HIV drug resistance and tracing outcomes among antiretroviral therapy defaulters in Malawi

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Background

- Up to 30% of people starting antiretroviral therapy (ART) in sub-Saharan Africa are lost to follow-up (LTFU) after three years

- Loss to follow-up (LTFU) at 12 months globally (2004-2012) 20% with prevalence increasing over time[1]

- Malawi has 700,000 people on ART as of June 2017 and an estimated prevalence of LTFU at 12 months of 25% [2]

[1] WHO Global report on EWI of HIVDR, 2016; [2]Malawi Ministry of Health

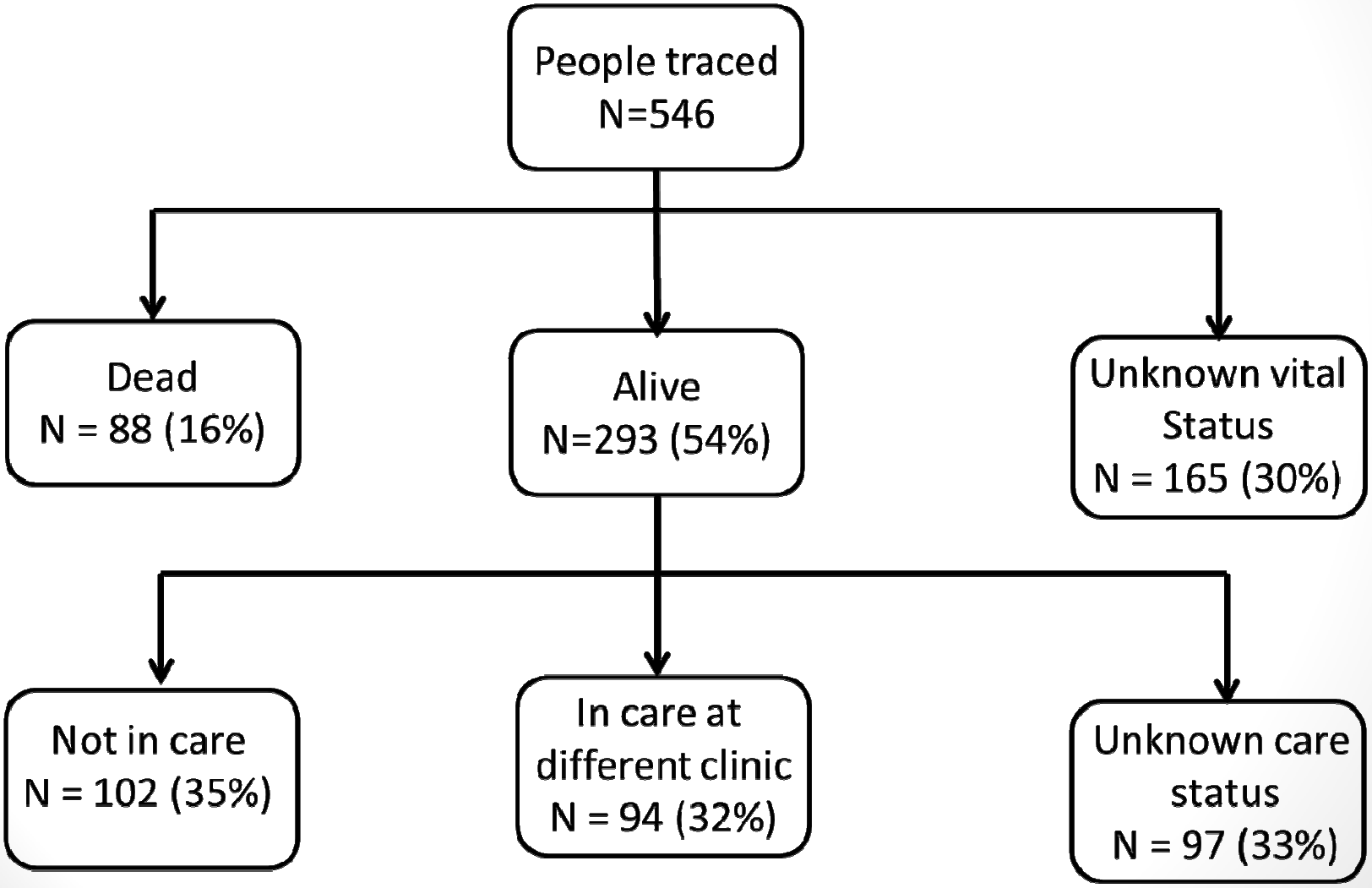
Methods (sampling and tracing)

