Low Level Resistance Mutations Correlate With HIV Therapy Failure in Pregnant Women 00511

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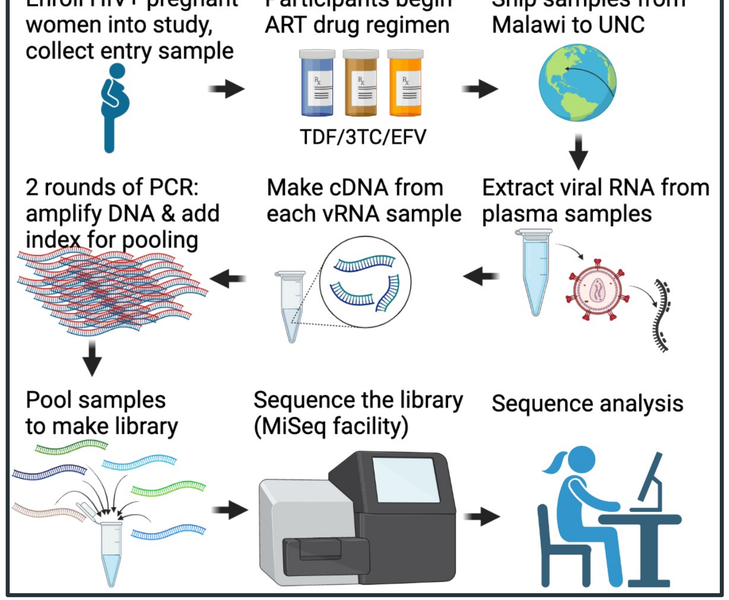
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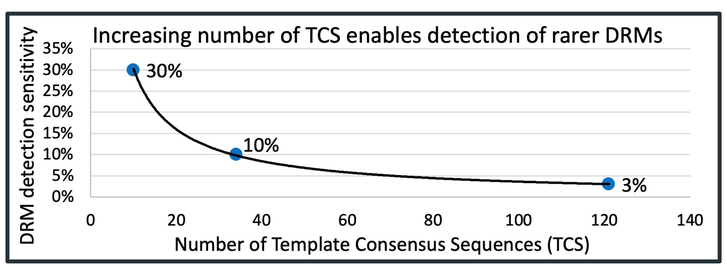
Background

Do low-frequency drug resistance mutations confer greater likelihood of treatment failure?

- HIV drug resistance mutations (DRMs) can be acquired at transmission, during untreated infection, or from poor adherence to antiretroviral therapy regimen (ART).
- High frequency DRMs increase chances of treatment failure (TF), but the association between **low frequency DRMs** and TF is unknown.
- A person who has taken ART before is ART-experienced, while someone who has no history of ART is ART-naïve

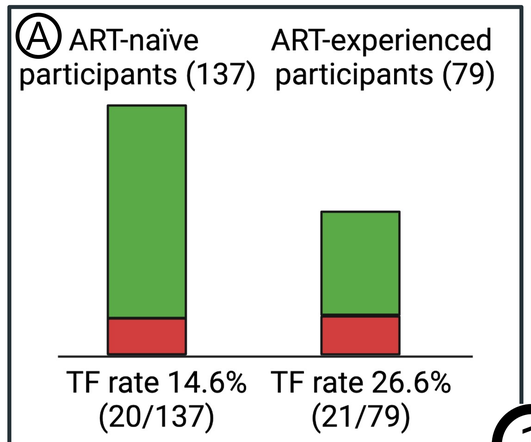
Methods

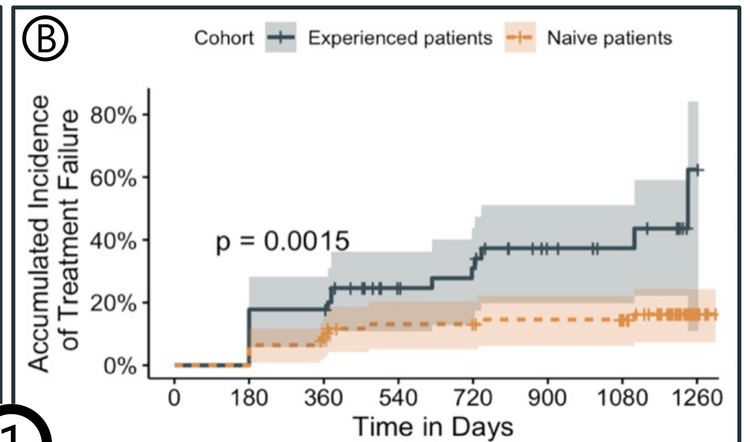




Previous ART experience, presence of DRMs, and *poor adherence* correlate with higher treatment failure rates.

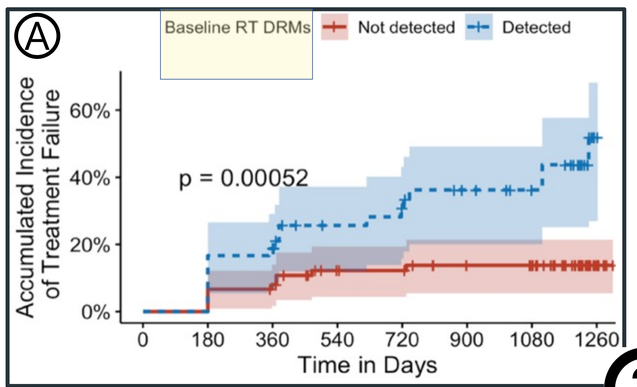
Results

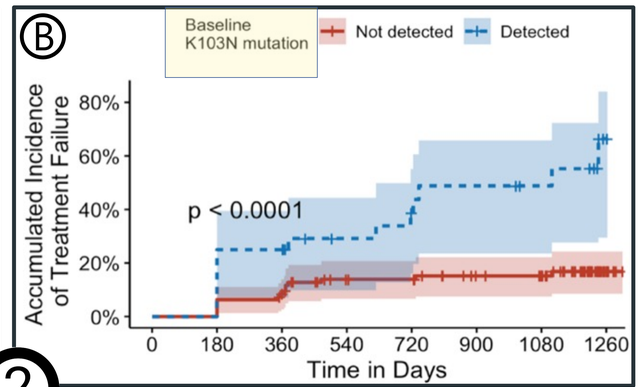




1

Experienced vs. Naïve participants: ART-naïve (N=137), ART-experienced participants (N=79) (Fig 1A) Over time, experienced participants were significantly more likely to have TF than naïve participants (Fig 1A) ($p < 0.01$), even when incidence of TF was stratified by previous ART experience ($p < 0.01$; Fig. 1B)





2

Presence of Reverse Transcriptase DRMs overall: Significantly associated with TF risk at 10% ($p < 0.01$) and 3% ($p = .002$) sensitivity (Fig. 2A)

K103N Mutation: Associated with TF at both sensitivity levels (10% shown in Fig. 2B)

Still an independent risk factor after stratification for previous ART, HR of 2.6 at 10% and 4.6 at 3%.

Conclusions

Highest treatment failure (TF) risk factors:

- **DRMs at entry, K103N**
- **Previous ART experience**
- **Poor adherence**

High *and* low frequency DRMs present in the population present significant TF risk with the TDF/3TC/EFV regimen; Malawi's recent switch to an integrase-based regimen should improve outcomes. ART-experienced PLWH may need more frequent check-ins or a novel regimen. Measures should also be taken to boost adherence for those on ART.

Acknowledgements

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Bwaila Family Health Unit in Lilongwe and UNC Project Malawi for sample collection ('S4' project, Clinical Trial NCT02249962) NIH