

Emerging Dolutegravir Resistance in Lesotho

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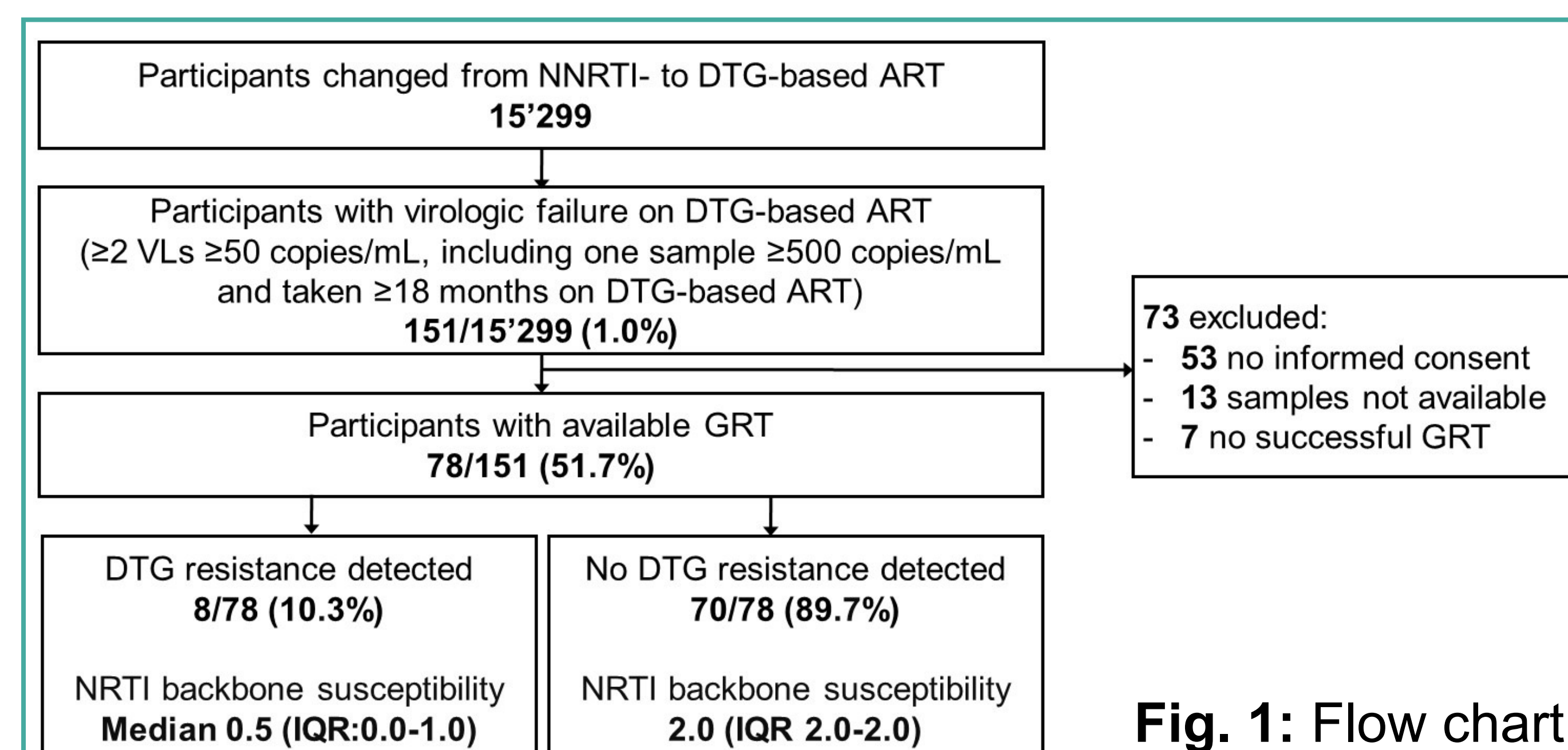
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BACKGROUND

