

# Molecular Characterisation of HIV Acquisition Events in the PARTNER Study



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*on behalf of the PARTNER Study Group*



# The PARTNER Study

- Prospective observational study of the risk of HIV transmission among serodifferent couples reporting unprotected sex while the positive partner was on ART
- 75 sites in 14 European countries
- PARTNER 1 (2010-2014) recruited and followed up heterosexual couples (n=548) and MSM couples
- PARTNER 2 extension (to 2018) recruited and followed up MSM couples only (= 972 MSM couples in total)



# The PARTNER Study: Main Analysis

**Incidence rate of  
HIV transmission**

**Number of phylogenetically linked HIV  
infections that occurred during eligible  
couple-years of follow-up**

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**Eligible couple-years of follow-up\***

\*Follow-up periods eligible for inclusion if couples had sexual intercourse without condoms and without PEP or PrEP and the HIV-positive partner had a viral load <200 copies/ml at the most recent visit (within the past year)



# HIV Acquisitions in PARTNER

- **22 HIV acquisitions** in participating couples
  - 11 in PARTNER 1 (10 MSM, 1 heterosexual)
  - 11 in PARTNER 2 (all MSM)
  - 16/22 events (15 MSM, 1 heterosexual) during eligible follow-up
  - 6/22 events (all MSM) outside eligible follow-up
    - Reasons for non-eligibility of follow-up period: no data on sexual behaviour (n=3), no condomless sex (n=1), PEP use (n=1), no viral load measurement in the HIV-positive partner (n=1)



# Aim of this Study

- To obtain a detailed molecular characterisation of HIV acquisition events
  - Include events that occurred during or outside eligible follow-up
  - Use sensitive techniques to characterise the viral strains\*
  - Perform anonymised phylogenetic analysis\*\* to determine linkage between viral sequences of putative source and putative recipient

\*Work supported by a  
BHIVA Research Award

\*\*Maximum-likelihood and Bayesian Markov Chain Monte-Carlo inferences

# Study Design

- When a HIV-negative partner was found to have become HIV-positive, a venous blood sample was taken from both partners to determine the genetic relatedness of the respective HIV sequences



