Viral ‘blips’ Clinical

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Clinical Questions:

1. What is the risk of transmission to others by sexual or other means?

2. Will the current treatment work sustainably (risk of failure)?
   - Antiretroviral medication factors e.g., effectiveness, resistance barrier
   - Viral factors e.g., prior resistance, regimen choice, dual therapy?
   - Human factors e.g., engagement in care, practicality, adherence, current or future side-effects

- Clinical VL assays have over time become more sensitive (lower limit of detection, LLD).

Undetectable = Untransmissible

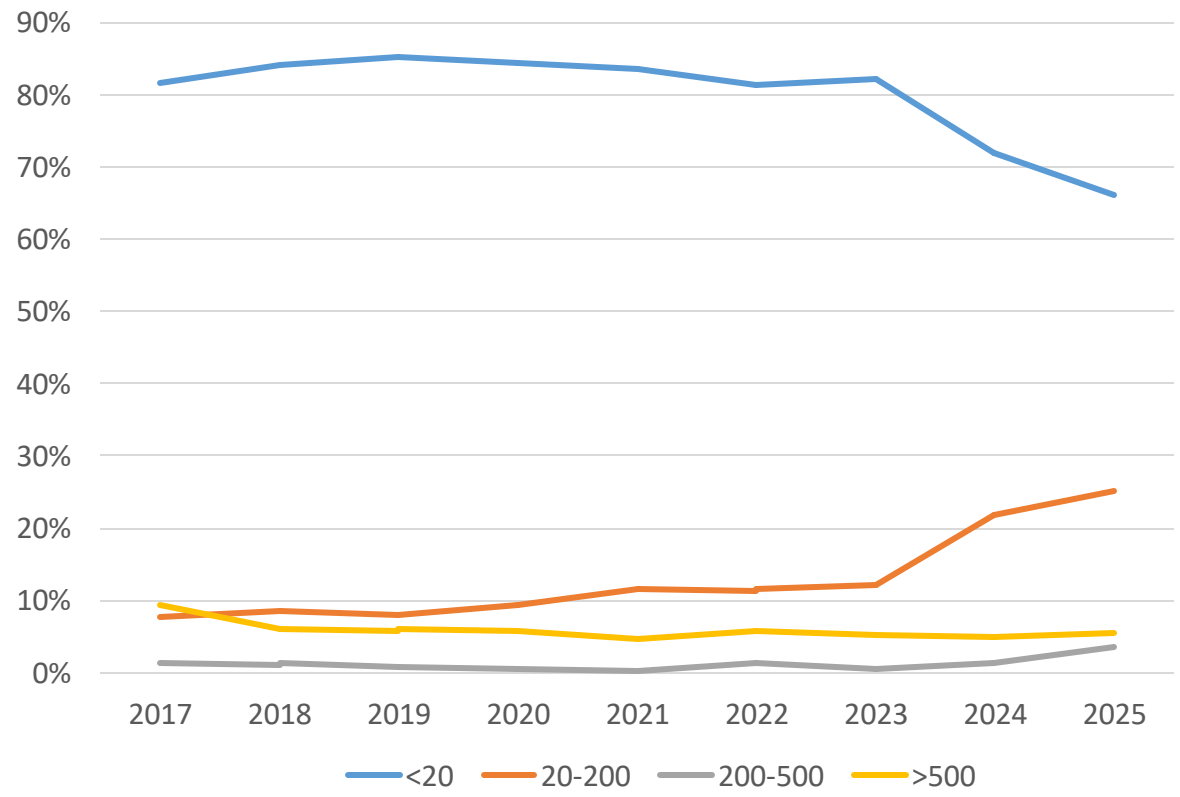
A person living with HIV who is on treatment and maintains an undetectable viral load has zero risk of transmitting HIV to their sexual partners.

Study	Study type	Partic-ipants	Partners	Follow up	Suppressed	Study outcomes	Partner HIV infn's when suppressed
HPTN052	RCT	1764	Hetero	5+ years	< 400	Early ART let to 93% less transmission	Nil
PARTNER1	Cohort	1166	MSM & Hetero	1.3 years median	< 200	11 acquired HIV, from other partners	Nil
Opposites Attract	Cohort	343	MSM	~1 year	< 200	3 unlinked HIV infections	Nil
PARTNER2	Cohort	782	MSM	2.0 years median	< 200	15 unlinked HIV infections	Nil

Clinical outcomes: PLHIV with a VL 20-199

- **Emergence of drug resistance mutations**: observed with persistent HIV RNA level ≥200 copies/mL, and especially >500 copies/mL
- **Disease occurrence or progression**: to date, there are no clear data indicating that a VL between the LLD and 200 copies/mL is clinically relevant in portending negative outcomes such as CD4 T-cell decline, cardiovascular disease, malignancy, or immunologic conditions.
- **Virological treatment failure** (VL >200-500). An association with future virological failure (VL 20-199), although most failure occurs in other settings e.g., stopping ART.

