HIV Drug Resistance among Adolescents and Young Adults Failing HIV Therapy in Zimbabwe

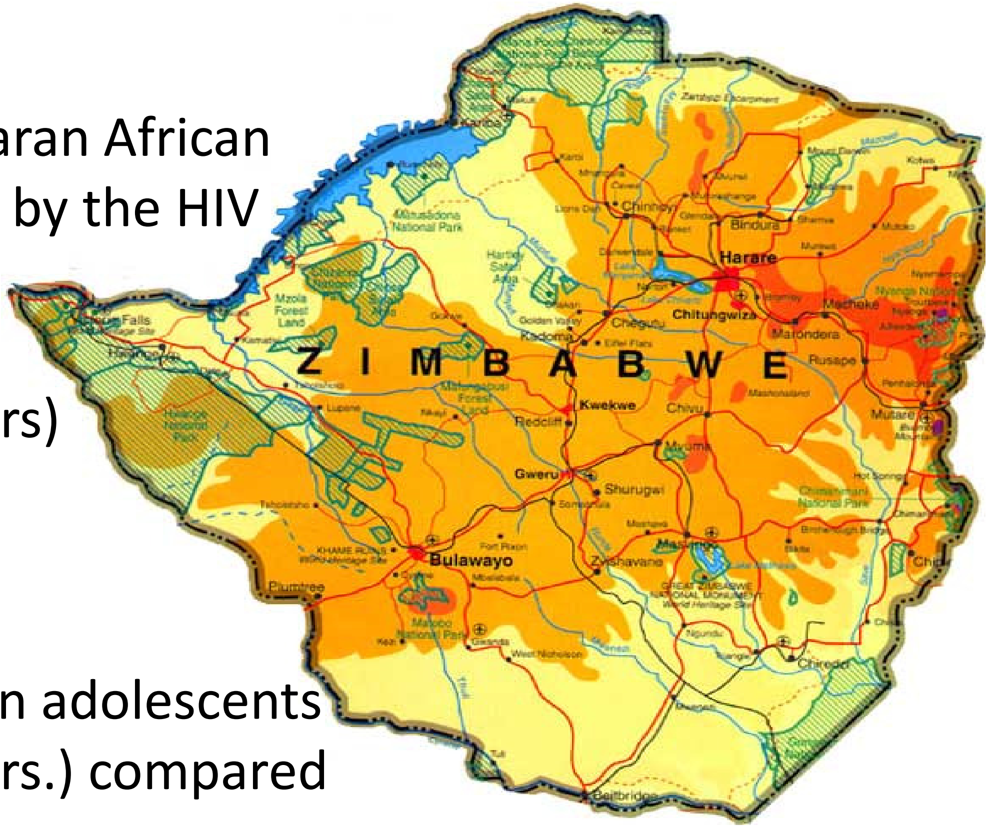
V Kouamou[1], J Manasa[1], D Katzenstein[1], A McGregor[1], CE Ndhlovu[1] & AT Makadzange[1].

[1] University of Zimbabwe

XXVII INTERNATIONAL WORKSHOP ON HIV DRUG RESISTANCE AND TREATMENT STRATEGIES

22 - 23 October 2018 Johannesburg, South Africa

Introduction



- Zimbabwe is one of the sub-Saharan African countries most severely affected by the HIV epidemic.
- HIV prevalence of 14.7% (15-64yrs)
- Overall ART coverage of 86.8%.
- Virological suppression is lower in adolescents and young adults 40.2% (15-24 yrs.) compared to older adults 71.1% (55 years or older)(Zimphia 2016).

Objectives

- To determine the patterns of DRMs among adolescents and young adults at a HIV tertiary clinic in Harare, Zimbabwe.

- To calculate genotypic susceptibility scores to infer adherence on current regimens and predict the activity of subsequent regimens.

XXVII INTERNATIONAL WORKSHOP ON HIV DRUG RESISTANCE AND TREATMENT STRATEGIES

22 - 23 October 2018 Johannesburg, South Africa

Results

- Of the 185 participants with confirmed VF , 160 (86%) were successfully genotyped.

