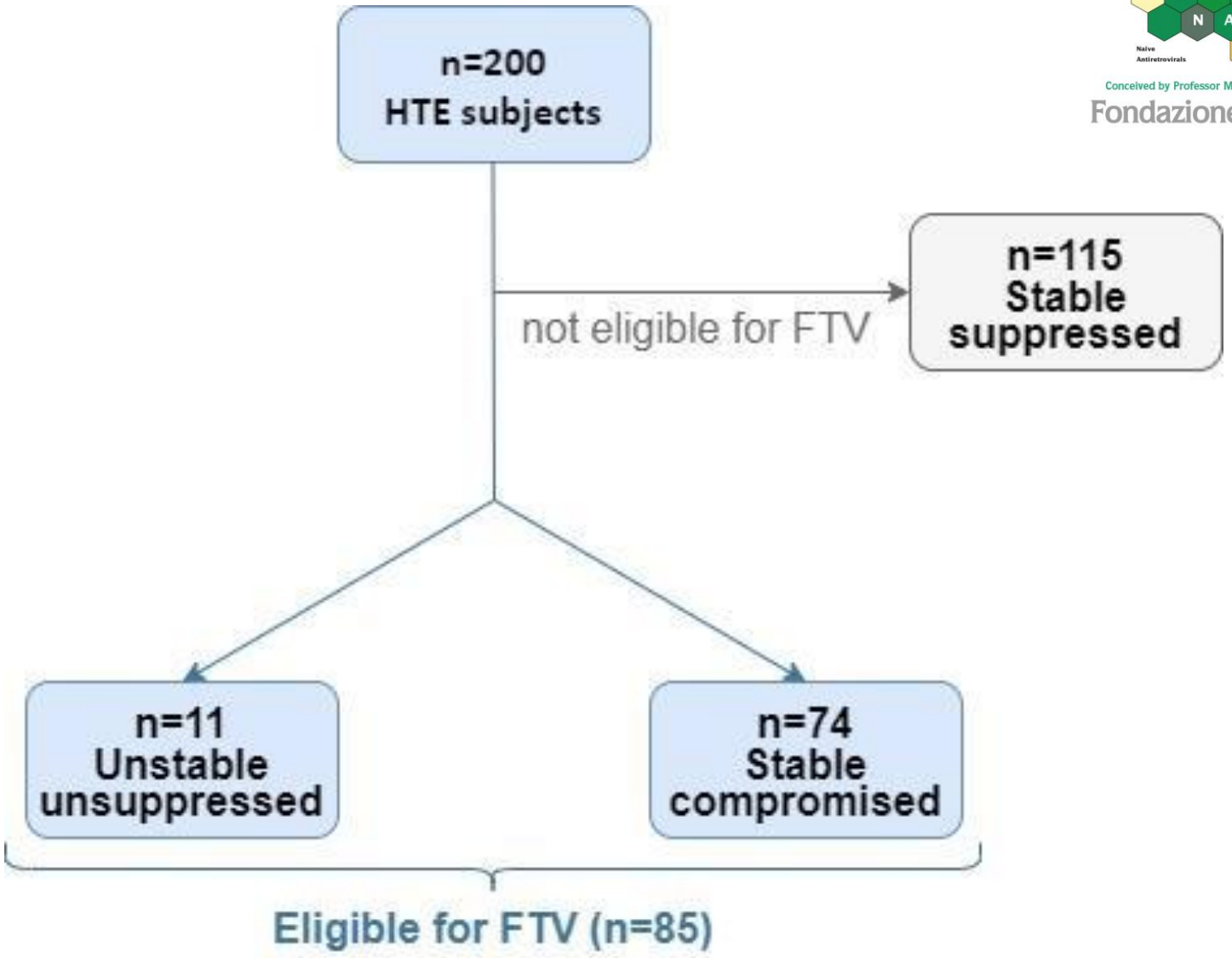
Results

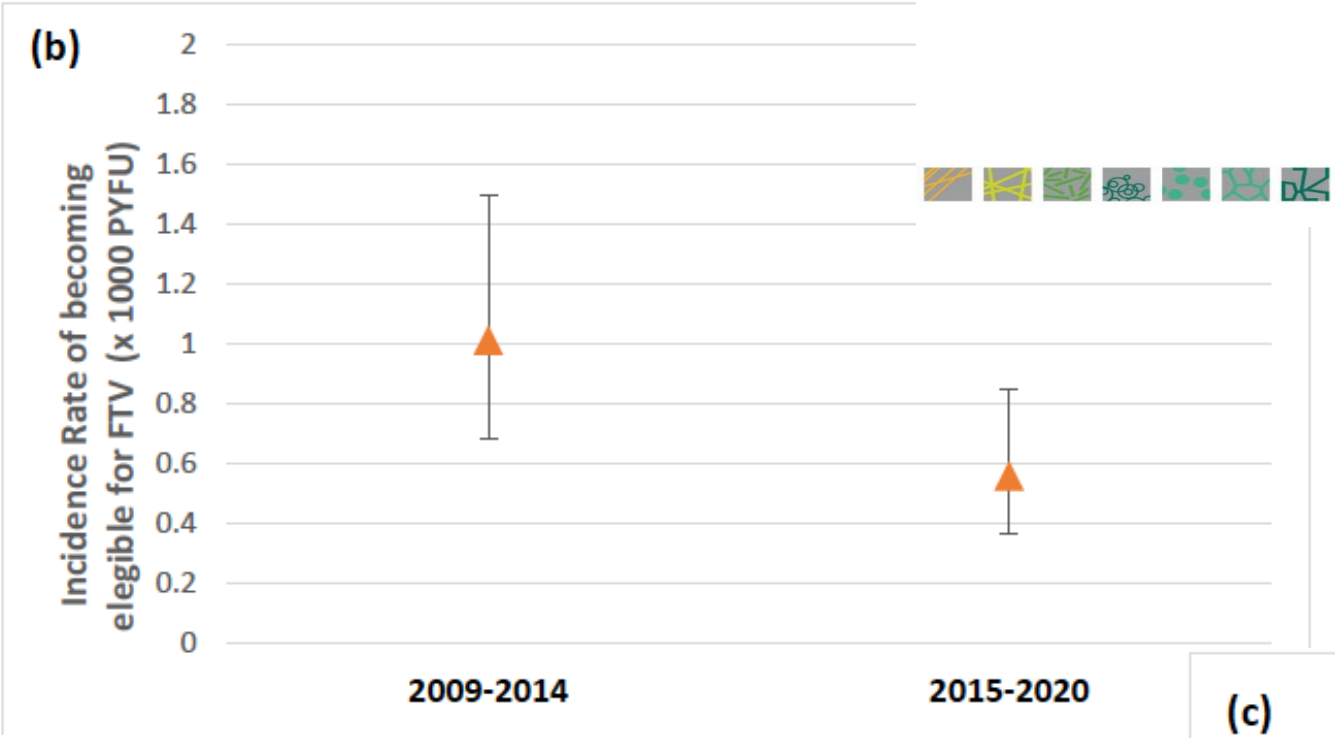
200 HTE patients

11 are unsuppressed (def 2A)

74 are virologically stable but compromised (def 2B)

We therefore identified **85 HTE** adults living with HIV-1 infection who are currently unstable unsuppressed or stable but