Partner on suppressive ART



HIV-1 DNA from PBMC

Newly positive partner

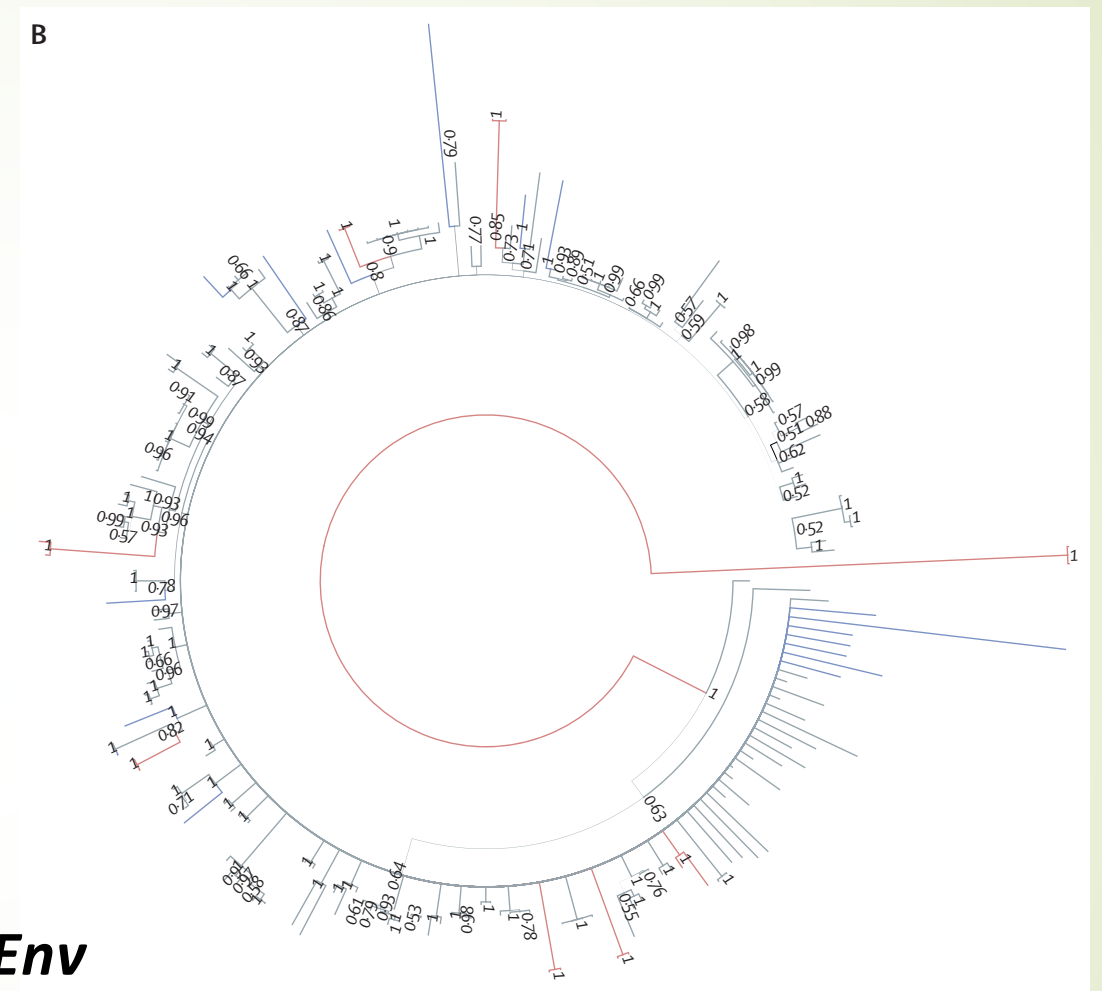
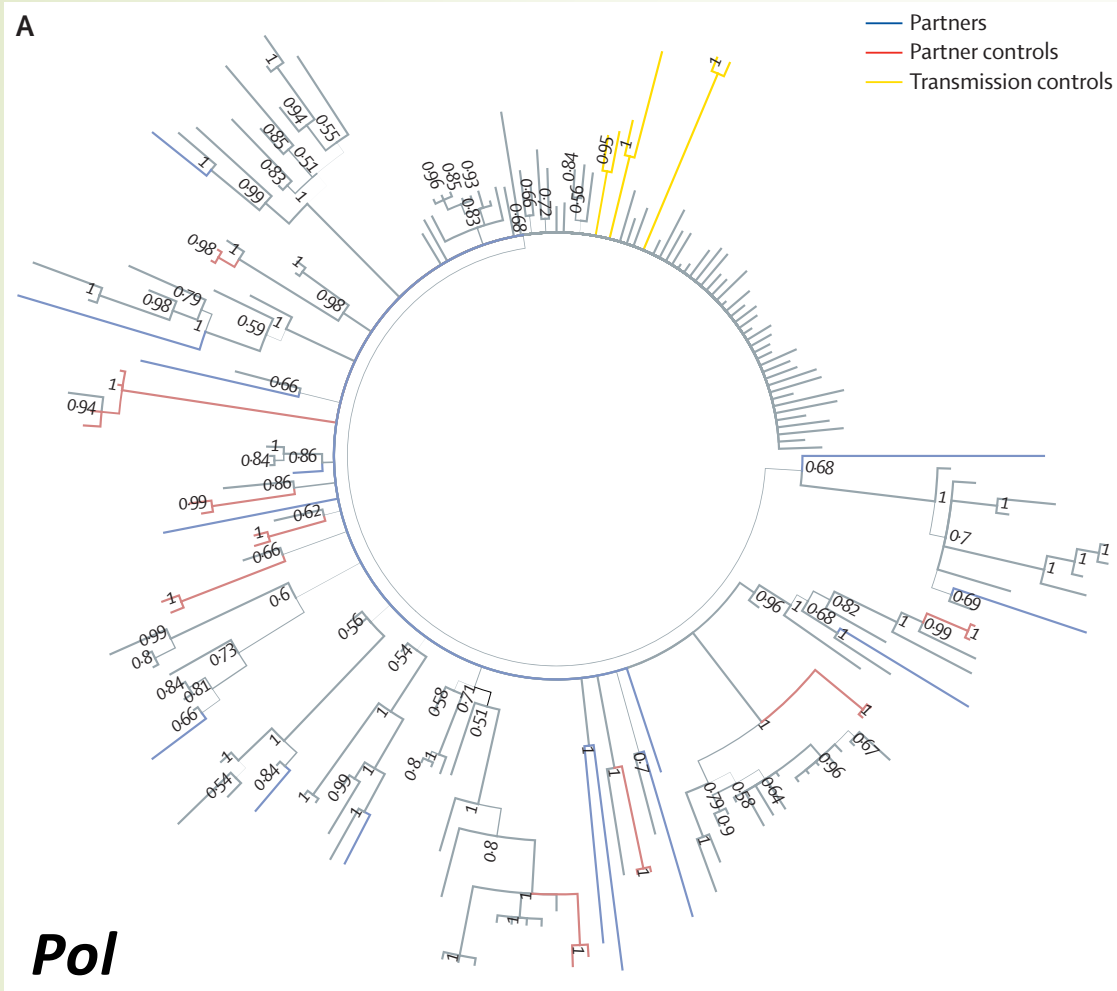


HIV-1 RNA from plasma

# Sequencing - Conventional

- Population (Sanger) sequencing of *pol* and *env*
  - 22/22 (100%) couples for *pol* and 18/22 (87%) couples for *env*
- 22/22 HIV-positive partners had subtype B
- 9/22 (41%) newly HIV-positive partners had non-B infections
  - A1, C, G, CRF02\_AG, CRF20\_BG, CRF29\_BF, CRF60\_BC , CRF14\_BG

**No linkage in any of the 22 couples**



Median pairwise genetic distance between PARTNER sequences consistently >0.040

*Pol* = median 0.069 (IQR 0.057–0.076)

*Env* = median 0.14 (IQR 0.125–0.169).