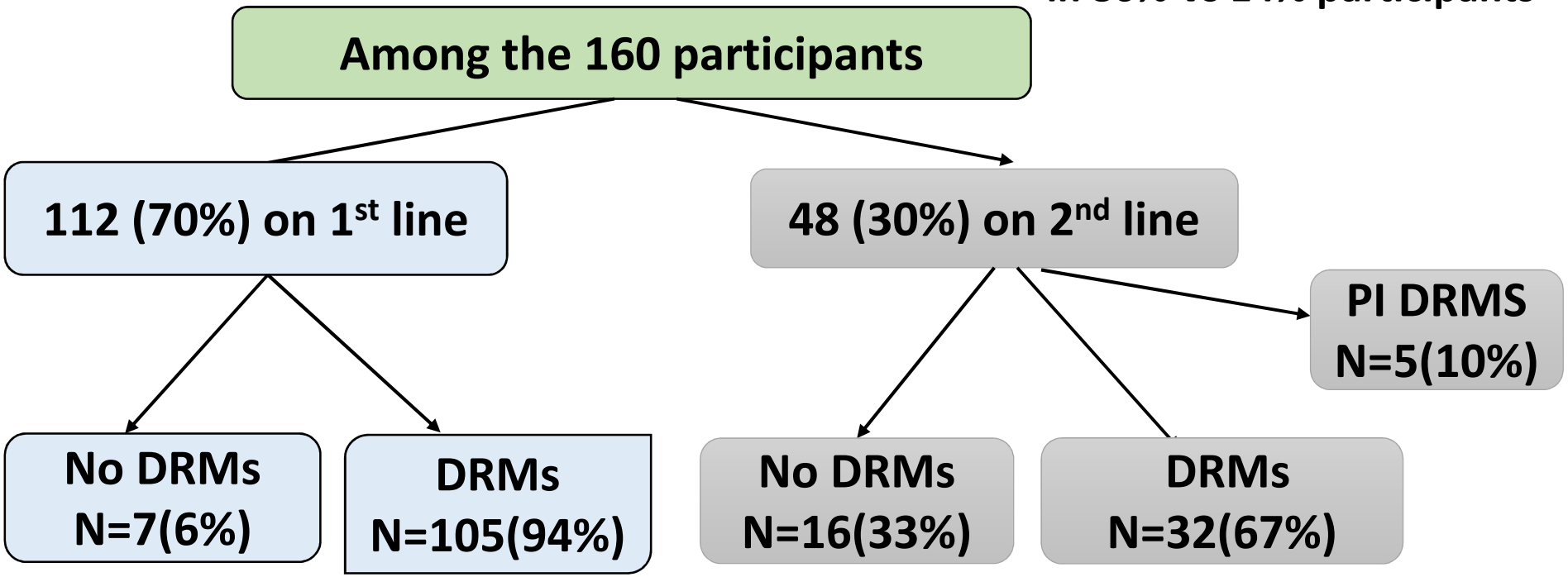
- 112/160(70%) were on 1st line ART(2NRTIs+1NNRTI)

- 48(30%) on 2nd line ART (2NRTIs+1 boosted PI)

Age at study enrolment years[median(IQR)]	18(15-19)
Gender, n (%) **Male**	83(52%)
Age at ART initiation years[median{IQR}]	11(9-14)
Plasma HIV-1RNA level, median log10 copies/ml(IQR)	4.51(4.05-4.93)
CD4 at enrolment, median cells/mm^3 (IQR)	197(47-359)
Duration on ART prior to enrolment, mean years ± SD	6.3 (± 0.25)
Duration on PI based ART prior to enrolment for those on 2nd line ART, mean years ±SD	3.6 (±1.19)