compromised, which constitute the 'target population' eligible for FTV (**42.5% of the HTE, 0.64% of total population**).





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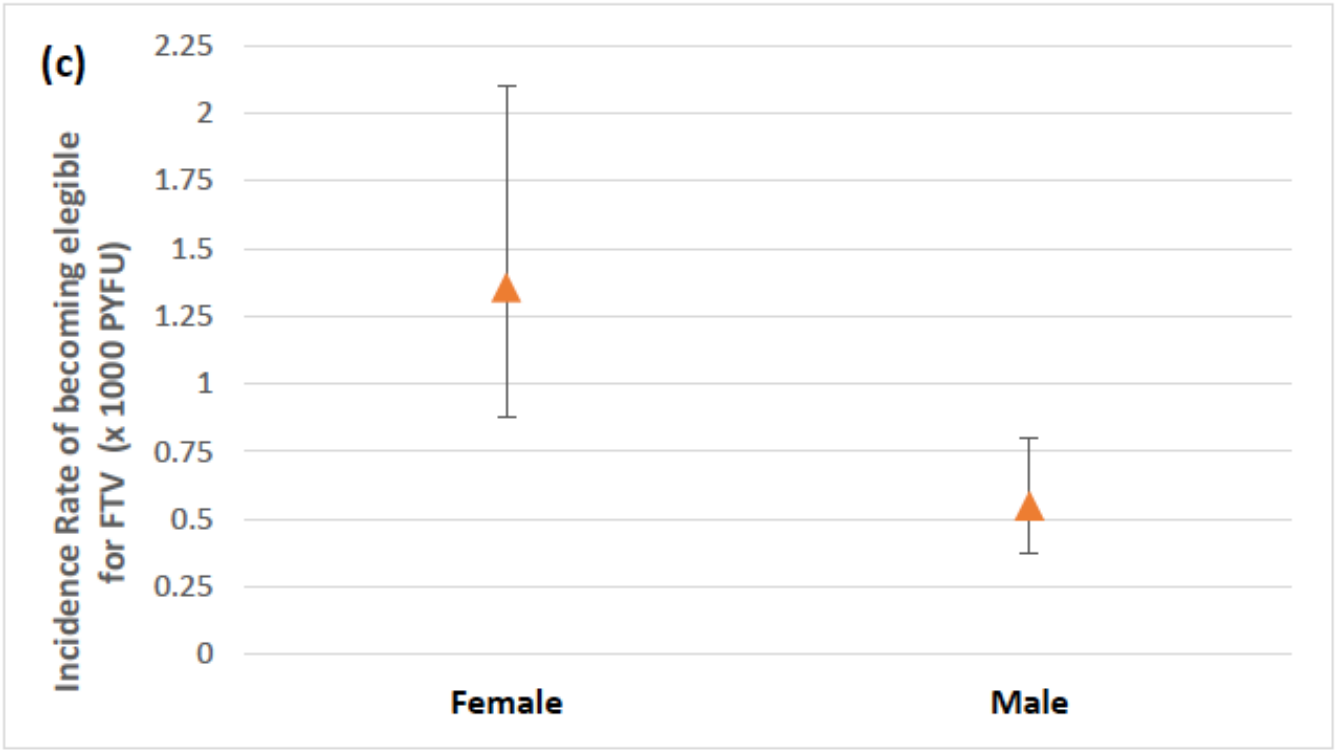
Incidence rate of entering in the 'target population' according to (a) gender and (b) calendar period

