Socio-Demographic Factors associated with Success of Antiretroviral Treatment among HIV Patients in Tanzania

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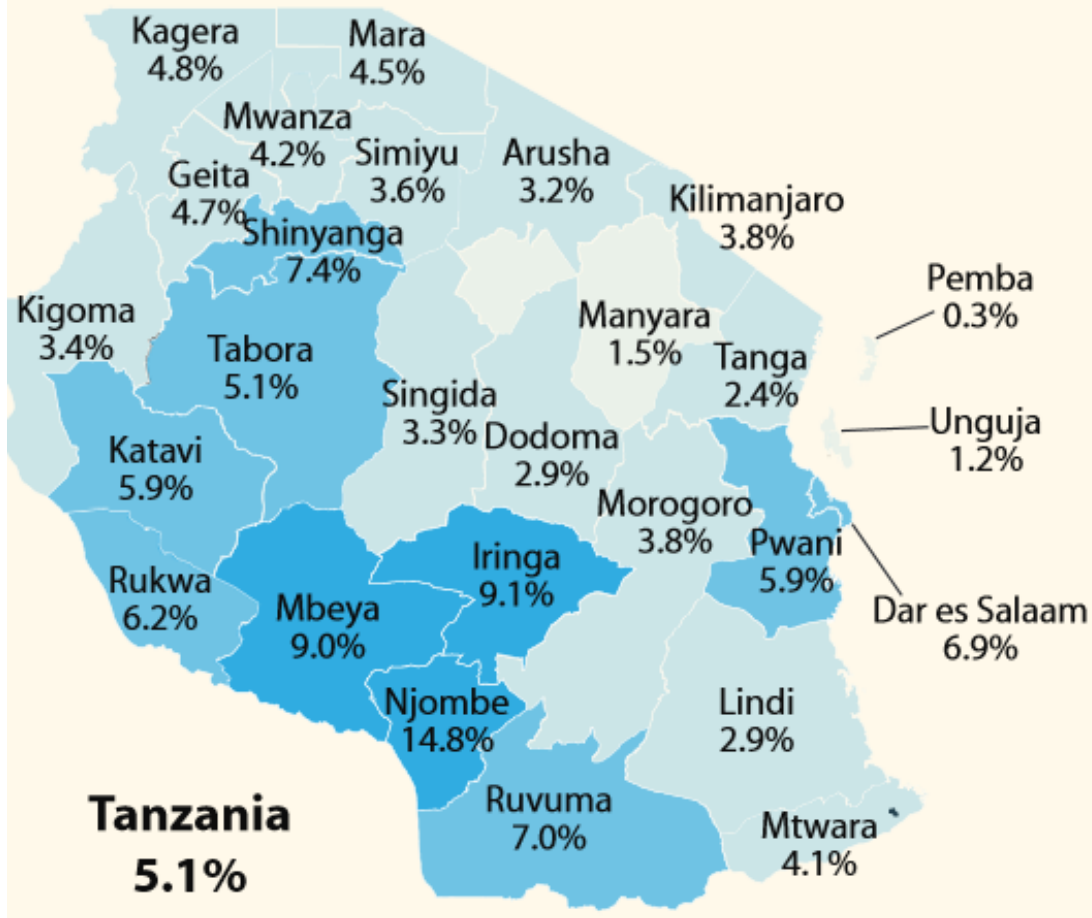**22nd October 2014**

Outline

- General Introduction

- Methods

- Research Studies

  - Gender differences in HIV disease progression and treatment outcomes among HIV patients

  - Factors influencing adherence to ART by HIV patients in an urban and rural setting

  - Clinical and virological response to ARV drugs among HIV patients on first line treatment

