High levels of HIV drug resistance pre-treatment and with first-line ART failure in Mozambique

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OPERATIONAL RESEARCH DAY, Brussels – 31 May 2019

Background

- In 2017, 21.7 million individuals on antiretroviral therapy (ART)
- HIV drug resistance (HIVDR) as an individual and public health threat
- WHO has developed a global strategy for surveillance and monitoring HIVDR
- 2017 WHO HIVDR report: 11 countries (3 in Africa) surveillance data
- Drug resistance testing (DRT) is not routinely available in low resource settings

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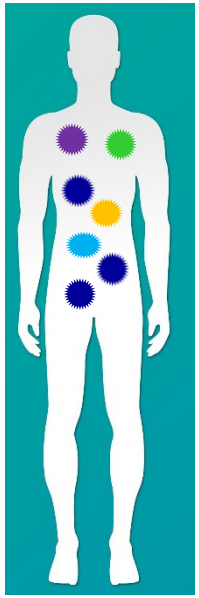
Three categories of HIVDR

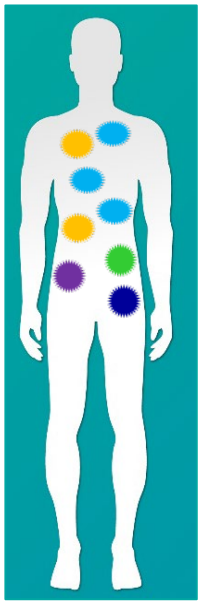
On ART



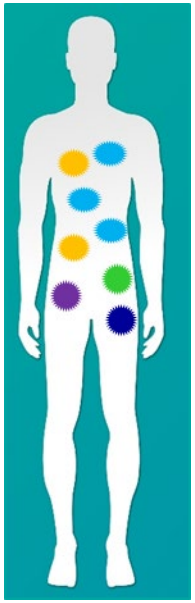
Non-Resistant HIV

Resistant HIV

New infection



non ARV pre-exposed or ARV pre-expose



Acquired DR (ADR)

Transmitted DR (TDR)

Pre-treatment DR (PDR)

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Study settings

- Tete province① (Changara and Marara district): 5% HIV prevalence
- Maputo city②: 16.8 % HIV prevalence

- MSF supports decentralized HIV programs in urban and rural settings

- Viral load (VL) testing scale-up since 2013
- In 2015 (programmatic data), VL ≥ 1 000 cps/ml:
  - Tete: 40 %
  - Maputo: 27 %

Objectives of the study

Acquired drug resistance

Assess the level of:

- Virological failure
- HIVDR
- Virological suppression at follow-up test

Pre-treatment drug resistance

Assess the level of:

- HIVDR among ART initiators regardless of prior exposure to ARTs
- HIVDR among those previously exposed to ARTs

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Study methods

	Acquired drug resistance (Oct 2017 – July 2018)	Pre-treatment drug resistance (Oct 2017 – Oct 2018)
Design	Cross-sectional	
Site	1 health centre in Maputo and 2 in Tete	1 health centre in Maputo and 7 in Tete
Eligibility criteria	age ≥ 18 years, on 1st-line ART for ≥ 6 months	age ≥ 18 years, ART initiator/re-initiators (interruption ≥ 3 months)
Sample size	1 100 participants	690 participants
Main assessments	• Plasma VL • DRT* if VL ≥ 1 000 copies/ml • Follow-up VL 3-6 months later	• Dried blood spot (DBS) VL • DRT* if VL ≥ 1 000 copies/ml

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*HIVDR interpretation using Stanford HIVdb algorithm v. 8.8:
sequence having predicted low-/intermediate-/high-level considered “resistant”

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Acquired drug resistance: Results

Characteristics of study population

Included, 1 113	N (%)
Sex, female	745 (67)
Age, years, median [IQR]	42 [34-50]
Time on ART, years, median [IQR]	4.5 [2-6.4]
CD4 count > 200 cells/mL	1 035 (93)
WHO stage 1 or 2	1 102 (99)
ART regimen TDF-based	968 (87)

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Prevalence of virological failure

HIV RNA copies/ml	N (%)	95%CI
< 1 000	988 (89)	87 – 91
≥ 1 000	**125 (11)**	**9 – 13**
1 000 – 10 000	37 (30)	22 – 38
≥ 10 000	88 (70)	62 – 78
2nd VL ≥ 1 000	***69 (77)**	**63 - 82**

