Oral Abstract Presentations 2

#5 High Levels of HIV Drug Resistance in Adult Patients with Unsuppressed Viral Load, Measured Through Routine Viral Load Programme Monitoring in South Africa, 2019

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High levels of HIV drug resistance in adult patients with unsuppressed viral load, measured through routine viral load programme monitoring in South Africa, 2019

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Monitoring of HIVDR in LMIC

- To maximize the long-term effectiveness of antiretroviral regimens and ensure sustainability of treatment programmes, it is essential to monitor and minimize the further spread of HIV drug resistance (HIVDR)
- In areas where limited/no routine HIVDR testing is available, nationally representative surveys are recommended to assess levels of acquired and pre-treatment HIVDR (ADR, PDR)
    - Uptake of these surveys in countries with high HIV burden has been slow and complex.
- Subsequent proposals to generate more timely surveillance data include
    - using programmatic viral load (VL) data to estimate the consequence of increasing HIVDR levels on first-line treatment outcomes
    - To use laboratory-based sampling of treatment failures

Monitoring of HIVDR in South Africa

- 7.9 million persons infected with HIV in 2017
- 4.4 million adults and children receiving ART through >4,000 public health care facilities
- VL testing @ 6, 12, 24 etc months
- National HIVDR estimates
  - ADR, 2014: >90% to NNRTI
  - PDR, 2017: >10% to NNRTI
- Explore the feasibility of using remnant VL specimens for updated ADR surveillance estimates

- South Africa has a strong network of 16 VL testing laboratories (National Health Laboratory Services)
- Contribute programmatically to VL testing with >80% coverage rates across 9 provinces
- 13% of 3.3million people had VL≥1,000cpm (2018)

Study Objective: to conduct nationally-representative surveillance of acquired HIVDR in adult patients with unsuppressed VL using leftover specimens from patients who had undergone routine VL monitoring

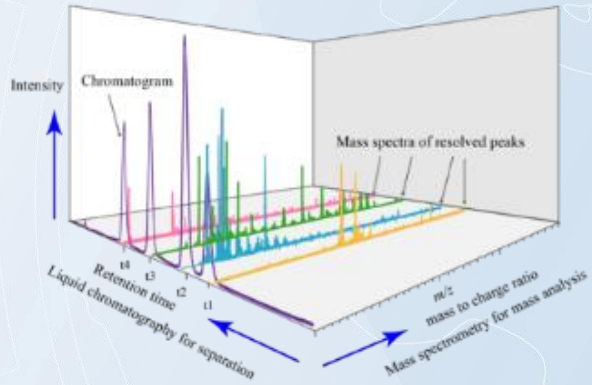
Sampling strategy and sample size

- A two-stage sampling approach was adopted.
- Stage 1
  - A systematic random sample of remnant VL test samples was selected over a five-day period at each of the 16 national VL laboratories
  - Basic demographic and VL test data was collected from the laboratory information system database and used to include specimens that were taken from adults and that had an unsuppressed VL.
- Stage 2:
  - A random sample of unsuppressed VL tests stratified by VL laboratory from those retained from stage 1 were selected.
- An effective sample size of 700 was estimated after adjusting for a 10% specimen rejection rate, 15% genotyping failure rate, and 6% specimen exclusion rate due to age. This would require a sample of 973 total specimens with VL ≥1,000cpm. To achieve this, a minimum sample total of 7,485 VL tests was required to be collected and stored during stage 1.

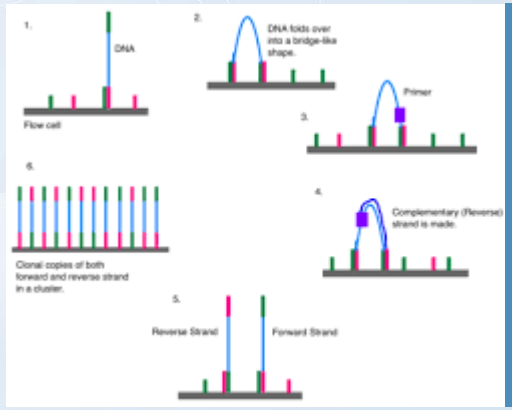
Proportion estimated	Error size	95% CI	Effective sample size	Genotyping failure (15%)	Unusable Sample (10%)	Underage Sample (6%)
0.5	0.037	1.96	700	824	915	973

Laboratory testing

- HIV Drug level testing
  - Liquid chromatography mass spectrometry
  - 3TC / FTC / NVP / EFV / LPV / ATV / DRV / DTG / RAL
  - Proxy for current treatment regimen



- HIVDR testing
  - In-house nested PCR coupled with NGS, results reported at Sanger-equivalent
  - FastQ sequences analysed using PASeq (paseq.org)