  - Prevalence of genotypic resistance to ARV drugs in treatment naïve youths

- Conclusion

HIV in Tanzania

HIV Prevalence by Region
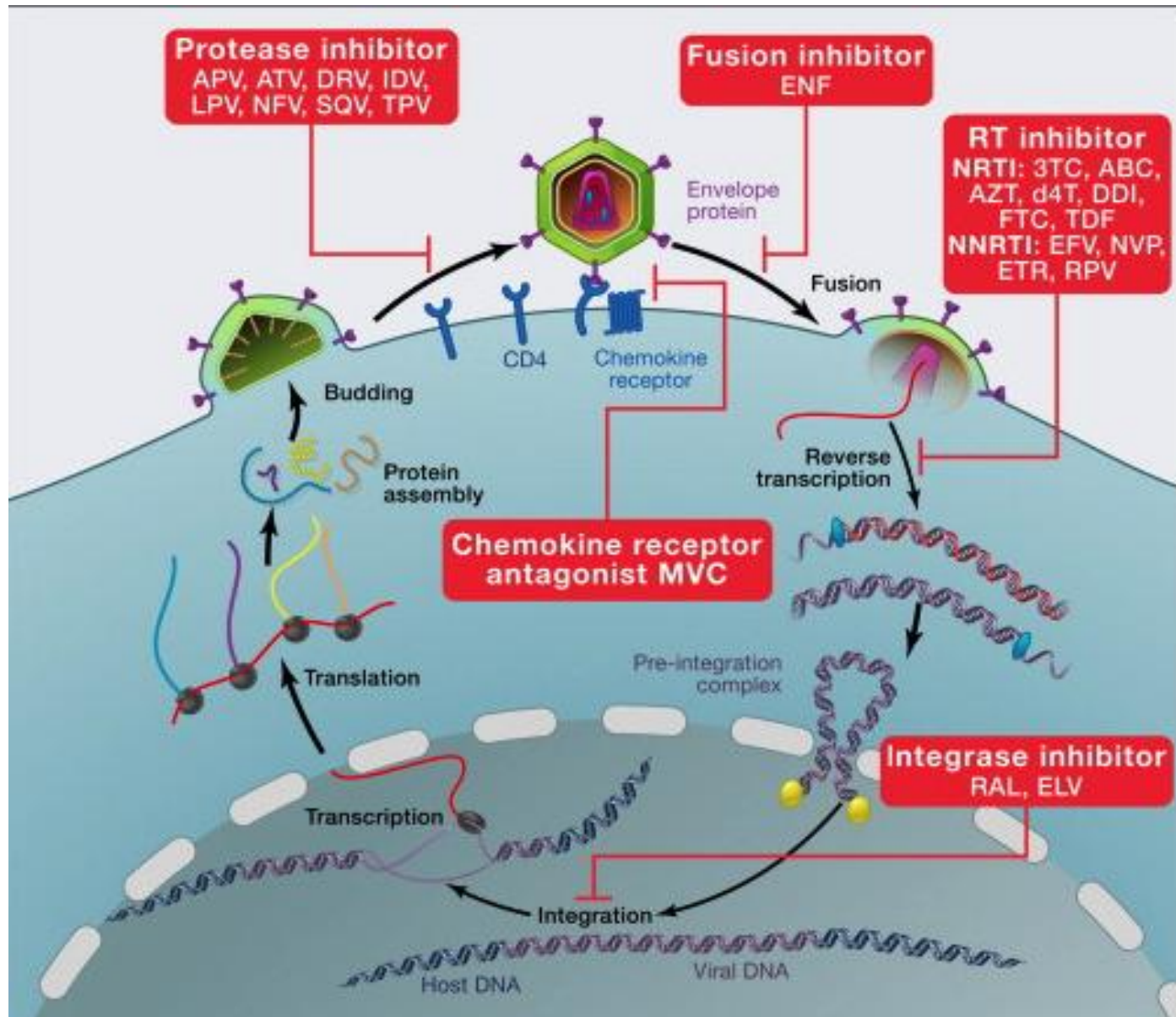*Percent of women and men age 15-49 who are HIV-positive*

Kagera 4.8%
Mara 4.5%
Mwanza 4.2%
Simiyu 3.6%
Arusha 3.2%
Geita 4.7%
Kilimanjaro 3.8%
Shinyanga 7.4%
Pemba 0.3%
Kigoma 3.4%
Manyara 1.5%
Tabora 5.1%
Tanga 2.4%
Singida 3.3%
Dodoma 2.9%
Unguja 1.2%
Katavi 5.9%
Morogoro 3.8%
Iringa 9.1%
Pwani 5.9%
Rukwa 6.2%
Mbeya 9.0%
Dar es Salaam 6.9%
Njombe 14.8%
Lindi 2.9%
Tanzania 5.1%
Ruvuma 7.0%
Mtwara 4.1%

- The estimated HIV prevalence is 5%
- ART is currently being scaled up
- CTC are being established to support HIV patients