* 21 patients were switched to 2nd line before the 2nd assessment

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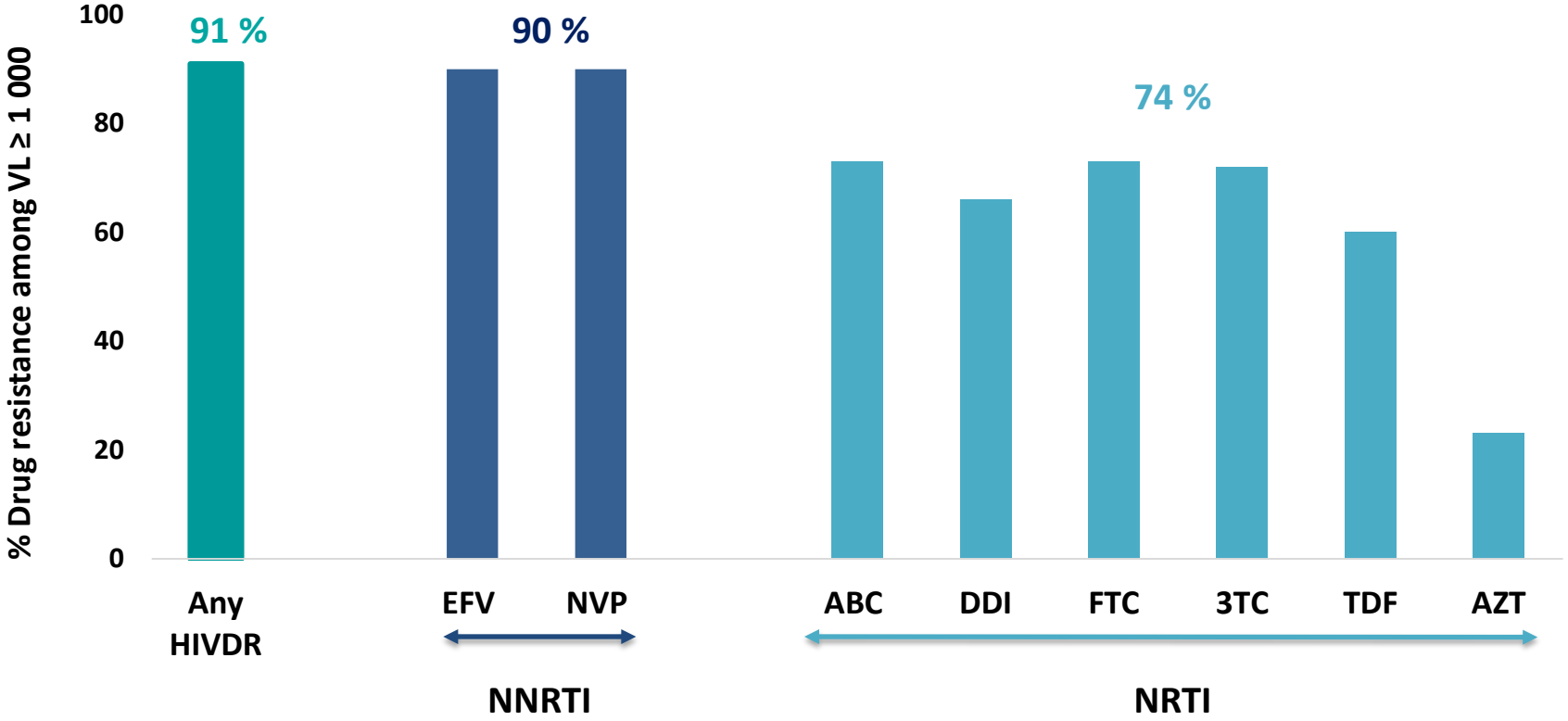
Resistance profile among VL ≥ 1 000



Definition: Any HIVDR = at least 1 resistance; NNRTI = resistance to EFV/NVP; Any NRTI = any resistance to any NRTI