Proportion of low level “blips” increased over time



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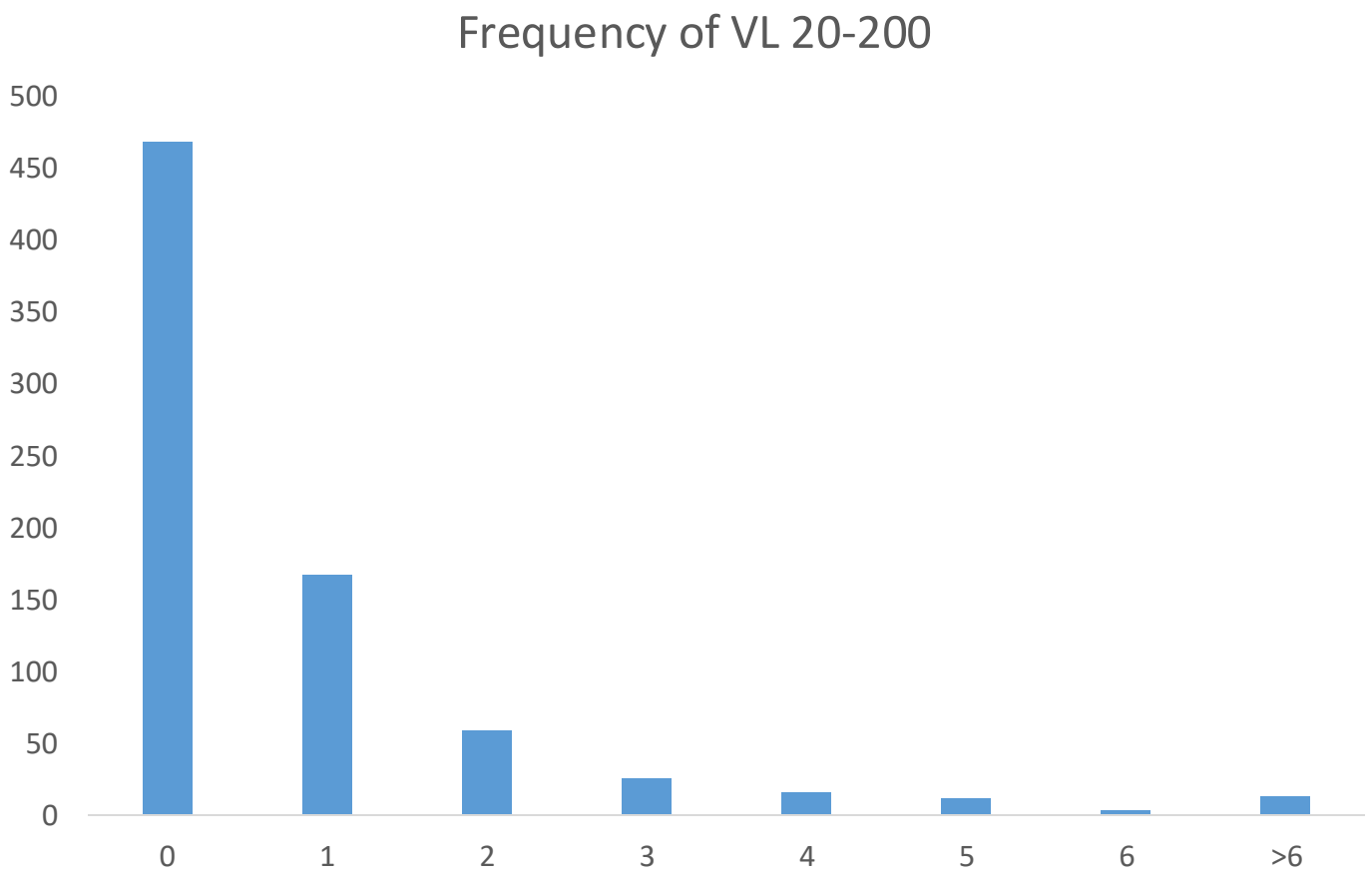
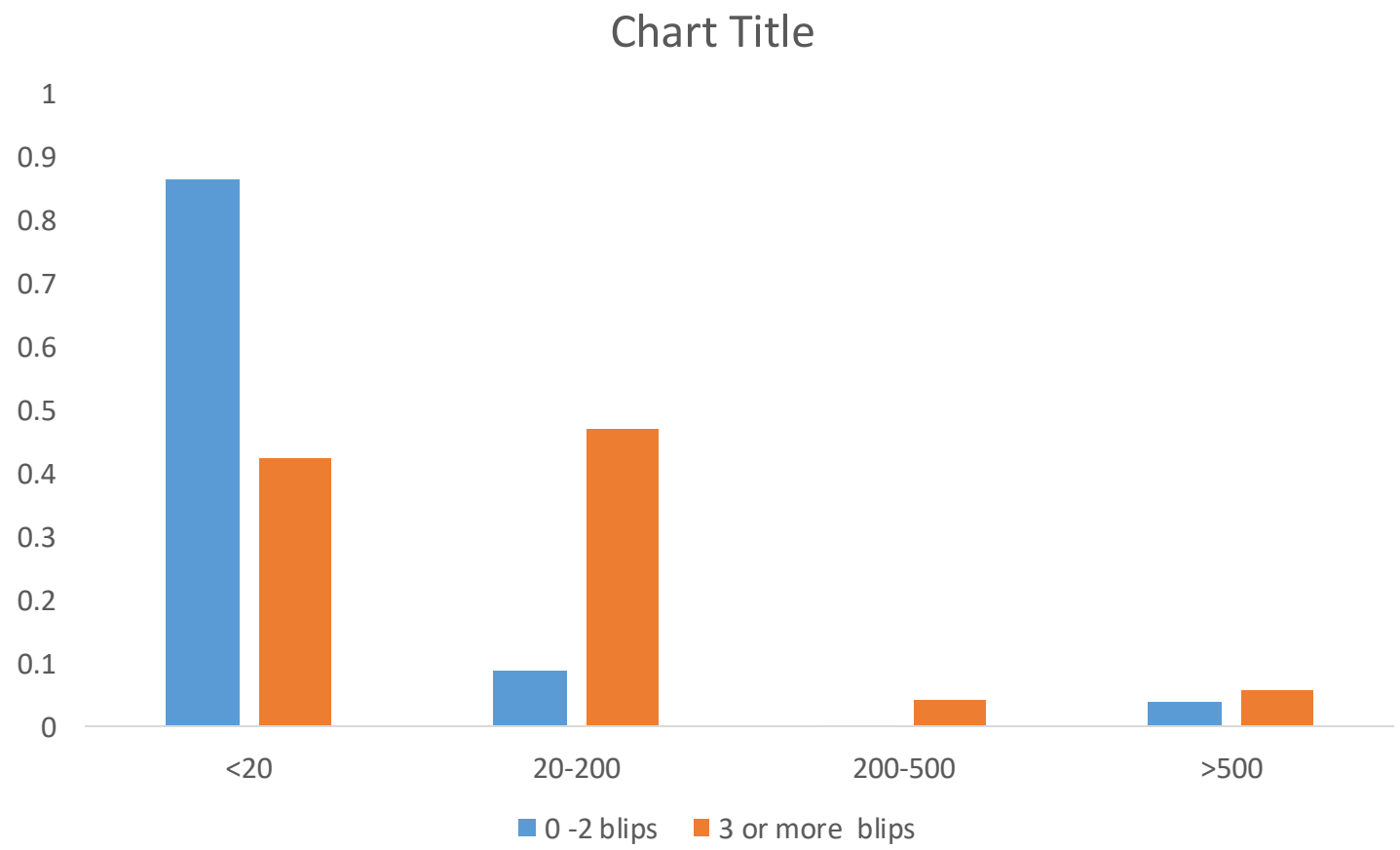
Patients and number of “blips”



