Increasing intra- and inter-subtype HIV diversity despite declining HIV incidence in Uganda

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BACKGROUND

- HIV incidence in eastern and southern Africa has declined by more than 50% with scale-up of HIV treatment and prevention programs; however, it is unclear whether such significant changes in the African HIV epidemic dynamics have affected viral diversity.
- Here, we used HIV sequence data generated over a 25-year period in southern Uganda to evaluate trends in inter- and intra-subtype HIV viral diversity.

METHODS

- **Study area:**



Figure 1. Rakai, Uganda with HIV prevalence of 8.1%

- **Study population:** We analyzed HIV genomic data from viremic persons with HIV collected between 1994 and 2018 from the Rakai Community Cohort Study, an open population-based HIV surveillance cohort in in Uganda.
- **Sequence data:** p24 and gp41 sequences between 1994 and 2009 (Sanger sequencing) and near full-length sequences between 2009 and 2018 (NGS) were combined and trimmed. Subtype analyses were performed using RIP.
- **Genetic diversity:** Inter-subtype diversity was measured using the Shannon Diversity Index (SDI), and intra-subtype diversity was calculated using pairwise TN93 genetic distance.

HIV-1 Subtype distribution (p24 & gp41)

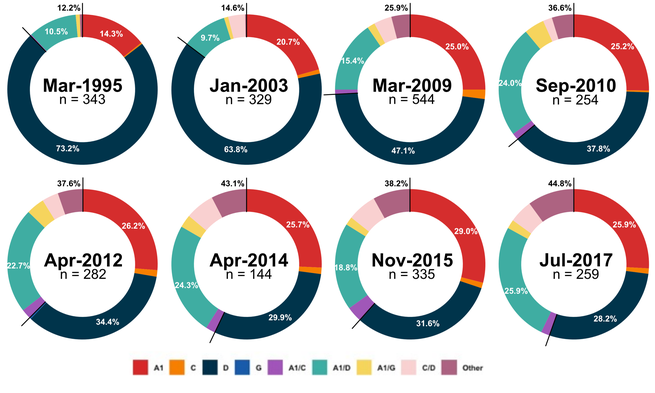


Figure 2. HIV subtype distribution by calendar time

In Uganda, HIV genetic diversity is on the rise despite a decrease in HIV incidence. This is attributed to an increasing prevalence of inter-subtype recombinant forms and growing intra-subtype genetic diversity in gp41.

RESULTS

- 5,532 (57.2%) RCCS participants living with HIV had HIV sequence data at ≥1 survey visit.
- The proportion of subtype A1 and recombinant viruses increased until 2012, whereas subtype D viruses consistently declined (p<0.0001) (**Figure 2**).
- The proportion of recombinant viruses significantly increased from 12.2% in 1995 to 44.8% in 2017 (p <0.0001) **(Figure 2)**.
- The SDI increased in p24 through the study period, while no significant changes were observed in gp41 from 2014 onwards (**Figure 3**).