38/85 subjects reached the HTE definition before 2009, over 63983 PYFU there was 47 new incident cases of subjects entering in the 'target population' during the study period 2009-2019. Incidence rate was 0.73 x 1000 PYFU (95%CI: 0.55-0.98). Again incidence rate was higher in female (1.3 x 1000 PYFU, 95%CI 0.87-2.1) compared to male (0.55 x 1000 PYFU, 95%CI 0.38-0.80) (log rank p= 0.001)



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Persistent poor clinical outcomes of people living with HIV presenting with AIDS and late HIV diagnosis – results from the ICONA cohort in Italy, 2009-2022

Annalisa Mondi[1], Alessandro Cozzi-Lepri[2], Alessandro Tavelli[3,*], Antonella Cingolani[4], Andrea Giacomelli[5], Giancarlo Orofino[6], Gabriella De Girolamo[7], Carmela Pinnetti[1], Andrea Gori[8], Annalisa Saracino[9], Alessandra Bandera[10], Giulia Marchetti[11], Enrico Girardi[12], Cristina Mussini[13], Antonella d'Arminio Monforte[3], Andrea Antinori[1], for the ICONA Foundation Study Group[§]

To asses **the impact of late HIV diagnosis** on **mortality** and **treatment outcomes** among **newly diagnosed PLWH who started ART over the last 14 years (2009-2022)**.

Study design and population

- **Prospective, observational, multicentric study** analysing data from Icona Foundation Study Cohort.
- All consecutive **HIV-infected subjects,** enrolled in ICONA cohort, who **started ART within 4 months from HIV diagnosis** from **January 2009 to December 2022**, were included in the analysis and divided according to CD4 cell count* and clinical presentation before ART initiation into three exposure groups:

NON LATE DIAGNOSIS (NON-LD)	Subjects with **CD4 count ≥350cell/mm3 without history of ADE regardless**
LATE DIAGNOSIS (LD)	Subjects with **CD4 count <350cell/mm3 and/or a diagnosis of ADE regardless of CD4 count**
- ASYMPTOMATIC LATE DIAGNOSIS (LD-ASYMPTOMATIC)	Subjects with CD4 count <350/mm3 **without a history of ADE**
- AIDS PRESENTERS (LD-AIDS)	Subjects **with diagnosis of ADE before ART initiation**

- We **excluded from the study population** subjects: - without at least a CD4 cell count available before ART initiation
  - without at least one-month follow-up after ART initiation
  - **who had a previously available CD4 count discordant with the group into which they were classified**

