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HIGH RATES OF VIRAL RESUPPRESSION ON FIRST-LINE ART AFTER INITIAL VIROLOGICAL FAILURE

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BACKGROUND

- ART achieves viral load (VL) suppression in the majority of HIV-infected patients in low and middle-income countries.
- WHO recommends annual VL monitoring, and switch to second-line ART without resistance testing if virological failure is confirmed (2x VL ≥1000 copies/mL).
- However, challenges exist regarding clinical response to VL results and management of treatment failure.

AIMS

- To study in a cohort of 69,454 patients the frequency of and risk factors for virological failure during first-line ART.
- To study the clinical follow-up in patients after virological failure in real life clinical care.
- To assess the frequency of viral resuppression on first-line ART after virological failure.

METHODS

- A cohort of **69,454** patients (**209,638** patient-years of follow-up on first-line ART) from 19 urban and 38 rural HIV treatment sites across four South African provinces was studied. Adult patients on first-line ART for ≥20 weeks were included.
- Virological suppression over time was assessed using multi-state models allowing for transition between suppression and non-suppression events.
- Risk factors for virological failure during ART were analyzed using mixed-effect logistic regression models, with provincial cohort as a random effect.
- Hazard for virological failure and switch after prior resuppression on first-line ART were calculated using Cox proportional hazard models.

VIROLOGICAL SUPPRESSION DURING ART

- The proportion of patients with a most recent VL <1000 copies/mL varied between 88.3% at 6 months and 91.0% at 6 years of follow-up *(figure 1)*.

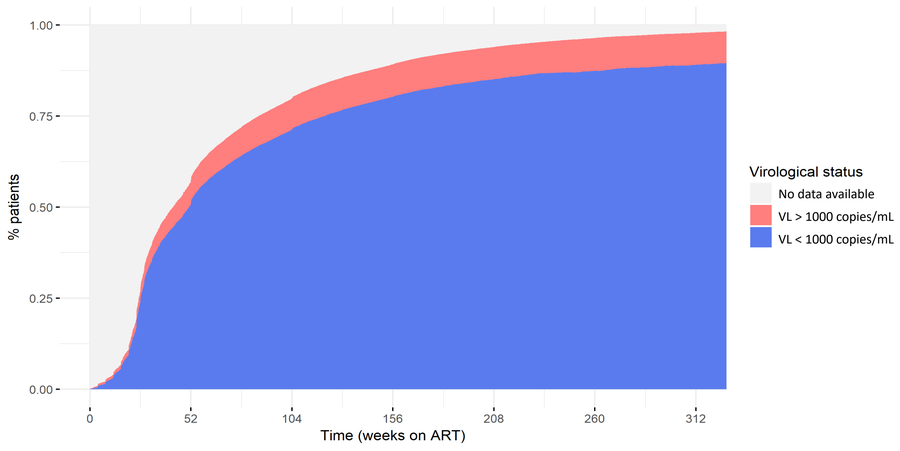


Figure 1 - Cumulative incidence of VL results - *Aalen-Johansen curves of 69,454 patients on first-line ART*

RISK FACTORS FOR VIROLOGICAL FAILURE

- In total, 20.7% of patients (14,380/69,454) experienced virological failure during follow-up. Risk factors for virological failure are displayed in *table 1*.

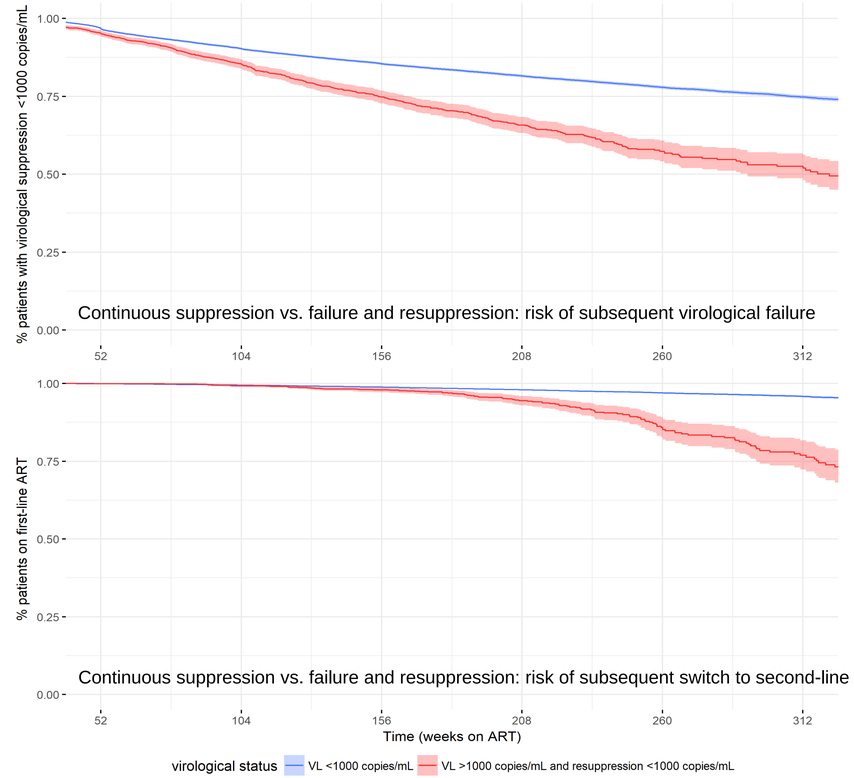
Table 1 – Risk factors - *Mixed-effect model for 69,454 patients on first-line ART*

	Virological failure		aOR
	yes	*no*	*[95% CI]*
Sex: female	64.4%	68.8%	0.76*** *[0.71 - 0.80]*
Age	34.9 years	36.0 years	0.79*** *[0.77 - 0.81]*
CD4 at start ART: ≤ 200 cells/mm^3	64.1%	52.4%	1.75*** *[1.63 - 1.89]*

Note: * = *p<0.05;* ** = *p<0.01;* *** = *p<0.001*. aOR = adjusted Odds ratio. 95% CI = 95% confidence interval. Provincial cohort was entered as random effect. aOR calculated for age increment of 10 years.

RESUPPRESSION WITHOUT SWITCH TO SECOND-LINE ART

- Of 9,351 patients with virological failure and available follow-up, failure was confirmed in 55.2%.
- The remaining 44.8% achieved resuppression <1000 copies/mL on at least one VL measurement without switch to second-line ART.
- Patients who resuppressed had an increased hazard of renewed virological failure (HR 1.90, 95%CI 1.75 – 2.07) and switch to second-line ART (HR 5.16, 95%CI 4.38 – 6.08).



FOLLOW-UP AFTER CONFIRMED VIROLOGICAL FAILURE

- Detection of failure → Confirmation of failure: **30 weeks [IQR: 17 - 53]**
- Detection of failure → Switch to second-line ART: **68 weeks [35 - 124]**

CONCLUSION

- In this large cohort, the proportion of patients with suppression <1000 copies/mL is 90%, while over 20% of patients ever experienced virological failure.
- After failure, resuppression on first-line ART was frequently observed, but these patients remained at increased risk of subsequent failure and switch.
- Significant delay in confirmation of failure and switch to second-line ART poses a potential risk for selection of drug resistance and onward transmission.
- These data confirm the relevance of timely confirmatory VL testing, and suggest that once virological failure is confirmed, diagnostic tools to discriminate between non-adherence and loss of drug activity may prevent unnecessary switches to second-line ART.

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