HIV drug resistance in adults failing protease inhibitor (PI)-based antiretroviral therapy (ART) in KwaZulu-Natal

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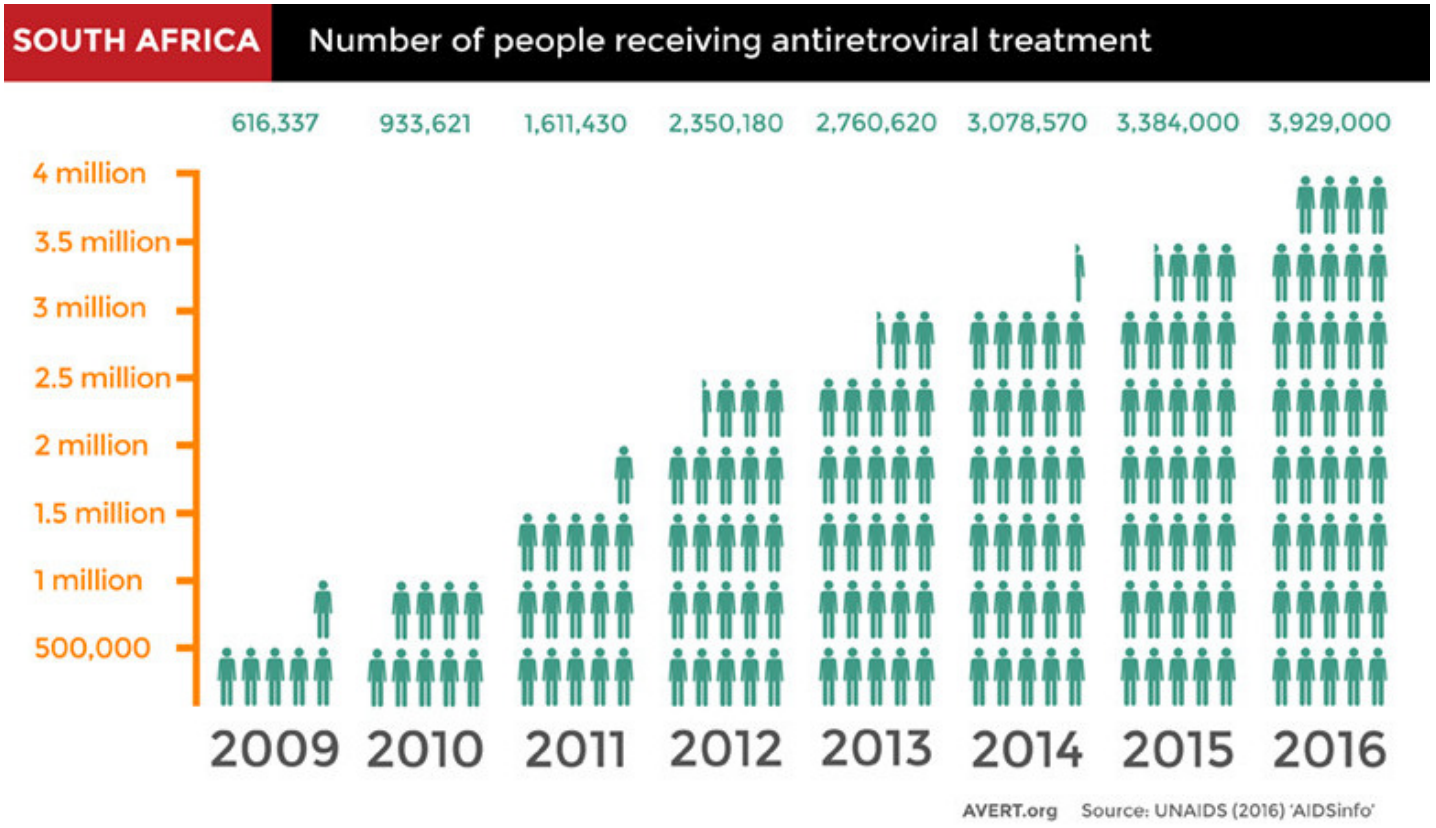
Background

South Africa has the largest ART program with ~3.9 million people receiving ART, by 2016.