- **Baseline = Date of ART initiation**

All Cause-Mortality
Kaplan-Meier Analysis

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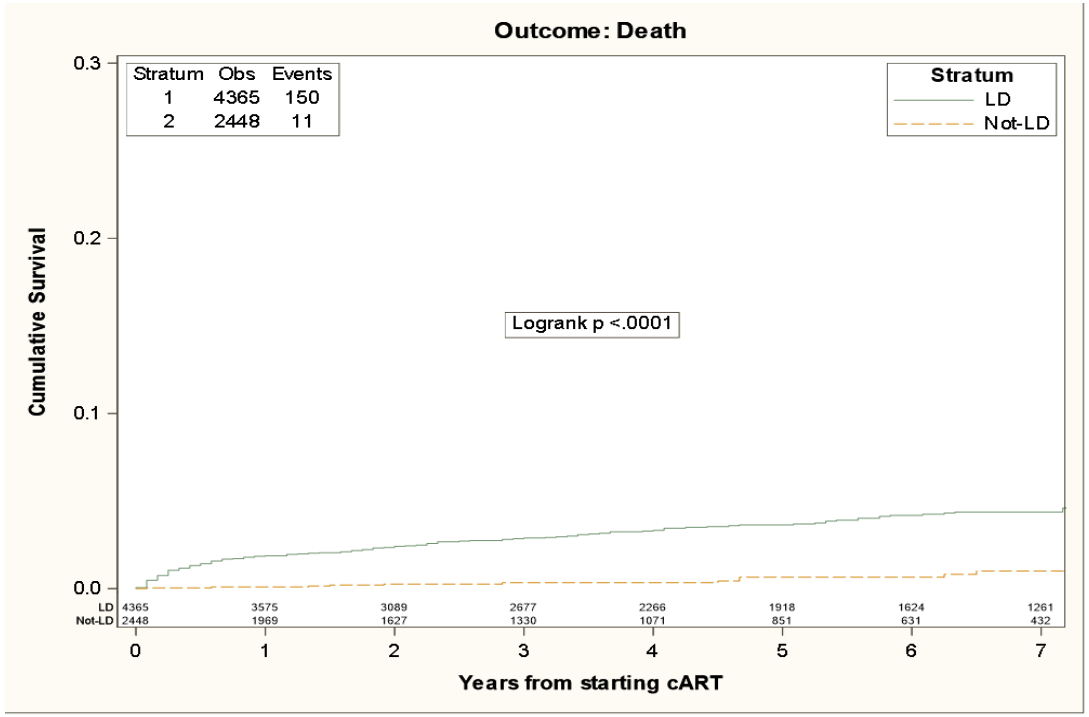

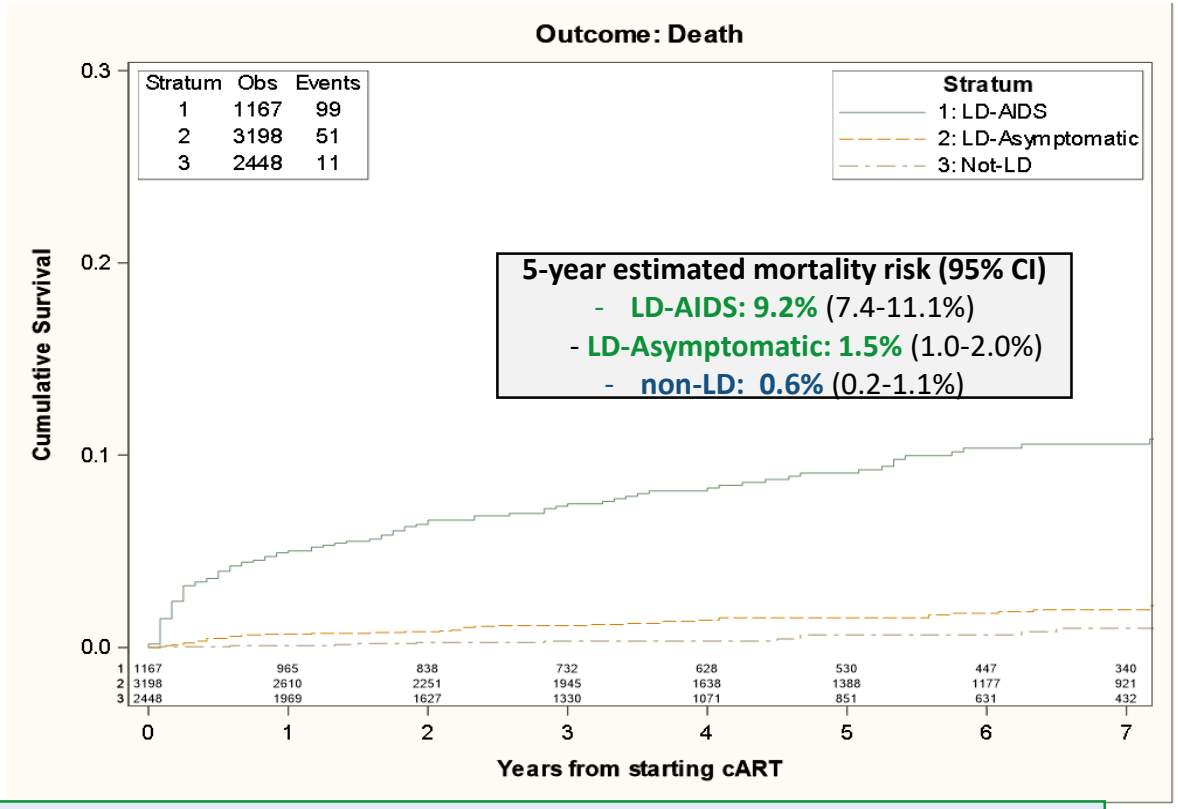

In the **LD-AIDS group**, the **estimated risk of death was highest over the first year after ART initiation** (**5.0%**) and **increased of approximately 1% per year thereafter** (**6.6% at 2 years, 7.5% at 3 years, 8.2% at 4 years and 9.2% at 5 years**).