Pre-treatment drug resistance: Results

Characteristics of study population

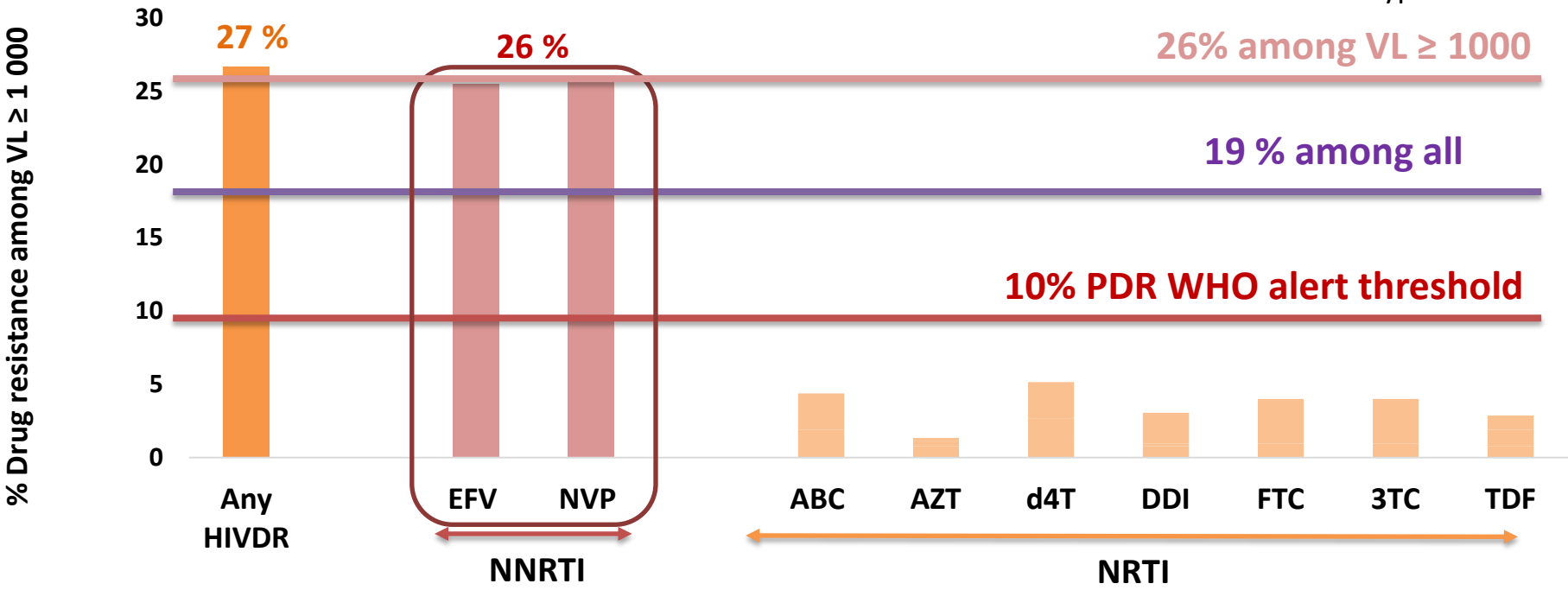
Included, 735	N (%)
Site, Maputo	343 (47)
Gender, female	413 (56)
Age, years, median [IQR]	34 [26-41]
CD4 count, median [IQR]	348 [193 – 508]
Prior ARV exposure	93 (13)
Type of ARV exposure:	
PMTCT	15 (16)
ARV interruption (≥3 months)	88 (95)

Viral load at inclusion

	N (%)	95%CI
VL ≥ 1 000	603 (82)	79 – 85

Resistance profile among VL ≥ 1 000

DRT amplification rate: 87.0%
HIV-1 subtype C: 98.8%



⇒ 1/5 of ART initiators / re-initiators would start a suboptimal regimen

Definition: Any HIVDR = at least 1 resistance; NNRTI = resistance to EFV/NVP; Any NRTI = any resistance to any NRTI

Resistance profile by prior ARV exposure among VL ≥ 1 000

	N (%)	95%CI
Pre-exposed (N=71)		
Any HIVDR	39 (55)	43 – 67
NNRTI	39 (55)	43 – 67
Any NRTI	8 (12)	5 - 21
Naïve (N=454)		
Any HIVDR	101 (22)	18 – 26
NNRTI	95 (21)	17 – 25
Any NRTI	20 (4)	3 - 7

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Summary

Acquired drug resistance

- Overall good virological suppression on first-line ART
- Virological failure driven by HIVDR
- Most of virological failures required a switch to 2nd line

Pre-treatment drug resistance

- Alarming level of PDR (NNRTI resistance): double the 10% threshold defined by the WHO
- In ART pre-exposed patients the level of PDR is twice as high as those who are ART-naïve

Conclusion

- **Fast switch** of regimen in patients with **virological failure** following the algorithm
- **More robust first line regimen** (integrase inhibitors –e.g. dolutegravir (DTG)) has to be considered
- If findings replicated at national level **urgent need** to pass to **DTG-based first-line regimen**
- HIV drug resistance surveillance should be implemented at national level (ADR and PDR)

Acknowledgments

- Study participants
- OR teams in Tete and Maputo
- Ministry of Health
- Ivan A. Pulido Tarquino
- Sherezade Fuentes
- Deise Vaz
- Birgit Schramm
- National Institute Communicable Diseases (NICD), Johannesburg

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Photo: Ivan A. Pulido Tarquino

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