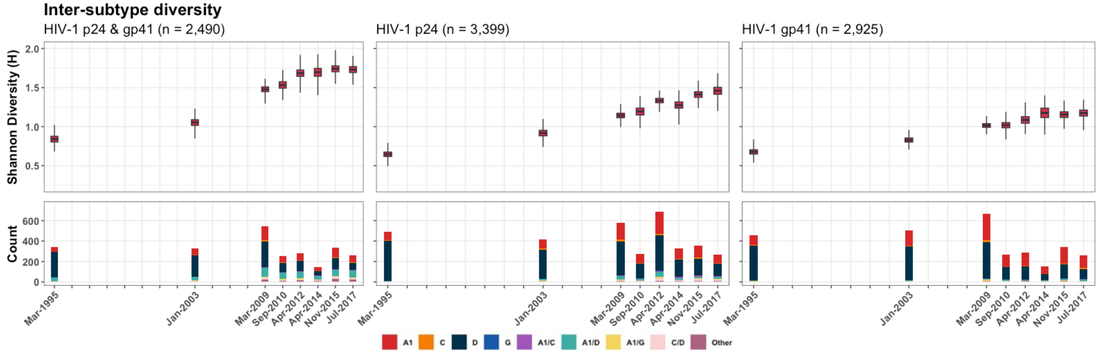


Figure 3. Shannon Diversity Index by calendar time

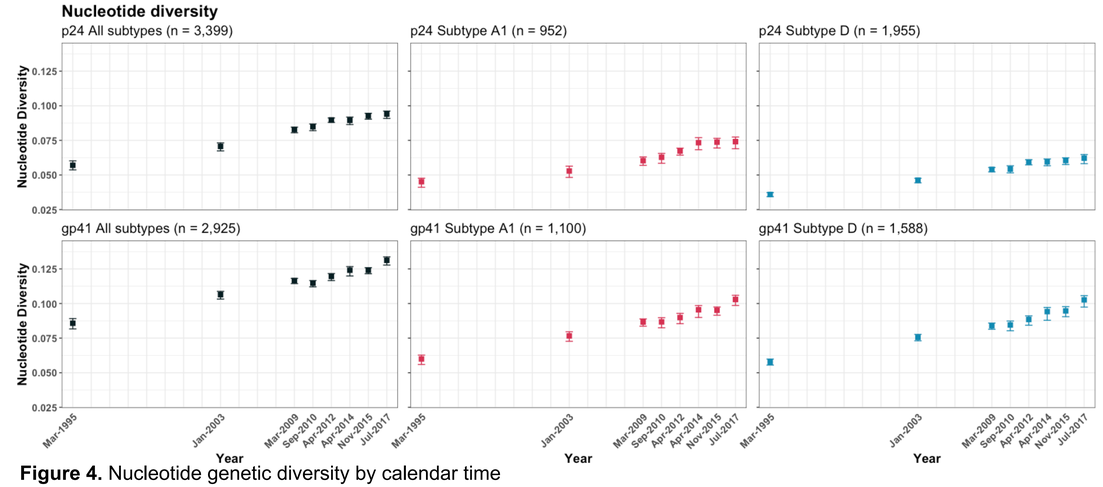


Figure 4. Nucleotide genetic diversity by calendar time

- Overall nucleotide diversity increased in both genes over the analysis period (**Figure 4**).
- Intra-subtype diversity in A1 and D p24 subtypes leveled off after 2014, while A1 and D gp41 nucleotide diversity increased continuously (**Figures 4 & 5**).
- These increasing trends were generally observed across all population sub-groups (**Data not shown**).

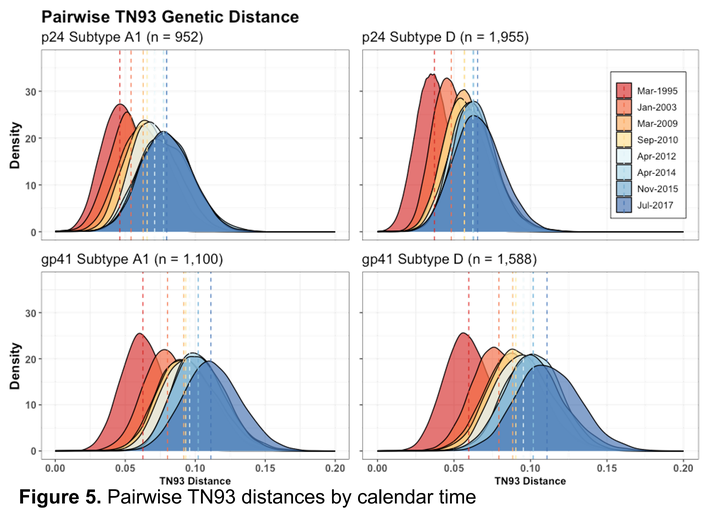


Figure 5. Pairwise TN93 distances by calendar time

CONCLUSIONS

- We observed continued HIV evolution, with a growing number of recombinant viruses and increasing intra-subtype evolution of gp41, despite declining HIV incidence.
- Comprehensive and wide-ranging molecular surveillance is essential for a better understanding of HIV dynamics driving population HIV evolution and the development of new HIV vaccines and treatments for epidemic control.

ADDITIONAL KEY INFORMATION

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