CAUSE-SPECIFIC MORTALITY COMPETING RISK ANALYSIS

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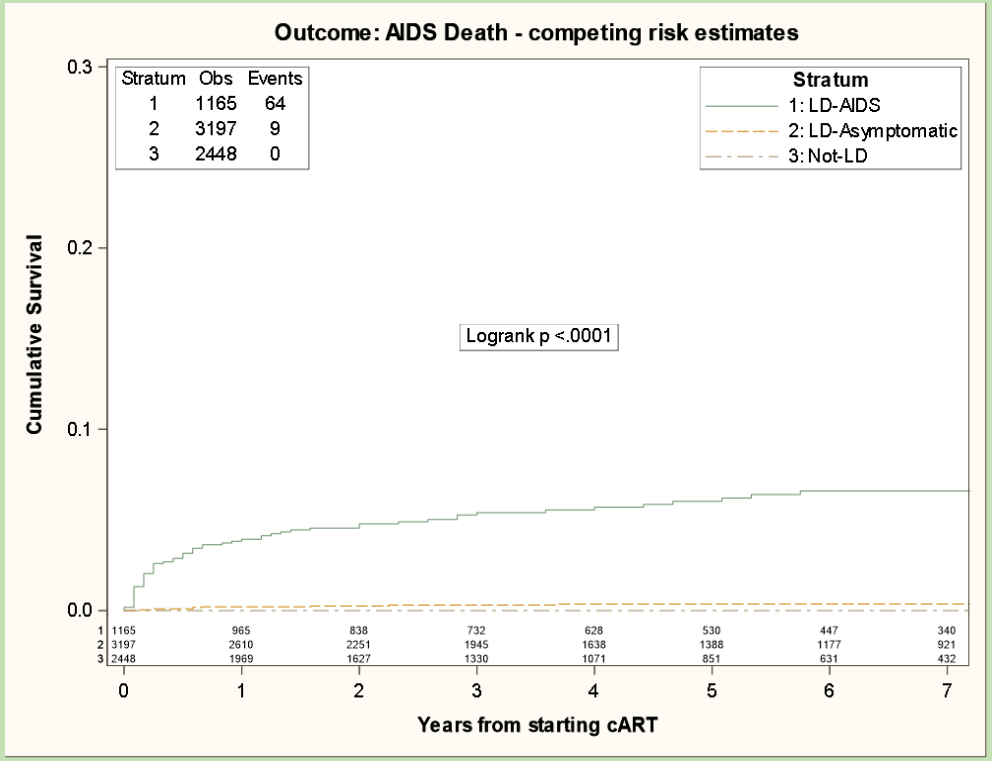
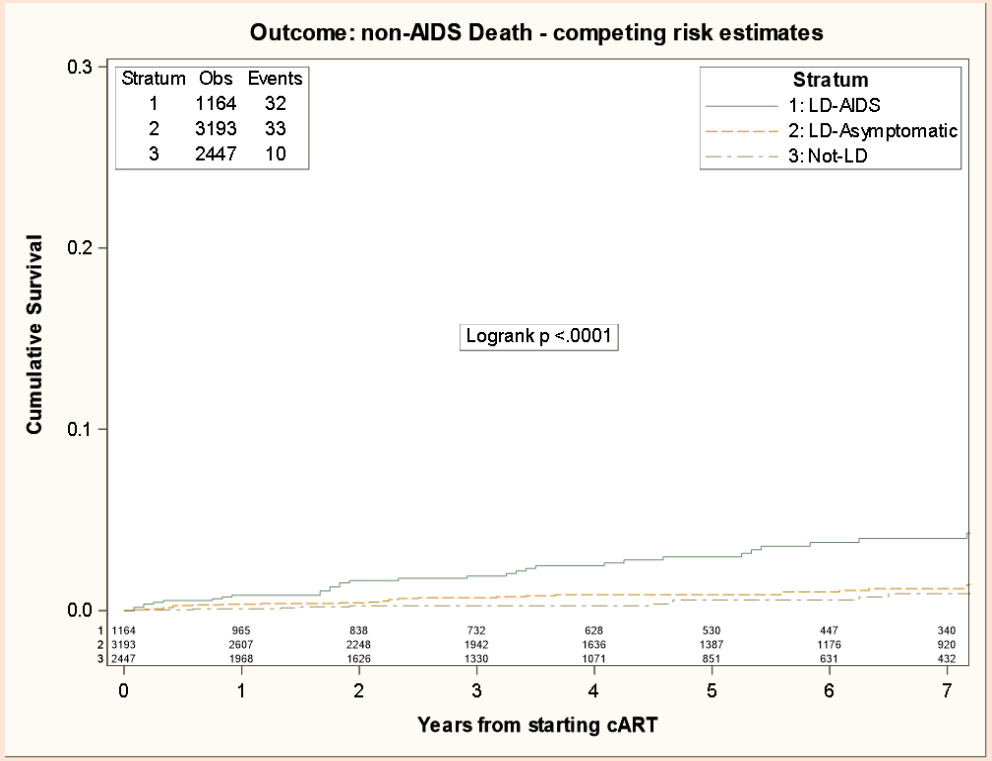
AIDS-RELATED MORTALITY