NACP, Tanzania

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HIV Disease Progression

Modified From: Fauci, A.S., et al, *Ann. Intern. Med.*, 124:654, 1996
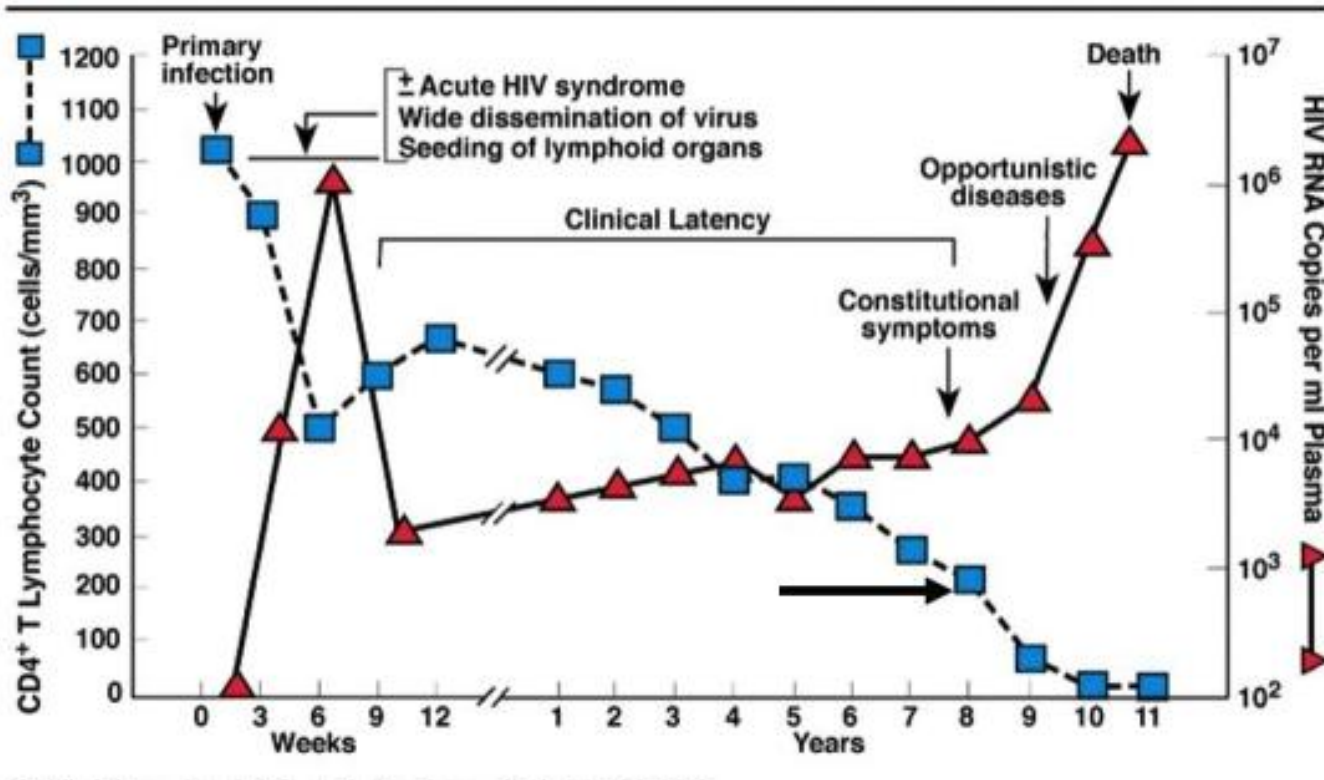
- Immunological markers
- Virological markers
- Clinical markers

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Treatment of HIV

Goldberg, virology 2012

ARV Drugs in Tanzania

- ARV for first line treatment in Tanzania:

  - 2NRTI+1NNRTI

  - 3NRTIs

- ARV for the second line treatment in Tanzania:

  - PI (Boosted LPV/r or ATV/r) + 2NRTI

  - PI (Boosted LPV/r or ATV/r) + 1NRTI

Objectives

- The purpose of our study was to:

  - Collect epidemiological data with regard to ART and treatment response in Tanzania

  - Provide evidence that can be used to set up affordable measures to improve treatment response in Tanzania

  - Investigate socio-demographic factors with a special focus on gender and adherence

  - Assess the impact of current treatment practices on drug resistance development and transmission of drug resistance