Latest viral load according to total number of prior blips



Viral Load (RNA copies/mL)	**Sexual Transmission?**	Clinically concerning?
Above 200	Transmission possible	Yes
51 - 200	U=U	Sometimes
20 - 50	U=U	Mostly not
‘Less than 20’, or ‘Not detectable’	U=U	No

What About U=U and…

Virologic "Blips"?	HIV RNA in Genital Secretions?	Breastfeeding?	Injection Drug Use?	Needlestick Injuries?
Patients on previously suppressive ART with newly detectable viral loads may be experiencing low-level transient viremia ("blips") and not virologic failure. Virologic blips likely occurred in individuals participating in HPTN 052, PARTNER, PARTNER 2, and Opposites Attract; still, there was no transmission from people whose measured HIV viral load was consistently suppressed.	There is no evidence that detectable virus in genital secretions while plasma viral load is undetectable is associated with transmission.	Studies demonstrate that ART *greatly reduces* the risk of HIV transmission from individuals who breastfeed their babies. However, research has not established that people whose HIV is undetectable do not transmit HIV during breastfeeding.	Studies demonstrate that ART *greatly reduces* the risk of HIV transmission through sharing of injection drug use equipment. However, research *has not* established that people with an undetectable HIV viral load do not transmit HIV through needle sharing.	Research *has not* established that people with an undetectable HIV viral load do not transmit HIV to people who are stuck by a needle containing their blood. HIV PEP may be indicated.