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Background

- Changes in second line-ART guidelines

- Before 2010: zidovudine (AZT), didanosine (ddI) and ritonavir-boosted lopinavir (LPV/r)

- After 2010: AZT after first-line tenofovir (TDF) **or** TDF after first-line AZT, with lamivudine (3TC) and LPV/r

- Proportion of patients requiring PI-based 2nd line ART is increasing, with approximately 144 000 receiving 2nd- line ART, by 2015 (UNAIDS, MDG Report 2015)

- However, there is limited knowledge of ART resistance profiles in patients who are not responding to PI-based ART, in KwaZulu-Natal (KZN) in South Africa

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Objective

To determine the drug resistance profiles in adult patients who are not responding to second-line PI-based ART in KZN.

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Methods

- Retrospective analysis of ART resistance data retrieved from request forms & Trakcare (Nov 2017 - Apr 2018) from the NHLS, Department of Virology, IALCH, in Durban.

- Adults failing 2nd-line PI-based regimens

- Data analyzed for PI, NRTI & NNRTI resistance

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Patient Characteristics

- Patient requests obtained: N = 166
- 87 males and 79 females
- Median age in years = 38.4
- Median HIV VL $\log_{10}$ c/ml = 5.72

ART Regimen	Number of Patients (%)
AZT+3TC+LPV/r	92 (55.4)
ABC+3TC+LPV/r	22 (13.2)
AZT+3TC+ATV/r	17 (10.2)
TDF+FTC+LPV/r	11 (6.6)
AZT+TDF+3TC+LPV/r	8 (4.8)
TDF+FTC+ATV/r	5 (3.0)
Other	11 (6.6%)
TOTAL	166 (100%)

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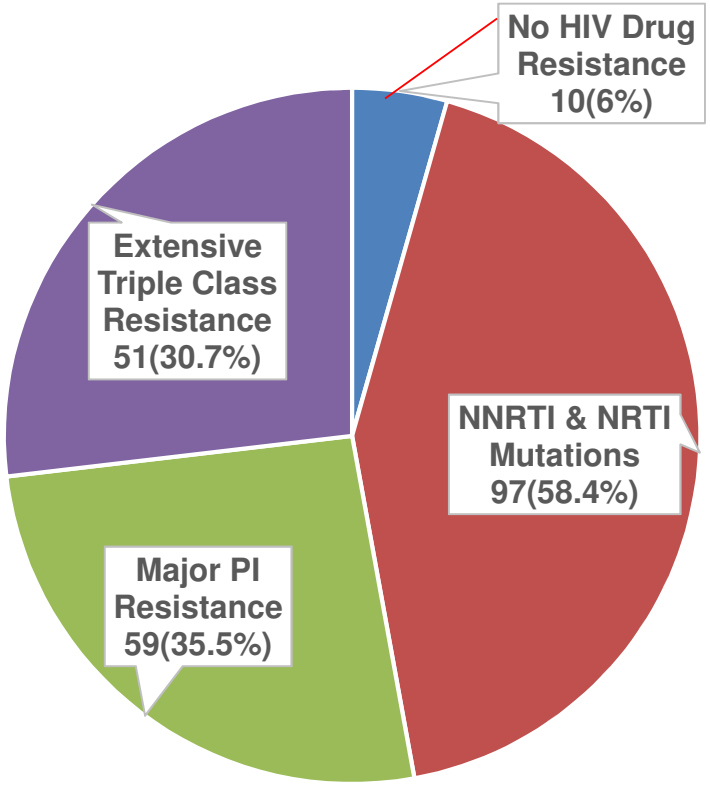
Results