Methods

- Prospective cohort and cross-sectional study designs

- Structured questionnaire and patients' record review

    - Socio-demographic

    - Clinical and treatment information

- We collected blood for CD4 testing, viral load testing and virus genetic analysis

- We performed epidemiological analyses using

    - Standard phylogenetic tests

    - Standard statistical tests

Gender Differences in HIV Disease Progression and Treatment Outcomes Among HIV Patients One Year After Starting ART in Dar es Salaam, Tanzania

To study the difference in clinical, immunological and virological HIV disease progression between men and women on ART

Mosha et al. BMC Public Health,2013

Differences on Baseline Characteristics Between Women and Men

- Women

  - Larger proportion tested for HIV before developing AIDS (P=0.04)

  - Started ARVs with higher mean BMI (P<0.01)

  - Started ARVs with lower Viral loads (P=0.05)

- Men

  - More educated (P<0.01)

  - Higher monthly income (P<0.01)

  - More knowledgeable on ARVs (P<0.01)

  - Started ARVs at Stage IV (P=0.04)

Outcomes After One Year of ART

- Death 35 (15%)

  - Women 21 (13%): Men 14 (20%); P=0.2

- Loss to follow up 63 (27%)

  - Women 42 (26%): Men 21 (30%); P=0.5

- More women than men

  - Had undetectable Viral load (P<0.01)

  - Higher mean BMI (P=0.02)

- More men than women

  - Mean CD4 increase (P=0.05)

Kaplan-Meier Survival Curves on Time to Death, for 234 patients

Kaplan-Meier survival estimates
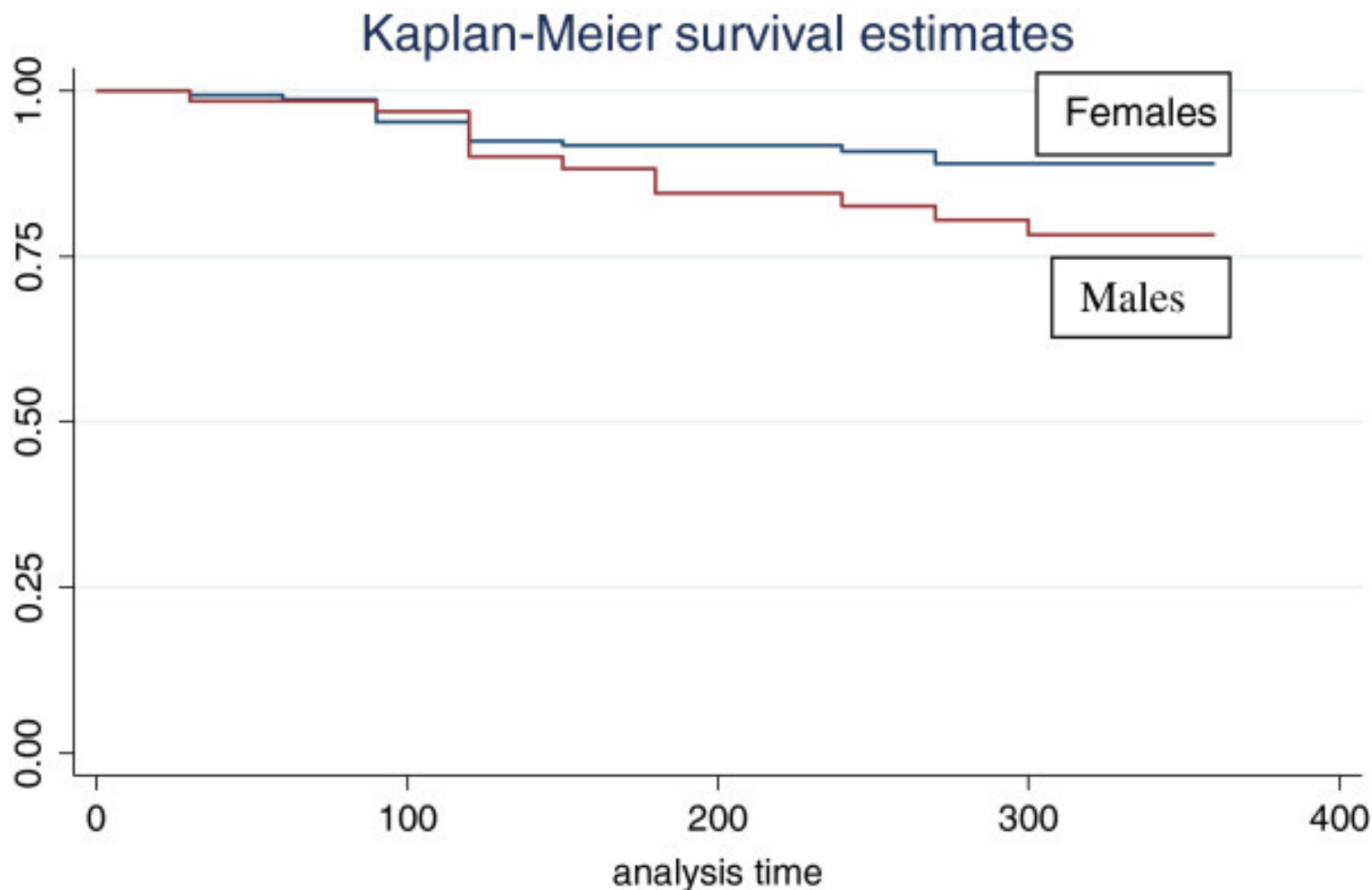
Relative hazard for death for males 1.94; P=0.08