DRM results

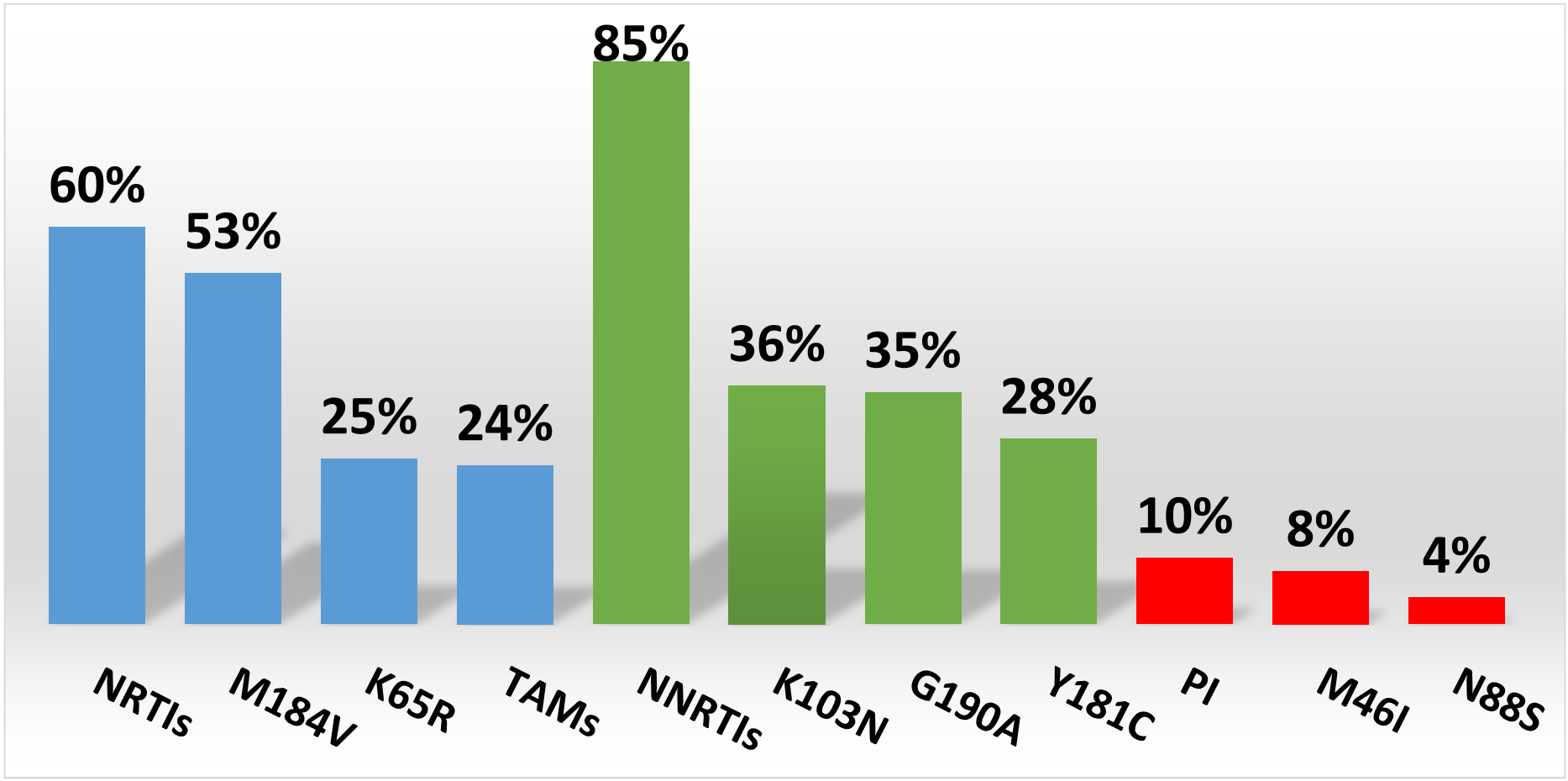
Overall, DRM was detected in 86% Vs 14% participants