- Random sample of 546 adults
  - Patients who made a visit to clinic between January 2013 and December 2014
  - Sampling January 2015; tracing January-March 2015
  - Classified as LTFU (>90 days late for last clinic or pharmacy appointment)
- Consent for tracing obtained per routine at time of treatment initiation
- Active tracing by peer health care workers
  - Outcome and care status: patient or surrogate
- When found alive and contacted in-person, venous blood specimens were collected

Methods (laboratory)

- HIVDR genotyping: British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada
- Deep Sequencing: Illumina MiSeq
  - Amplicon coverage: RT 90-234
  - MiSeq data processed through in-house pipeline
  - 20% prevalence threshold for reporting
  - Previously demonstrated high concordance with Sanger sequencing
- Drug susceptibility was predicted using the Stanford HIVdb algorithm (version 8.4)

Outcomes and care status amongst patients lost to follow up from HIV care



Proportion of people reporting given reason for stopping care at original ART clinic (N = 92)[a,b]

Reason	N	% of people reporting reason (95% CI)
Had traveled away from clinic catchment area	18	20% (13-29)
Afraid of scolding at clinic	13	14% (8-23)
No transport to clinic	12	13% (7-22)
Had other source of ART	10	11% (6-19)
Experiencing side effects from medication	8	9% (4-17)
Work obligations	8	9% (4-17)
Too ill to travel	6	7% (3-14)
Had to take care of children or family members	5	5% (2-13)
Felt better and thought s/he did not need care	5	5% (2-13)
Unspecified	13	14% (8-23)