Main Findings

- Males were reporting for care with a more advanced disease than females

- Patients accessed care after developing AIDS

- Males had a better economic status and knowledge

- After one of year on ART, females lost their immunological advantage

- Significant number missed their monthly appointments

- Mortality is likely to be underestimated due to the high number of Lost to follow-up

Factors Influencing Adherence to ART by HIV Patients in an Urban and Rural setting, Tanzania

To investigate factors affecting adherence to ARV drugs in an urban and rural setting in Tanzania

Mosha et al. Accepted BMC 2014

Comparison of Adherence to ARV Drugs Between Urban and Rural Settings

ART adherence questionnaire

Please place an "X" on the line below at the point showing your best guess about how much of your current antiretroviral medication you have taken in the **past 30 days**

0% means you have taken none of your current antiretroviral medication, 50% means you have taken half your current antiretroviral medication, 100% means that you have taken every single dose of your current antiretroviral medication in the past 30 days.

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%   Estimate percent indicated   ☐☐ %

- Adherence based on consistency of keeping appointments

  – Urban 318 (77%); Rural 293 (55%); P<0.01

- Adherence based on consistency of taking ARV (VAS)

  – Urban 234 (56%); Rural 428 (81%); P<0.01

- Adherence based on 4 days recall

  – Urban 362 (87%); Rural 423 (80%); P<0.01

Predictors of Adherence

- Positive predictors with statistical significance

    – Being on ART > 1 year (Both)

    – Satisfaction with Health Services (Both)

    – Early presentation to CTC (Both)

    – Attending CTC > 1 year (Both)

    – Having treatment support (Both)

    – Knowledge on ARV use (Both)

- Negative predictors with statistical significance

    – Paying transport cost to CTC (> Rural)

    – Use of traditional Medicine (> Rural)

    – Taking alcohol (> Rural)

    – Employment (> Urban)

Main Findings

- Adherence in this study was lower compared to previous studies

- Differential attention in rural compared to urban settings are needed to influence ARV adherence

- Patients in the rural settings will benefit more from:

  - A better transport system

  - Easy access to CTC

  - Seeking in traditional medical practitioners allies

- Patients in the urban areas may benefit more from access to CTC outside working hours

# Clinical and Virological Response to ARV Treatment in Dar-es-Salaam, Tanzania

- To investigate factors predicting ART clinical response and associate them with virological response in patients taking ARV drugs in Tanzania

Mosha et al. JIDC, 2014

Characteristics of ART Clinical non-responders and responders

- Clinical responders (71) than non-responders (79) were more likely to have:

  - Better immunological response (P=0.03)

  - Better percentage weight gain (P<0.01)

- 25 viraemic 10 [(14%) responders; 15 (19%) non responders: P=0.3]

- Any ARV resistance mutation 20 (83%) (P=0.13)

- Dual NRTI and NNRTI resistance mutations 16 (67%) (P=0.7)