Distribution of Drug Resistance Mutations



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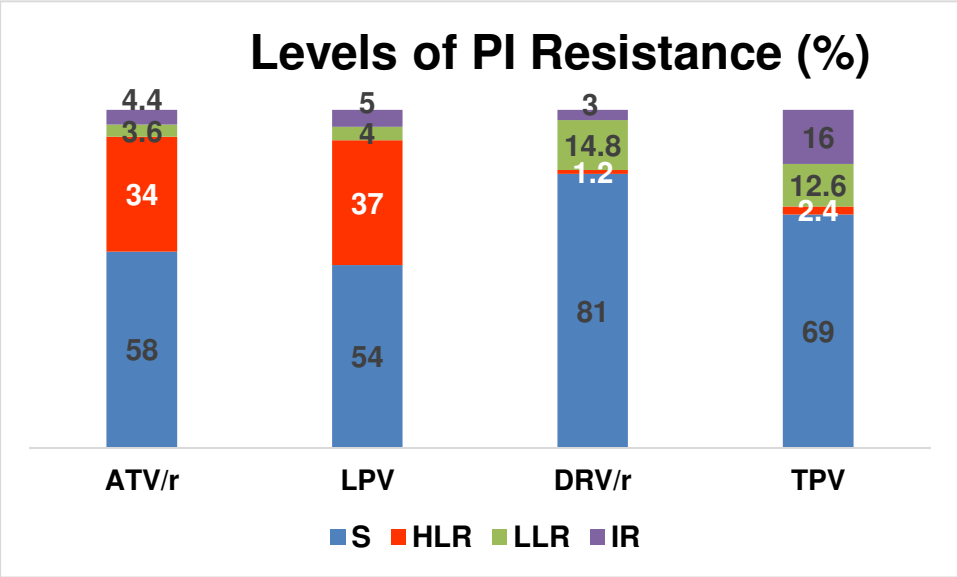
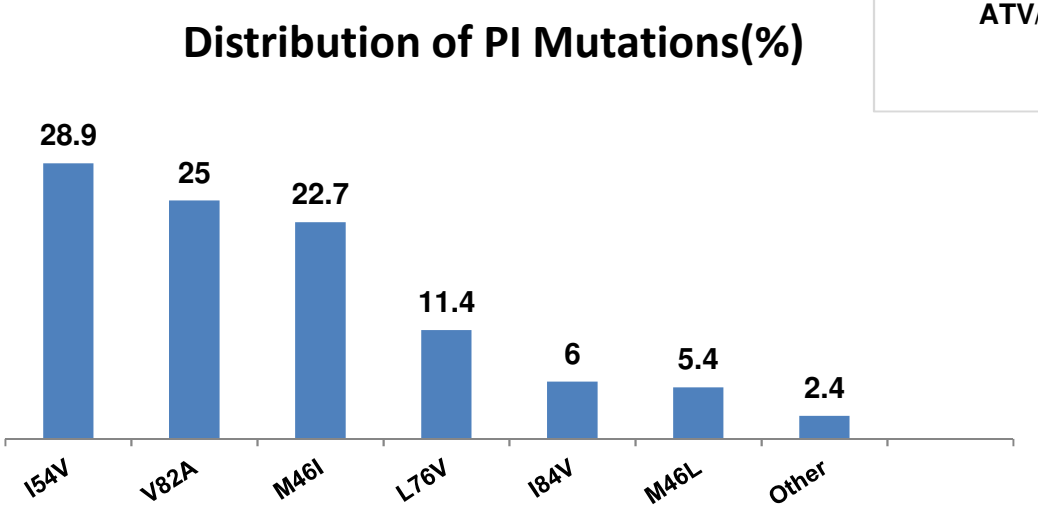
Results

- 35.5% had Major PI resistance mutations
- 30% PI resistance with ≥3 PI major mutations