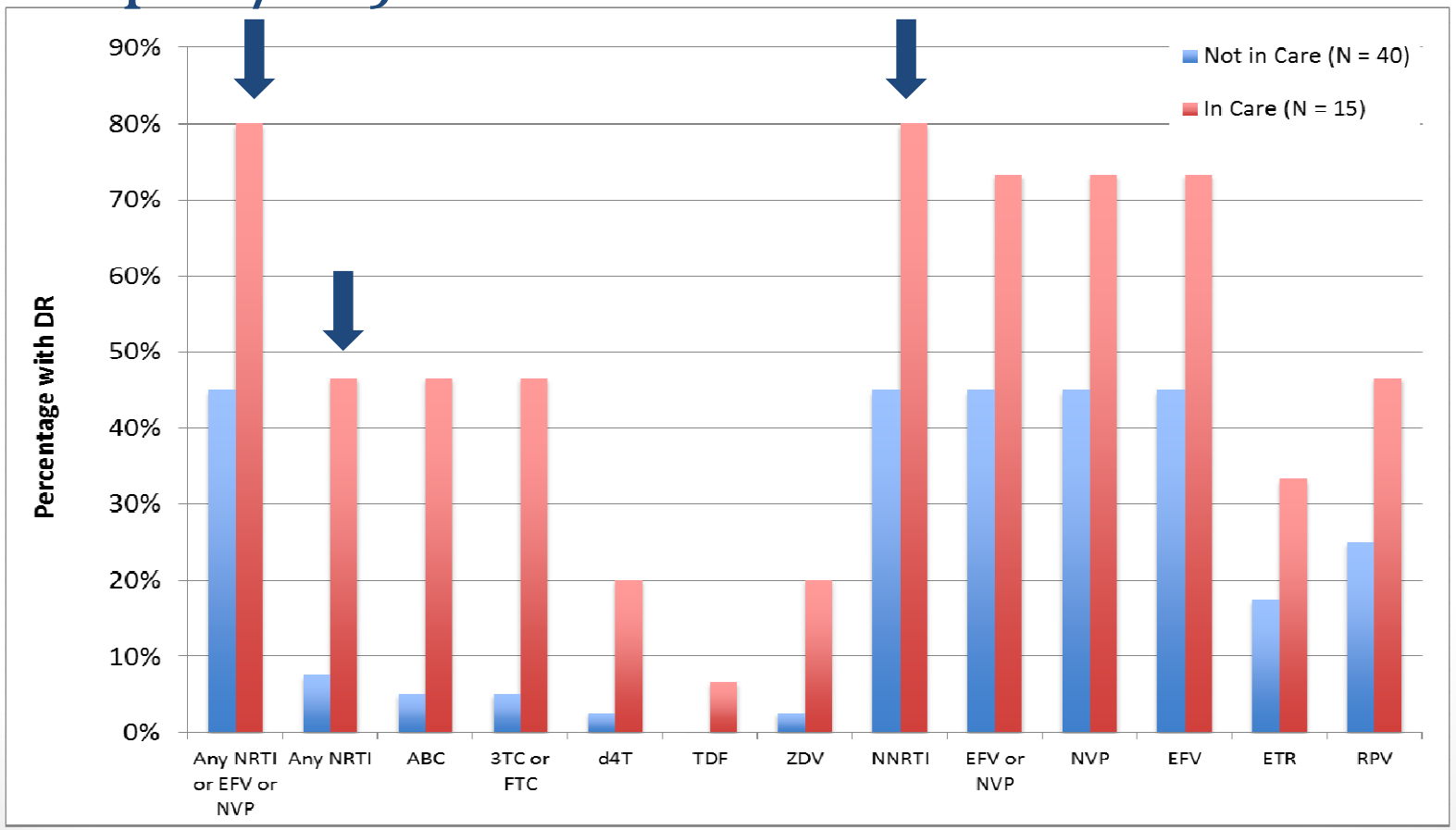
[a]Of 293 persons documented to be alive, 92 were contacted in person and responded to the questionnaire. [b]Reasons reported by 5% or more of people

Proportion of people reporting given reason for attending a different clinic (N =75)[a,b]

Reason	N	% of people reporting reason (95% CI)
New clinic is closer to where I live	29	39% (28-50)
Declined to answer	14	19% (11-29)
New clinic was less expensive	12	16% (9-26)
New clinic is more convenient	6	8% (4-17)
Traveling or moved	6	8% (4-17)
Switch was related to pregnancy (ANC or PMTCT care)	4	5% (2-14)
Received an official transfer	4	5% (2-14)
Unspecified	8	11% (5-20)