- NRTI resistance mutations 17 (71%) (P=0.5)
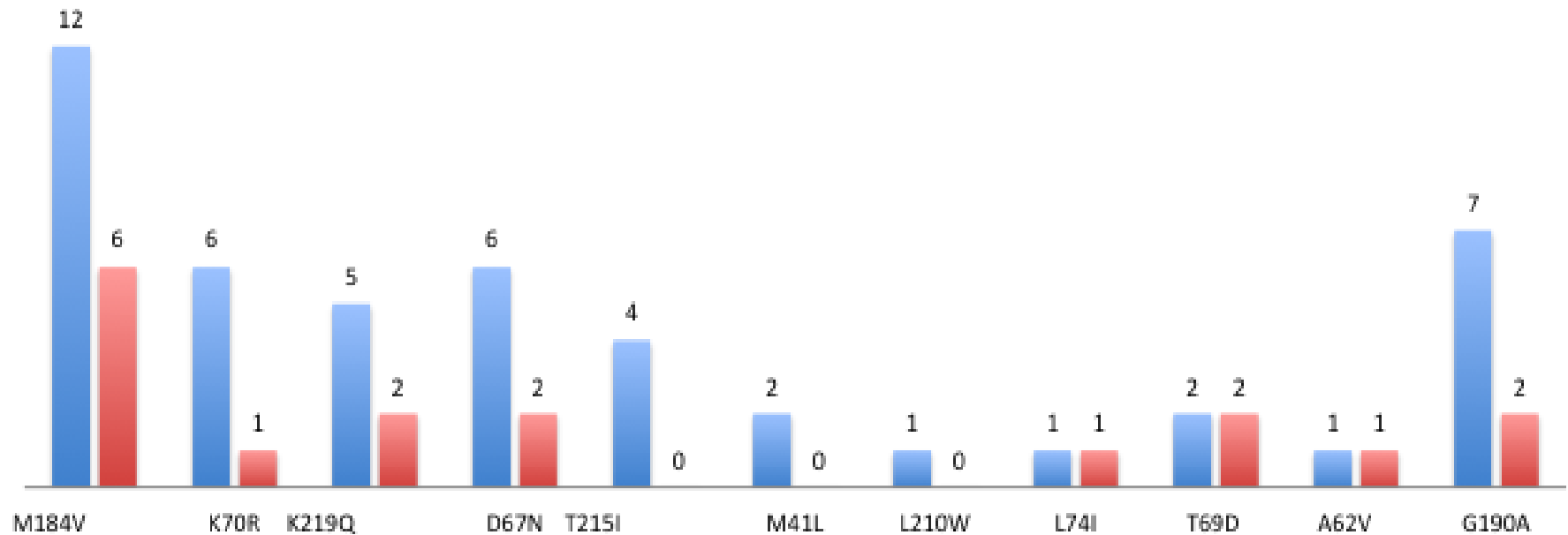
- NNRTI resistance mutations 19 (79%) (P=0.4)

Percentage of observed Subtypes and Recombinants

Legend:
- A
- C
- CRF02_AG
- CRF10_CD
- D
- URF_AC
- URF_CA
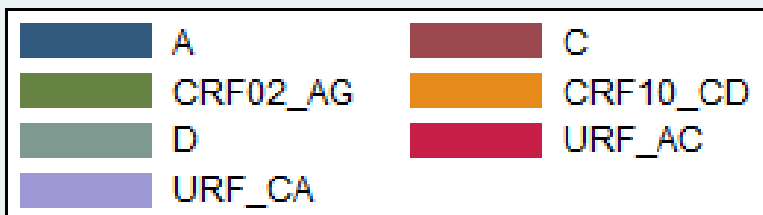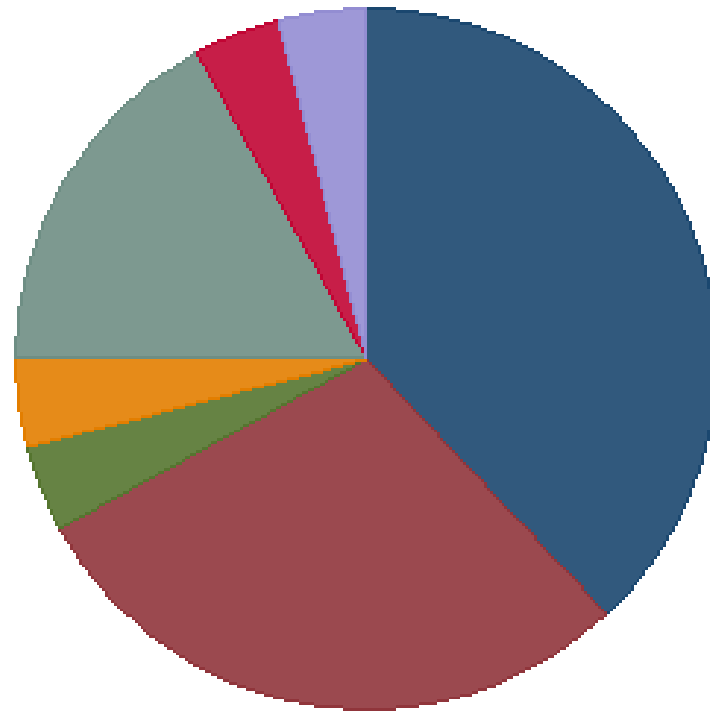
Observed ARV Resistance Mutations