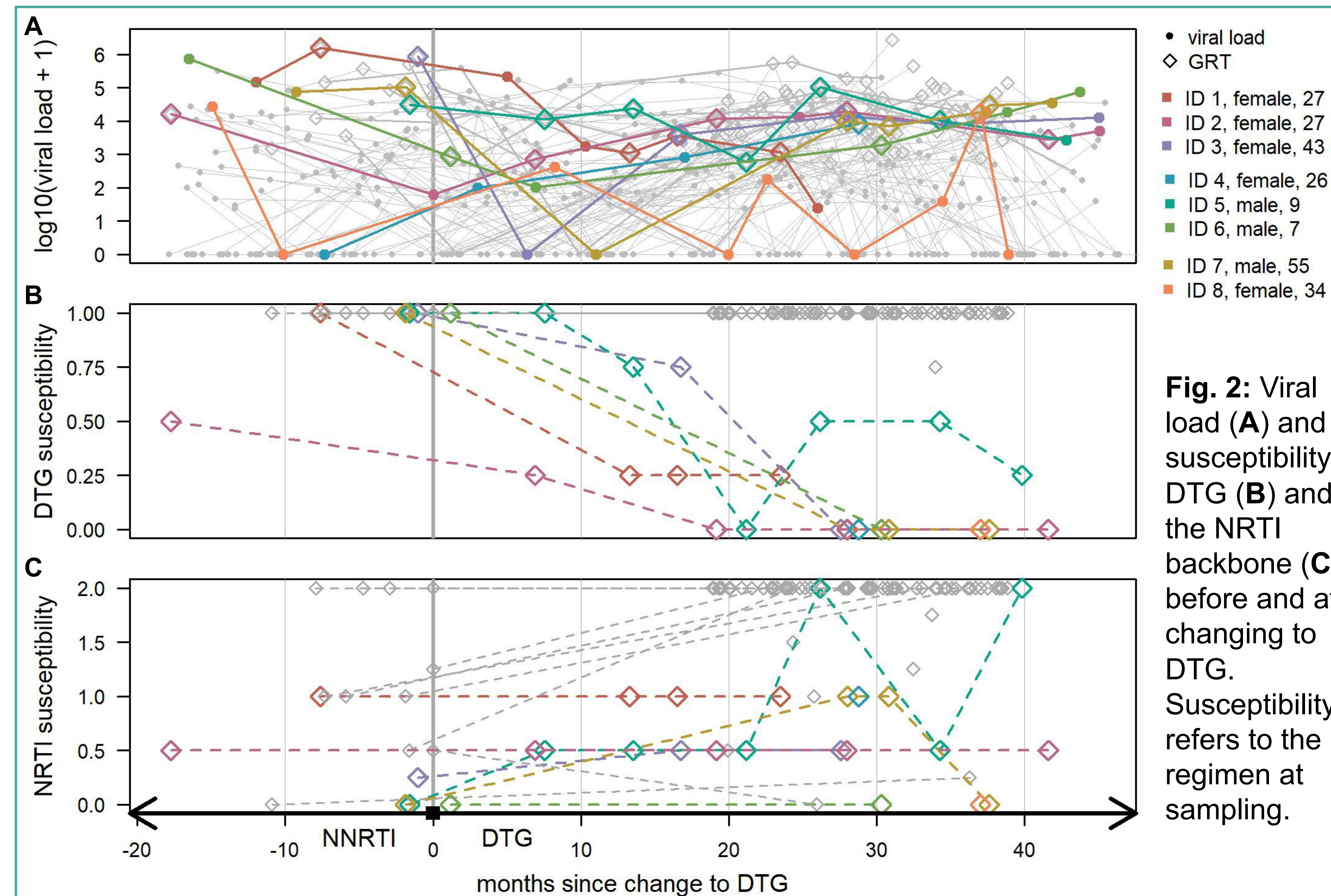
- The WHO has recommended dolutegravir- (DTG-) based antiretroviral therapy (ART) as first-line for all people with HIV
- This has triggered large-scale programmatic transitioning to DTG-based ART across Africa, often without recent viral load (VL) or genotypic resistance testing (GRT)
- Evidence gap:** Real-world data on emergent DTG resistance after transition to DTG in Africa are scarce