# Sequencing - Deep

- Illumina MiSeq
- Plasma virus from 8 HIV acquisition events
  - 6 in eligible and 2 in non-eligible follow-up
- ~1,000bp *pol* amplicon (codons 14 to 345 of RT)
- Virus variants of putative recipient detected with sensitivity  $\geq 1\%$
- Haplotypes analysed phylogenetically for relatedness to the PBMC sequence of the putative source

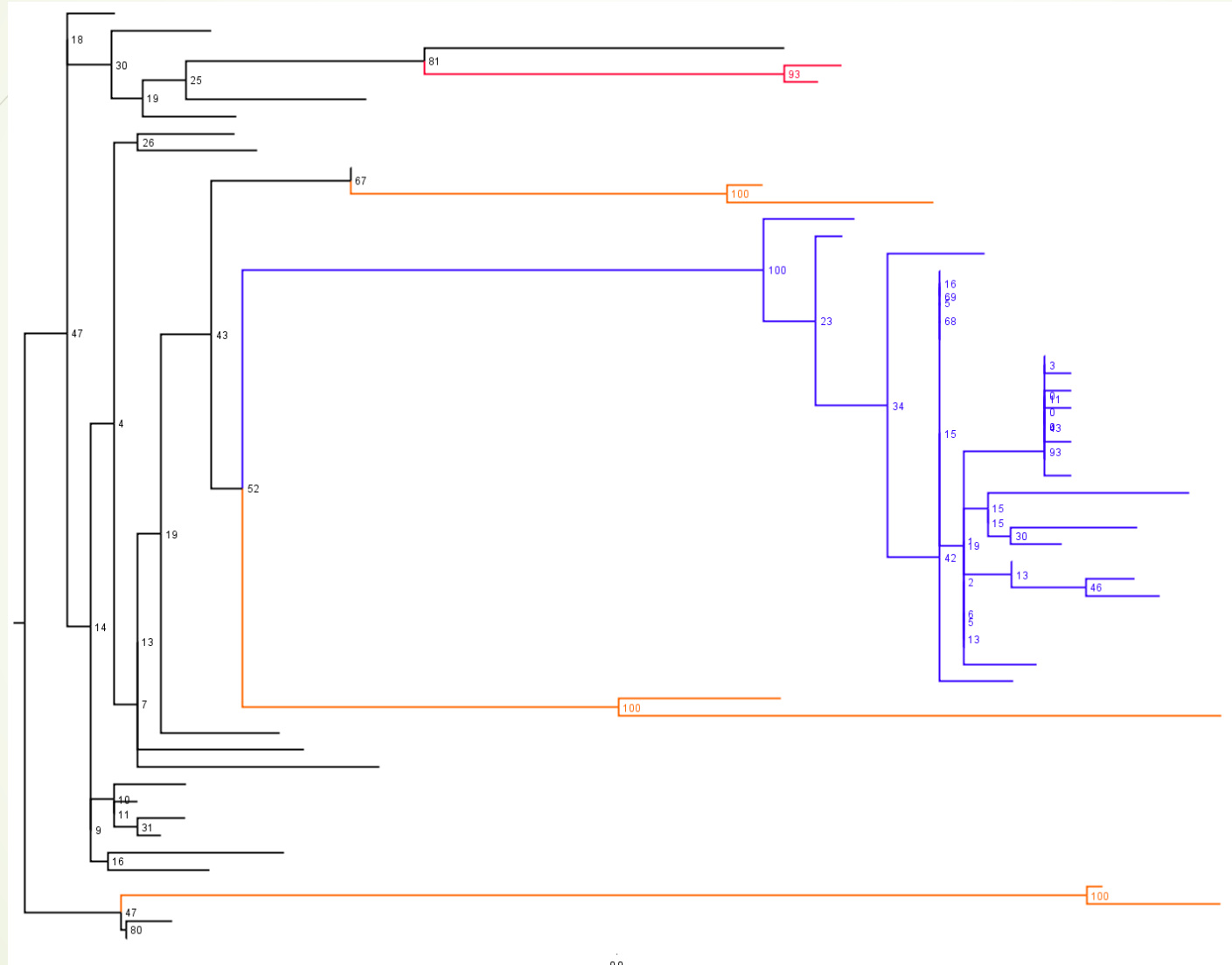
**No linkage in any of the 8 couples**



Putative transmitter's sequences

Viral haplotypes

Control sequences



# Conclusions

- Using both conventional and sensitive sequencing methodologies, and including HIV acquisition events occurring in non-eligible periods, there was no evidence of within-couple transmissions in PARTNER





# Thank you

- Apostolos Beloukas, John Ambrose<sup>1</sup>
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- Valentina Cambiano<sup>3</sup>, Alison Rodger<sup>3</sup>
- Tina Bruun<sup>4</sup>, Jens Lundgren<sup>4</sup>
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