Main Findings

- Initiation of therapy at advanced disease stage was associated with clinical and not virological treatment failure

- The criteria for defining clinical failure to ART are not reflecting the actual virological failure

  - There were many patients defined to have clinical failure that were actually not virologically failing

- The prevalence of ARV drug resistance was high among virologically failing patients

Prevalence of Genotypic Resistance to Antiretroviral Drugs in Treatment Naive Youths infected with Diverse HIV-1 Subtypes and Recombinant Forms in Dar es Salaam, Tanzania

- To establish the prevalence of ARV drug resistance in drug naïve population

Mosha et al. AIDS Res Hum Retroviruses 2011

Subtype and Recombinant forms

Subtype	Env Region	Gag Region	Pol Region	Full genome
Subtype A	16 (46%)	12 (25%)	16 (36%)	7 (27%)
Subtype C	6 (17%)	13 (27%)	16 (36%)	6 (23%)
Subtype D	1 (3%)	7 (15%)	6 (14%)	1 (4%)
Unclassified	12 (34%)	0	0	0
C-like	0	2 (4%)	0	0
D-like	0	2 (4%)	0	0
Recombinant AD	0	2 (4%)	2 (5%)	2 (8%)
Recombinant AC	0	8 (17%)	1 (2%)	6 (23%)
Recombinant AB	0	0	1 (2%)	0
Recombinant CD	0	0	1 (2%)	3 (12%)
CRF10_CD	0	2 (4%)	1 (2%)	0
Total	35	48	44	26

Observed Resistance Mutations Among the 44 pol Sequenced Samples

Subtype	NRTI mutations	NNRTI mutations	Gender	CD4 count (cells/ul)
AC	M184V, T215F	K103N, Y181C	Female	83
D	M184V	K103N	Female	175
AC		Y181C	Male	39
C	K65R	Y181C	Female	374

- The median CD4 T-cell count was 228 cells/μL

Main Findings

- Low median CD4 T-cell counts in a supposed recently infected youth

- High prevalence of ARV resistance mutations in ARV naïve

- Could not measure effect of subtype on ARV resistance mutations

- High genetic diversity with unclassified recombinants
  - Implication on treatment
  - Implication on vaccination strategies

Conclusion

- Despite using ARVs, some patients still experience disease progression and death

- Some of the observed challenges:

  - The limited resource and skills to monitor therapy efficiency

  - The late initiation of antiretroviral therapy

  - The size of the epidemic, which precludes efficient treatment for all that need it

- Many viraemic patients are not uncovered as failing patients

  - Risk for resistance development

Conclusion

- After one year of ART, women lost their immunological advantage

- Observed behavioral factors with effect to ART include:

  - Alcohol consumption

  - Use of drugs of abuse and traditional medicine

  - Knowledge on the use of ARV

- Need for differential attention in rural compared to urban settings while rolling out ART

- The existence of diverse HIV subtypes and recombinants complicates treatment monitoring

Limitations

- Small sample size

- Patient self-reporting might result in recall bias

- Use of the routinely documented data in the ART clinic files

- We studied patients retained in care, but lacked data on patients' LTF

Recommendations

- More comprehensive studies on ART involving more patients
  - Focusing on gender differences on adherence to ARV medication
  - Observed ART adherence difference between rural and urban settings
  - Testing the cost-efficiency of virological monitoring for treatment response
  - Follow up the observed predictors of non-adherence as described in our study

- Early diagnosis and treatment of HIV

- Monitoring of the emergence of drug-resistant HIV

- Reduce gender inequalities on accessing the health care

Thank you