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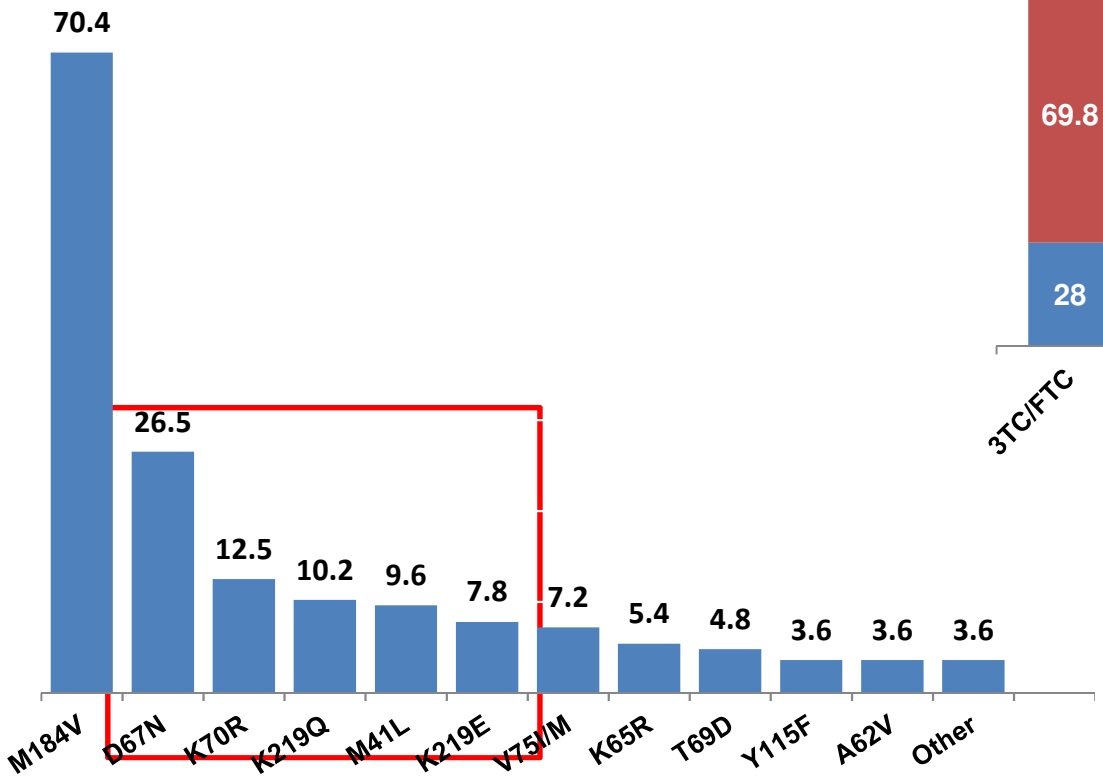
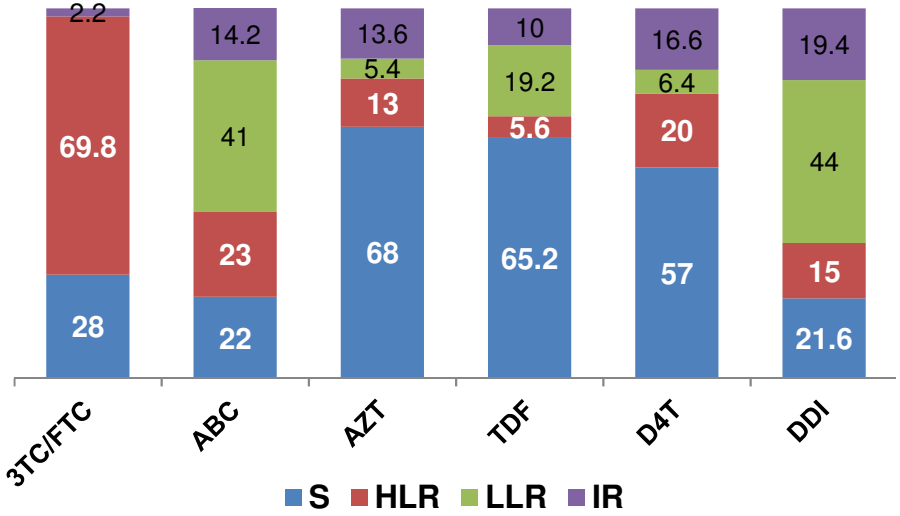
Results

Distribution of NRTI Mutations(%)



Levels of NRTI Resistance (%)



- Most frequent NRTI mutations - Thymidine Analogue Mutations (TAMs).
- 68% and 65% remained susceptible to AZT and TDF respectively

