## ABSTRACT

### Background:

HIV superinfection (SI) has been detected at a substantial rate in several settings, but its impact on disease course remains poorly characterized. Understanding the consequences of SI has important implications for counseling HIV-infected individuals, as well as estimating transmission risk in epidemic modeling. Prior studies have suggested that SI may lead to a transient increase in viral load (VL) and sustained acceleration in VL increase
over time, however these studies were small (analyzing 2-12 cases of SI) or did not distinguish between coinfection and SI. We recently screened a cohort of HIV-infected high-risk women in Mombasa, Kenya, for superinfection. Among 145 women singly infected at baseline, 21 acquired SI during follow-up.

**Methodology:**

Detailed clinical and laboratory data collected at quarterly intervals were used to compare disease progression between superinfected and singly infected women from the Mombasa cohort. Linear mixed effects models were used to compare post-acute VL and CD4 counts over time. Cox proportional hazards analysis was used to determine the effect of SI on time to clinical progression (CD4 < 200, ART initiation or death).

**Results:**

Overall, 124 singly infected and 21 superinfected women contributed 925 person-years of follow-up, during which 1788 VL and 1532 CD4 counts were collected and 91 progression events occurred. VL increased more rapidly following SI than during single infection (increasing at 0.14 vs. 0.08 log10 copies/ml/year respectively, p=0.04). Conversely, CD4 counts decreased more rapidly in SI cases than singly infected women (at 1.57 vs. 0.97 √CD4+cells/ml/year respectively, p=0.05). Prior to SI acquisition, there was a trend for ultimately superinfected women having lower setpoint VL than singly infected women (-0.37 log10 copies/ml, p=0.09). Adjustment for viral subtype, genital infection at HIV acquisition and HLA alleles reported to
modify HIV progression had negligible effect on the results. We did not detect a significant effect of SI on time to clinical events, though this may have been due to limited statistical power. We also did not detect transient changes in VL or CD4 at the time of SI detection, though sampling was not optimal for this analysis.

**Conclusions:**

This is the largest study to date examining the effect of SI on HIV progression. Our findings suggest that SI may accelerate disease
progression and, through elevated VL, increase infectivity, arguing for greater awareness among clinicians and patients of the consequences of SI.
Additionally, the observation that VL setpoint may be lower pre-SI than in women who remain singly infected suggests that low initial viral replication may be
associated with SI, prompting further investigation of viral fitness and immune responses in the setting of SI.