METHODS

- The Viral load Cohort North-East Lesotho (VICONEL) includes all individuals who get HIV viral load testing at one of the 24 clinics (3 hospitals, 21 health centers) in the districts Mokhotlong and Butha-Buthe in Lesotho
- Participant selection for GRT:
 - Changed from non-nucleoside transcriptase inhibitor- (NNRTI-) to DTG-based ART (**Fig. 1**)
 - ≥2 VLs ≥50 copies/mL while taking DTG, including one ≥500 copies/mL ≥18 months after starting DTG
- Sample selection for GRT (next-generation near-full-length sequencing):
 - Last sample with VL ≥500 copies/mL while taking DTG
 - If DTG resistance found, prior samples ≥500 copies/mL while taking DTG
 - Last sample (if VL ≥500 copies/mL) before starting DTG
- Susceptibility scores: high, intermediate, low, potential low, and no resistance to a drug (Stanford algorithm) assigned values 0.00, 0.25, 0.50, 0.75, and 1.00, respectively



10.3% of people with persistent or recurring HIV viraemia ≥18 months after changing to DTG-based ART had DTG resistance



RESULTS

- Among 15'299 VICONEL participants who changed from NNRTI-to DTG-based ART, 78 (0.5%) met criteria for and received a successful GRT (**Fig. 1**)
- 8/78 (10.3%) had DTG resistance (2 intermediate-, 6 high-level)
- Fig. 2** shows VL results and susceptibility scores to DTG (possible range: 0-1) and the NRTI backbone (possible range: 0-2) over time; **Fig. 3** shows resistance mutations
- Among the 8 individuals with DTG resistance:
 - the majority had a history of treatment failure with NRTI and NNRTI resistance
 - the last VL before changing was ≥50 copies/mL in six and ≥100,000 copies/mL in four individuals
 - all were in care at peripheral nurse-led health centres, as opposed to hospitals

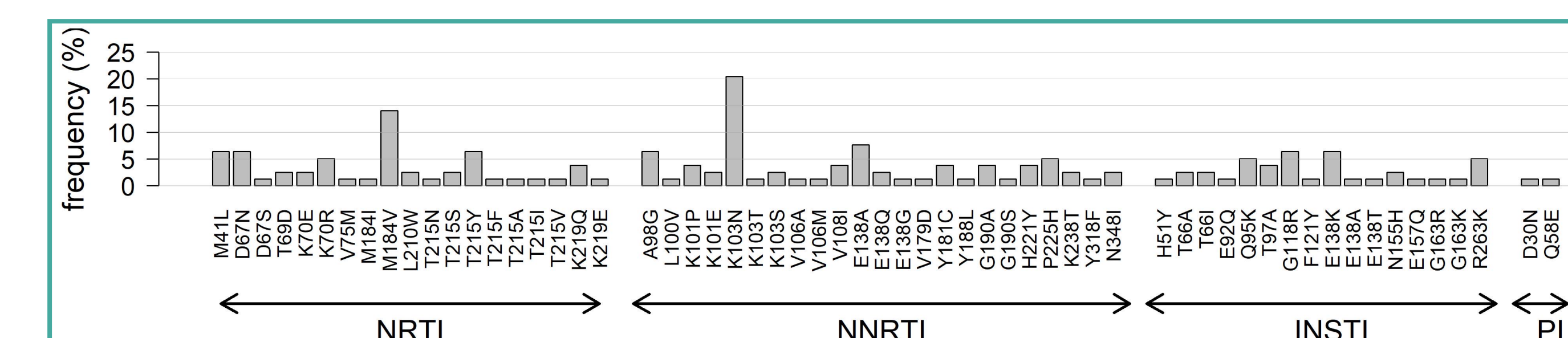


Fig. 3: Resistance-associated mutations (>5% variant frequency, multiple per position and participant possible)

CONCLUSIONS

- Implications:** DTG resistance is an emerging public health threat
- Measures needed to sustain the advances achieved through the roll-out of DTG in Africa:
 - Programmatic surveillance for emergent DTG resistance
 - Timely diagnosis of DTG resistance at individual level
 - Access to effective, well-tolerated alternative regimens

ADDITIONAL INFORMATION

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