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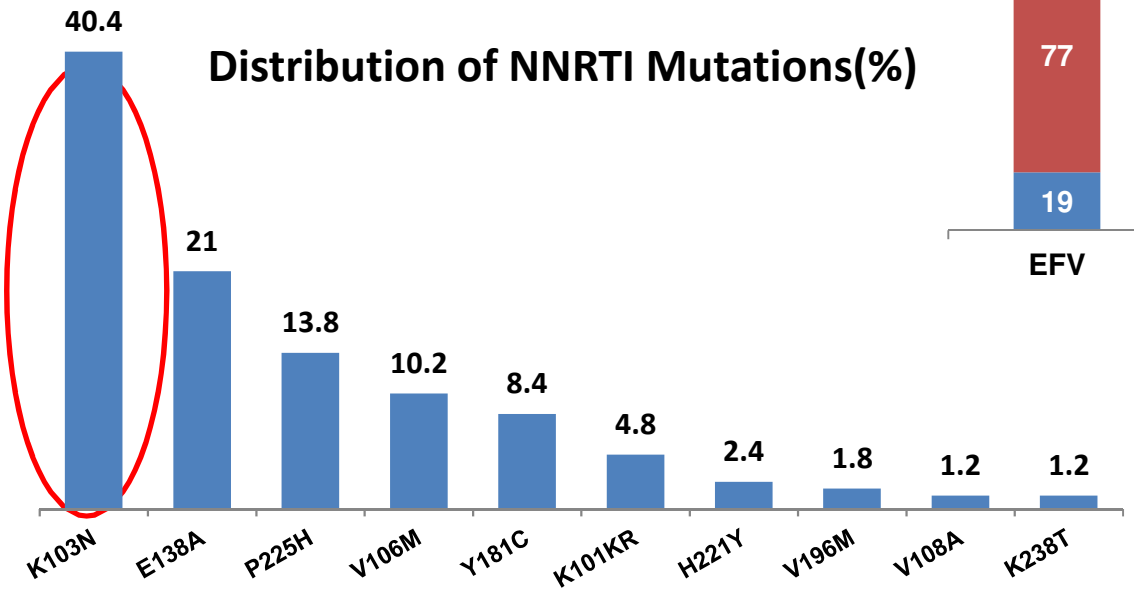
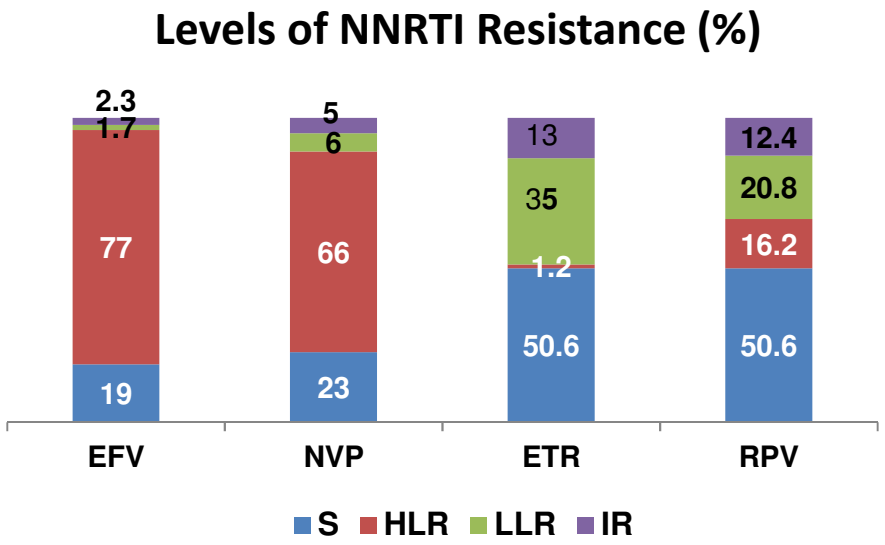
Results





- >50% - high-level resistance to 1st-generation NNRTIs
- ETR may be promising, despite a higher frequency of intermediate and low level resistance