NON AIDS-RELATED MORTALITY



INDIPEDENT RISK OF MORTALITY BY EXPOSURE GROUP

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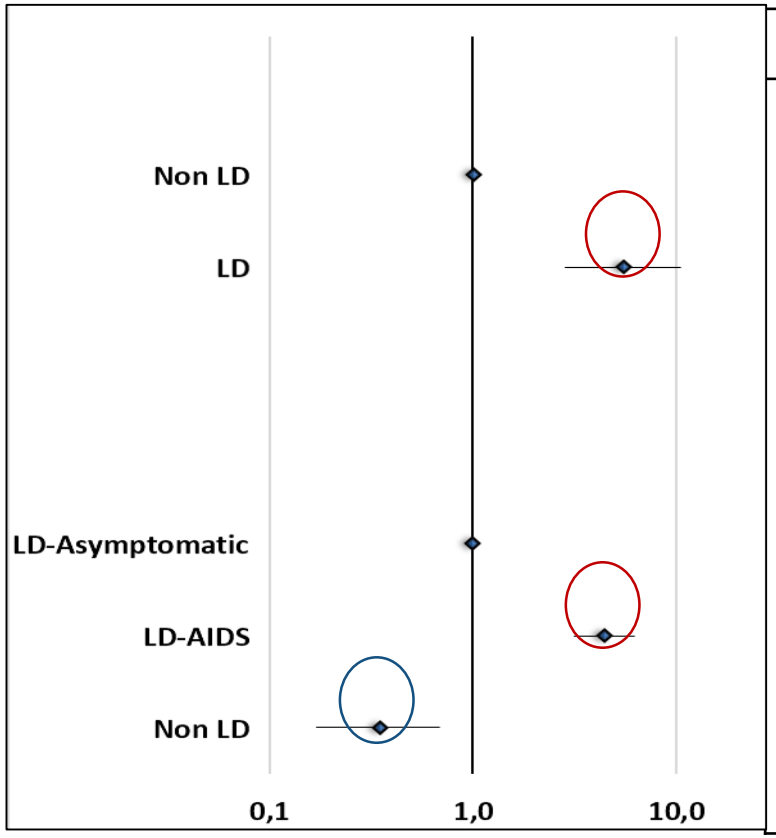
ALL-CAUSE MORTALITY

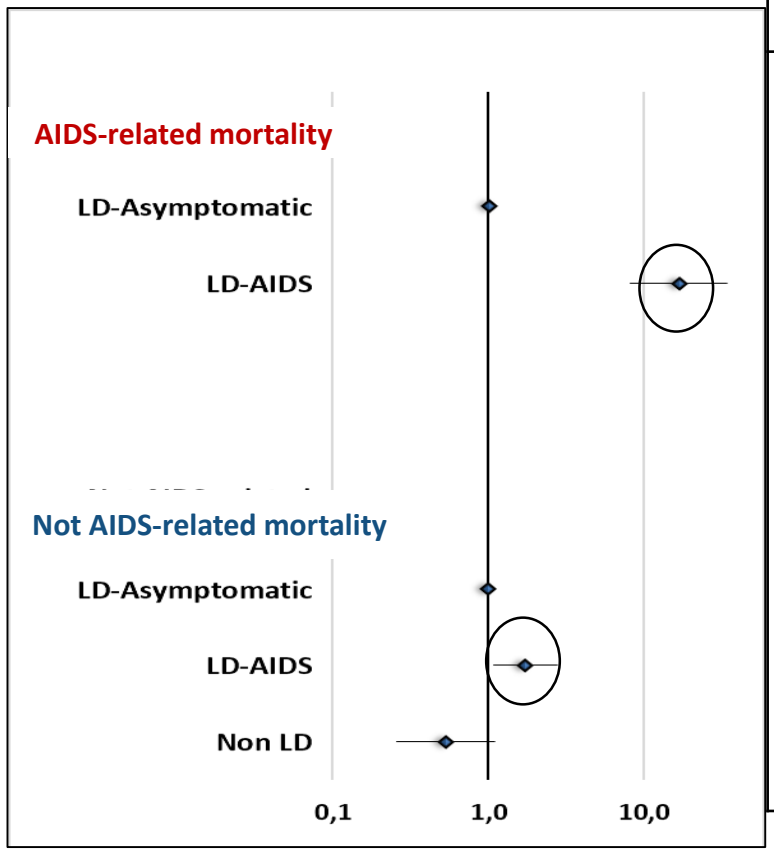
(standard Cox regression model)