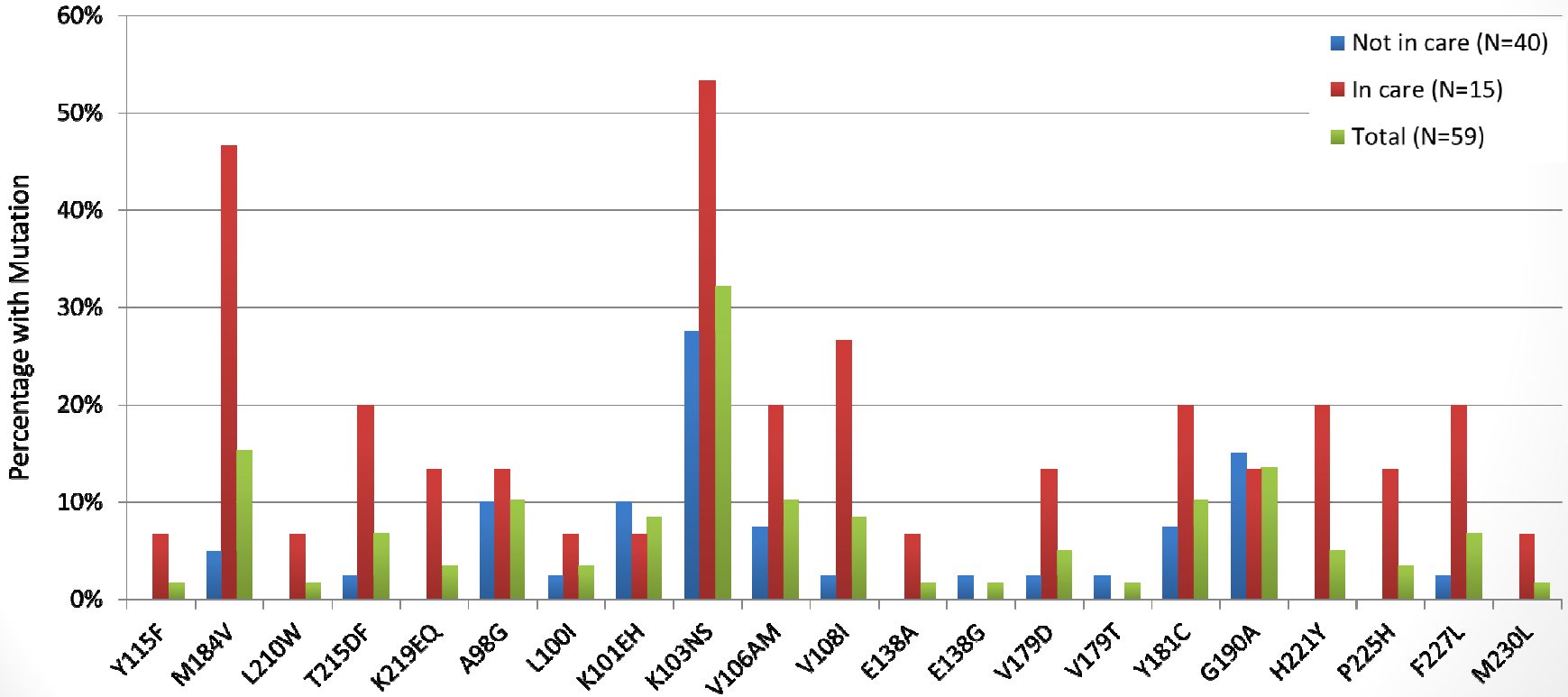
[a]Of 94 persons in care at a different clinic, 75 completed the questionnaire. [b]Reasons reported by 5% or more of people

HIV drug resistance (20% threshold) among people classified as lost to follow-up and successfully traced (N=59, plasma VL > 1000 copies/ml)[a]



[a]four people with undefined care status; none with resistance

Frequency of reverse transcriptase inhibitor drug resistance mutations among physically traced patients (N=59, plasma VL > 1000 copies/ml)[a]



[a]four people with undefined care status; none with resistance

Discussion & conclusions

- Socio-economic factors and travel away from the clinic catchment area are major reasons for stopping care or attending a different clinic.
- Levels of resistance are very high in this sample of LTFU
  - HIVDR is significantly higher amongst those reporting to be in care and with plasma VL > 1000 copies/mL
- Maximizing retention and routine viral load testing/prompt switch to second-line ART critical to minimizing HIVDR
- Where LTFU is high, assessments of HIVDR that do not include lost patients underestimate population-level magnitude and potential impact of drug-resistant virus
- Use of non-NNRTI based regimens in people with prior treatment may be considered

Acknowledgments

- Ministry of Health Malawi
  - Epidemiology unit
  - National HIV reference laboratory
  - HIV department

- Patients and health care providers at:
  - Nkhotakota Distric Hospital;
  - Queen Elizabeth Hospital;
  - St Martin’s Mission Hospital;
  - Ndirande Health Centre