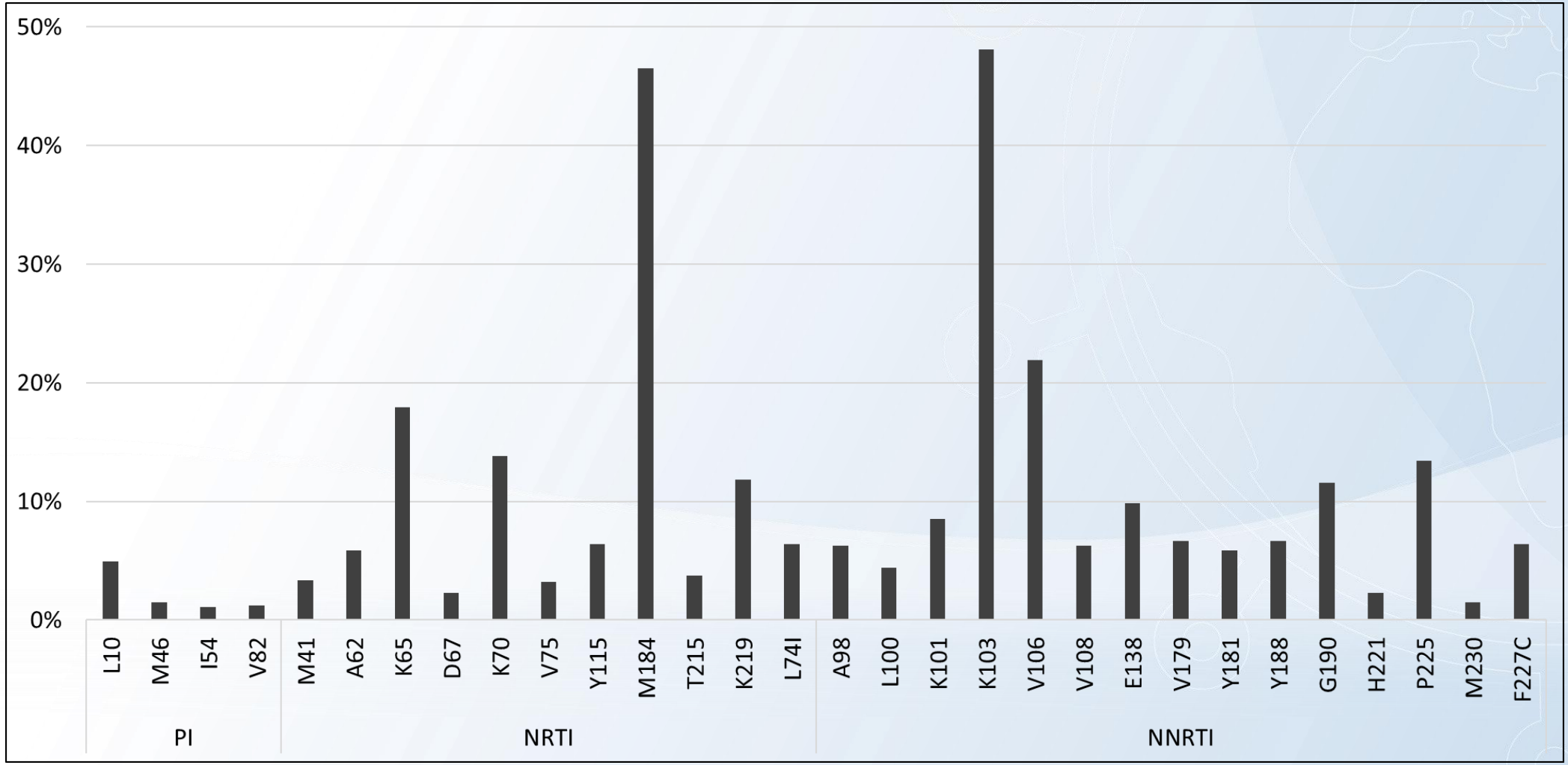


VL specimen collection and testing outcomes:

- 8,202 VL specimens collected between May - July 2019
- 1,052 had VL≥ 1,000 cpm and were from adult patients
- 779 randomly selected for further testing
- 56% of specimens tested positive for ARVs
- HIVDR testing successful in 753 (96.7%)

	Proportion	95% CI
All specimens		
HIVDR	72%	67 – 77%
NNRTI resistance	71%	65 – 76%
PI resistance	2%	1 – 4%
NRTI resistance	49%	45 – 53%
ART detected		
HIVDR detected	86%	80 – 90%
ART not detected		
HIVDR	56%	47 – 90%
NNRTI-based regimen		
HIVDR	87%	82 – 90%
PI-based regimen		
HIVDR	82%	62 – 93%
PI resistance	32%	18 – 52%

HIVDR mutations detected



Conclusion

- 72% of patients with unsuppressed VL in the public sector harbour resistance to ART
  - NNRTI resistance was most common, with 71% of specimens harbouring resistance to NNRTI, 49% of specimens harbouring NRTI resistance and 2% of specimen exhibiting PI resistance.
- Notably, 45% of patients on ART and presenting for routine VL testing had undetectable levels of ART. HIVDR was lower in patients that had undetectable levels of ART, presumably due to lack of drug selection pressure ($p<0.0000$).
- The survey adopted a novel approach to specimen collection and testing for HIVDR, and was successful in obtaining a nationally representative sample
- However, demographic and clinical data was not available through the laboratory information systems.

Acknowledgements

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