	aHR* (95%CI)	p-value
Non LD	ref	
LD	5.51 (2.87-10.60)	**<0.001**
	^interaction test p=0.41	
LD-Asymptomatic	ref	
LD-AIDS	4.42 (3.14-6.22)	**<0.001**
Non LD	0.35 (0.17-0.69)	**0.002**
	^interaction test p=0.07	

CAUSE-SPECIFIC MORTALITY

(Fine-Gray regression model)



	aSHR* (95%CI)	p-value
AIDS-related mortality		
LD-Asymptomatic	ref	
LD-AIDS	16.86 (8.24-34.46)	**<0.001**
	^interaction test p=0.42	
Not AIDS-related mortality		
LD-Asymptomatic	ref	
LD-AIDS	1.74 (1.08-2.78)	**0.022**
Non LD	0.53 (0.26-1.11)	0.093
	^interaction test p=0.65	

*adjusted for age, gender, mode of HIV transmission, nationality, calendar year for ART initiation, hepatitis-coinfection and type of ART regimen
^ interaction test exposure group and calendar year of ART start

TREATMENT FAILURE

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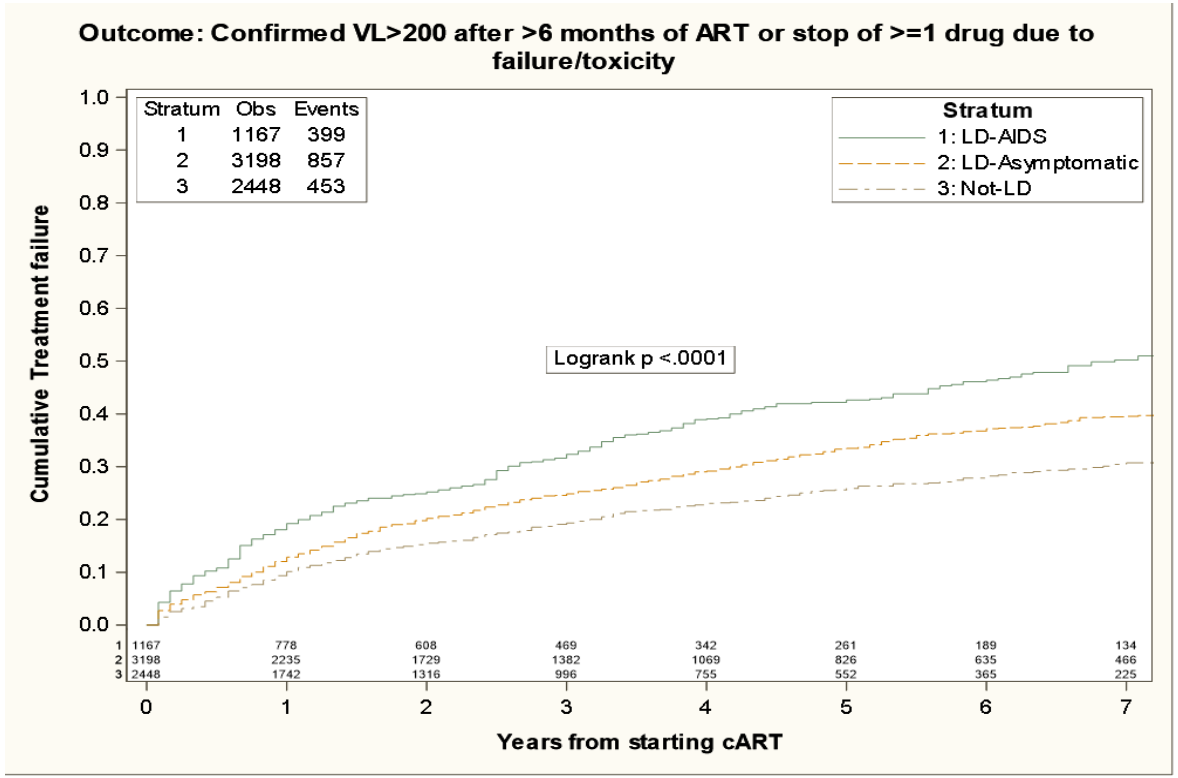
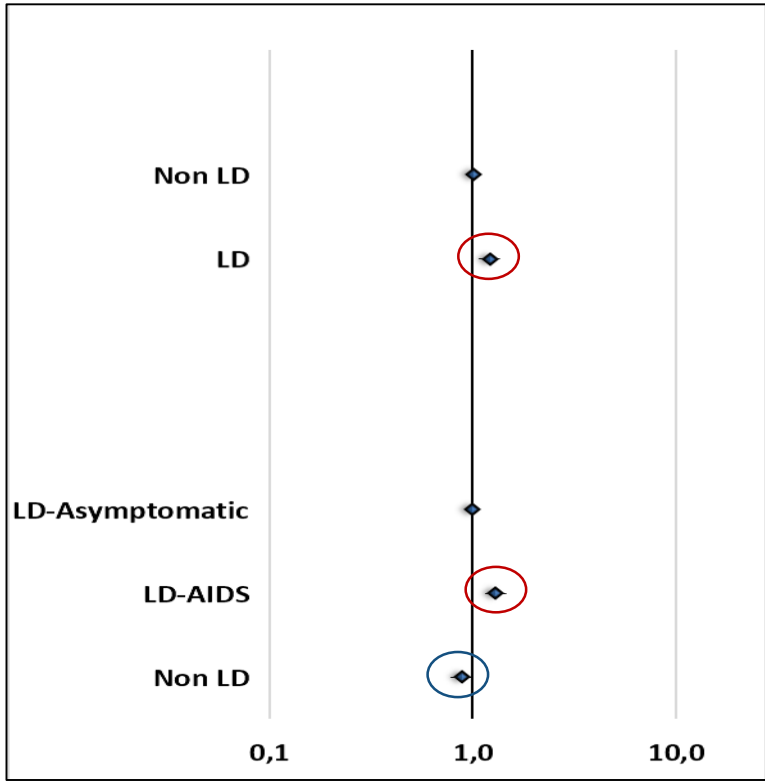
ESTIMATED PROBABILITY OF TREATMENT FAILURE BY EXPOSURE GROUP (KAPLAN-MEIER ANALYSIS)