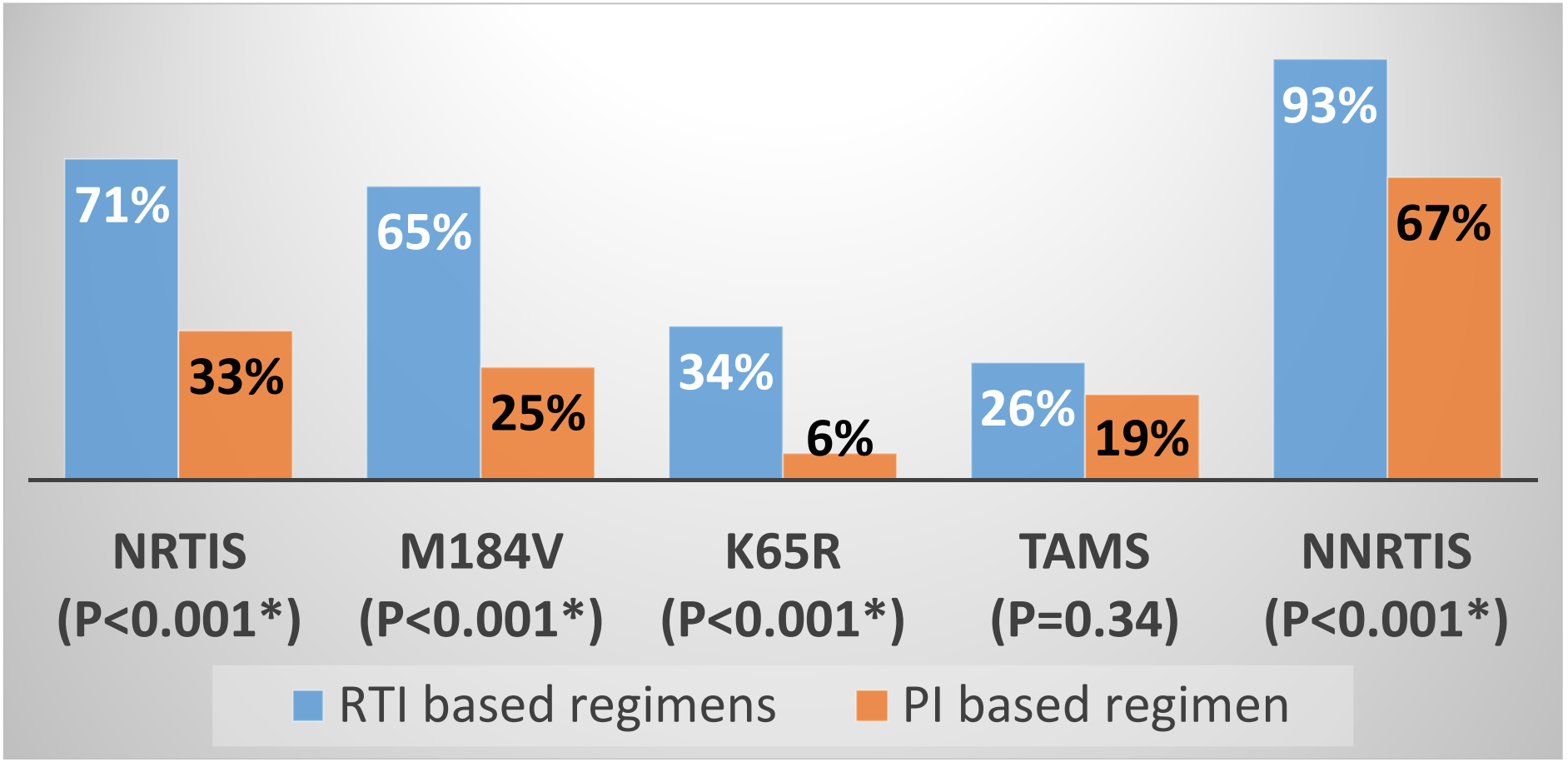
- (86)77% on TDF Vs 23% on AZT
- 74% on EFV Vs 26% on NVP

