Source and recipient characteristics of HIV transmission pairs identified in the HPTN 071 phylogenetics project

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Outline
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Background
Understanding heterogeneities are crucial to achieve UNAIDS goals

>70% of infected population virally suppressed
<30% reduction in rates of new infection

UNAIDS 2018 report
A cluster-randomised trial of HIV treatment as prevention
• Ran from 2013 to 2018
• Primary outcome: HIV incidence at 36 months
• Three arms:
  1. Prevention intervention with rapid testing plus immediate ART
  2. Prevention intervention with rapid testing plus ART by national guidelines
  3. Standard of care
• 21 communities in Zambia and South Africa
• Total population ~1 million
• Random sample (population cohort) of 2,500 from each community used to monitor outcome
• Hayes et al, *NEJM*, 2019
Participants, methods and data
Participants

- Genomic data was collected as part of the HPTN 071 study
- Zambia only
  - 9 of 12 study communities
- Phylogenetics data was acquired from two sources:
  - Patients in the population cohort, enrolled to measure the primary endpoint of the trial
  - Patients attending HIV clinics (HCFs) within the trial areas
Source attribution

• We have not sampled everyone
• If we can identify which people we have sampled were infected by which others, we can characterise source and recipient populations
• Characterising sources can help better target interventions
• But how to identify pairs?
Phylogenetics helps us determine how individuals are related in the transmission chain.

This normally requires multiple sequences per host.

We infer that person A may be the source of infection for person B.

The analysis is anonymised.

We are only interested in exploring the characteristics of transmission by comparing many such pairs, *not* identifying exactly who infected who.
Phylogenetic methods

- The methodology we use allows us to use the HIV genome to:
  - Estimate the time of infection of each individual
  - Identify likely transmission pairs within the study area
  - Reconstruct the likely direction of transmission between those pairs
- We restrict to pairs where we estimate the transmission took place during the trial
- We classify sources of transmission by:
  - Age
  - Sex
  - Community of residence
  - Drug resistance mutations
  - Recency of infection
- We weight the set of pairs such the recipient set is representative of the overall HIV+ population in the trial areas
**Summary of recruitment**

**HCF**
- 5,729 approached
- 55 ineligible
  - 26 withheld consent
- 5,648 samples collected
- 36 samples not received
  - 293 viral load too low
- 5,319 samples successfully sequenced

**PC**
- 27,467 recruited
  - 20,786 negative at end of trial
  - 5,599 baseline positive
  - 585 seroconverters
- 1,146 withheld consent
  - 2,182 not asked
- 2,856 samples collected
- 188 samples not received
  - 863 viral load too low
- 1,805 samples successfully sequenced

**Summary**
- 300 directed pairs (estimated infection during trial)
- 355 directed pairs (consensus of methods)
- 295 directed pairs (phyloscanner topology)
- 264 pairs (recency estimate)
- 468 probable transmission pairs
- 5,818 with sufficient coverage
- 7,124 samples
Results

3
High level first line DR
From different community
Infected < 1 year prior
Female aged 20−35
Male aged 25−40
Source risk factors

Weighted percentage

Source risk factors

- Male aged 25−40
- Female aged 20−35
- Infected < 1 year prior
- From different community
- High level first line DR
Conclusions
Conclusions

• Men aged 25-40 are responsible for 43.2% of transmissions
• Women aged 20-35 are responsible for 30.3% of transmissions
• Given prevalence, the number of new infections from young men per HIV+ young man is 2.93 times the same number for young women
• Most infections are:
  • Not from outside the community
  • Not drug-resistant
  • Not from a source who was recently infected
HIV transmission is driven by “typical” sexual interactions and control strategies must take this into account
The PANGEA-HIV consortium

Map from Dwyer-Lindgren et al., 2019
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