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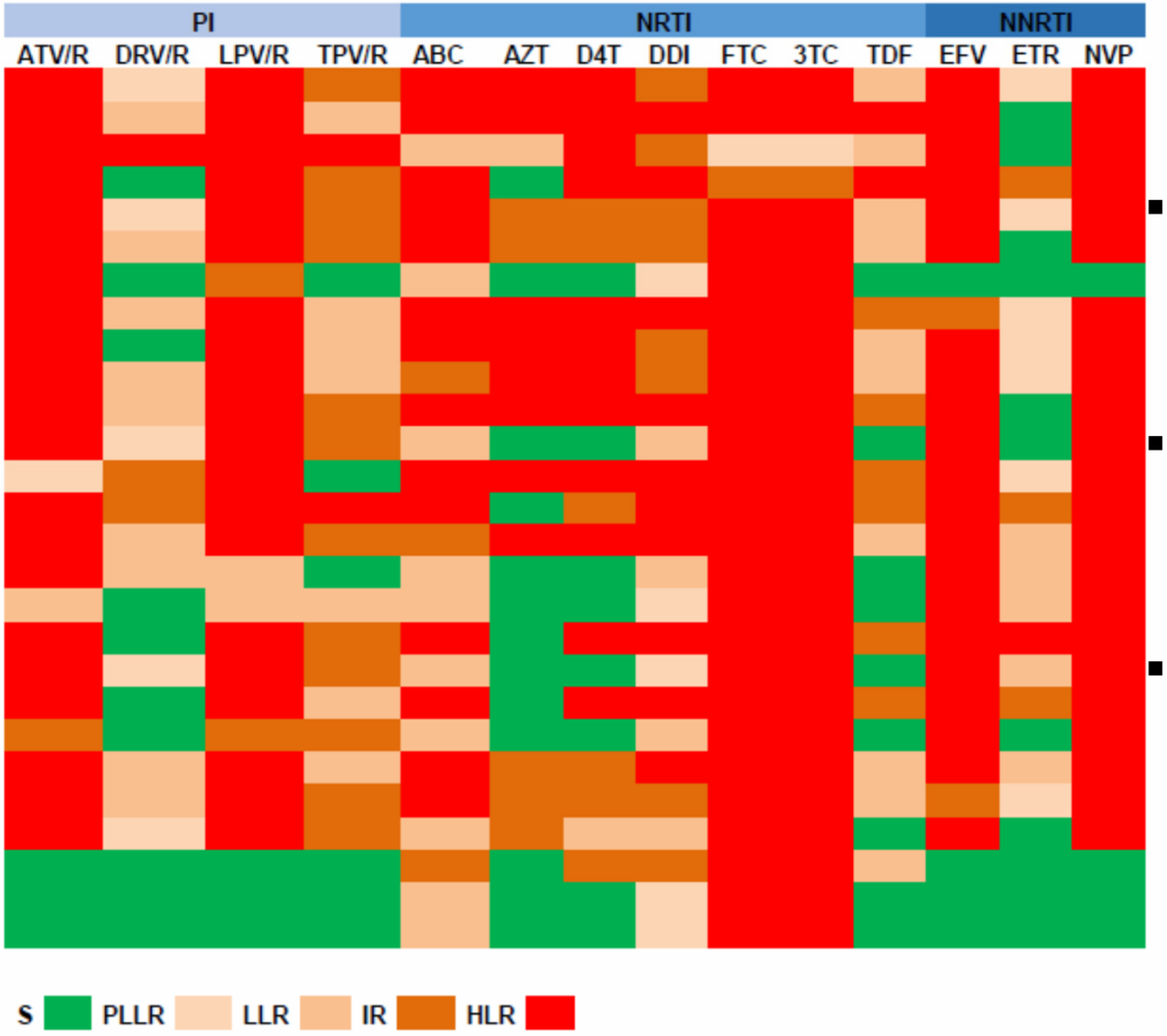
Results



- Triple-class resistance (n=27 of 51 patients)
- 51(30.7%) - triple class resistance
- DRV/r and ETR remain good options as 3rd-line drugs in most patients

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Conclusion

- Increasing frequency of PI resistance: 35.5% (current) vs 6.7% (2009-2010) [Wallis et.al.,2010]
- Increasing triple-class resistance in patients with 2nd-line failure
- Prevalence of complete susceptible profiles is decreasing: 6% (current) vs 38.7% (2009- 2010) [Wallis et.al.,2010]
- Relatively low levels DRV, ETR, AZT & TDF resistance observed in those with ART failure may warrant use of these ARV's in third line regimens
- Continued surveillance of drug resistance levels in our settings is needed to guide management of patients on ART.

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