- 83% on ATV/R Vs 17% on LPV/R
- (28)58% on TDF Vs 15% on AZT
- 27% on ABC

Frequency of DRMs among the 160 participants



Comparison of the frequency of DRMs between 1st and 2nd line recipients



Multiple drug resistance (MDR) among the 5 participants with PI DRMs on 2nd line regimen

PI MUTATIONS	NRTI MUTATIONS	NNRTI MUTATIONS*
M46I, I54V, N88S	M184V, T215Y	**Y181C, G190A, H222Y**
M46I, I84IV, N88NS	M184V, K70R, T215F, K219Q, D67N, T69D	**V108I, Y181C**
V82M	M184V, K70R, D67G, T69D,K219Q	**A98G, K101E,Y181C,G190A**
M46I	M184V, K65R, A62V	**A98G, Y181C,G190A**
M46I, L90M	M184V, M41L,K70N,L74I,V75T, L210W,T215Y	**K101E, E138A,G190A**

tGSS to infer adherence to the 1st line failing regimens

- **Current regimens:**
  - Of the 105/112 (94%) failing on 1st line with DRMs,
  - All 105 had tGSS<2 on their failing regimens.
  - Only 7 participants (6%) failing 1st line without evidence of DRMs, (tGSS=3)-suggesting an adherence problem.

- **Predicted 2nd line regimens:**
  - 70/105 (67%) were susceptible , tGSS of >=2.
  - 45(33%) had tGSS<2- (had M184V and TAMS/K65R).

tGSS to infer adherence to 2nd line and optimize the next regimens

- **Current regimens:**
  - All 5/48(10%)failing with PI DRMs had a tGSS of <2
  - Of the 43(90%) failing with no PI DRMs, 39/43(91%) had tGSS>=2

- **Predicted 3rd line regimens**:
  - All 5 (100%) was susceptible, tGSS of >=2.

Discussion

- Among participants failing 1st line failure a high prevalence of DRMs (86%)
  - DRM among adolescents and young adults on 1st line (70-90%) (Sigaloff et al, 2011).

- The most common mutation was M184V(53%) which is usually the first mutation to emerge in combination therapy,
  - K65R Significant in TDF(34%) vs AZT(3%) regimens (p=0.0003*)

- The most common NNRTI mutations found among 1st line participants were K103N (51%) and G190A(50%).
  - Mutations reflecting first line NNRTI Drugs (EFV and NVP.)

Discussion

- Among the 48 participants on 2nd line regimen, only 10% (5/48) developed PI DRMs – evidence of reduced adherence
- Frequency of PI DRMs similar to Wallis et al (2011) who reported 7% major mutations in patients.
- the rate of NRTI mutations; M184V, K65R, TAMs were significantly lower in second line regimen failure compared to first line failure. ($p<0.001$*).
- **The increasing prevalence of NNRTI associated mutations among 1st line experienced patients as transmitted and acquired resistance, respectively, has led to consideration of integrase inhibitors InSTIs for first line treatment**

Conclusion

- A significantly higher proportion of adolescents failing RTI based 1st line regimens had at least one clinically significant HIVDRM unlike those failing the PI based 2nd line regimens with lower frequency of clinically significant HIVDRM; suggesting inadequate adherence.

- **In addition to enhanced adherence counseling, more adolescent friendly drug regimens are critical for optimal HIV care.**

- Consider InSTI for 2nd line ?

- tGSS can be used in LMICs, as an approach to differentiated care to optimize regimens to achieve virologic suppression

Acknowledgements

- All study participants, clinicians and staff
- All my supervisors
- USAID grant number (AID-OAA-A-14-00046)
- NIH R21 grant (1R21AI124402-01).
- All my supervisors for their mentorships.

JOHN SNOW, INC.
Promoting and Improving Health

KNOWLEDGE · DILIGENCE · INTEGRITY

NIH National Institutes of Health
Turning Discovery Into Health

USAID


The End
You can all smile
now..
Is it?