INDIPENDENT RISK OF TREATMENT FAILURE BY EXPOSURE GROUP (COX REGRESSION ANALYSIS)



	aHR* (95%CI)	p-value
Non LD	ref	
LD	1.21 (1.08-1.36)	**0.001**
	^interaction test **p<0.01**	
LD-Asymptomatic	ref	
LD-AIDS	1.30 (1.15-1.47)	**<0.001**
Non LD	0.88 (0.78-1.00)	**0.046**
	^interaction test **p<0.01**	

*adjusted for age, gender, mode of HIV transmission, nationality, calendar year for ART initiation, hepatitis-coinfection and type of ART regimen according to the third drug.
^ interaction test exposure group and calendar year of ART start

Table 3

HR and aHR for treatment failure associated with late HIV diagnosis (non-LD vs LD, Table 3a and non-LD vs LD-asymptomatic vs LD-AIDS, Table 3b) from fitting a standard Cox regression model.

Table 3a. Treatment failure	HR	95% CI	*P*-value	aHR[a]	95% CI	*P*-value
Non-LD	1	-		1	-	
LD	1.51	1.35-1.68	**<0.001**	1.21	1.08-1.36	**0.001**
[X]*interaction test exposure group and calendar year of ART start: P <0.01*						
Table 3b. Treatment failure	**HR**	**95% CI**	**P-value**	**aHR[a]**	**95% CI**	**P-value**
LD-asymptomatic	1	-		1	-	
LD-AIDS	1.36	1.21-1.53	**<0.001**	1.30	1.15-1.47	**<0.001**
Non-LD	0.72	0.65-0.81		0.88	0.78-1.00	**0.046**
[X] *interaction test exposure group and calendar year of ART start: P <0.01*						

[a] Adjusted for age, sex, mode of HIV transmission, nationality, calendar year for ART initiation, hepatitis-coinfection, and type of ART regimen according to the third drug.Abbreviations: aHR, adjusted hazard ratio; ART, antiretroviral therapy; CI, confidence interval; HR, unadjusted hazard ratio; LD, late diagnosis; non-LD, non-late diagnosis.

CONCLUSIONS

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- Even in more recent years, **subjects presenting late to care, and particularly AIDS presenters, despite a prompt linkage to care after diagnosis and ART initiation, still presented significantly poorer outcomes in terms of both survival and treatment durability** compared with the rest of ART-naïve subjects.

- The **risk for all-cause mortality** was approximately **5.5-fold higher in LD individuals** than in those without late diagnosis, and **4.5-fold higher in AIDS presenters** compared to the remaining late diagnosed patients.

- Considering the persistent mortality gap of LD and AIDS-presenting subjects, also in high-income countries, **public health strategies for unveil hidden HIV infections are urgently needed.**

Icona Foundation Study Group

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