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

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Outline

1. Background
2. Participants, methods and data
3. Results
4. Conclusions

Background

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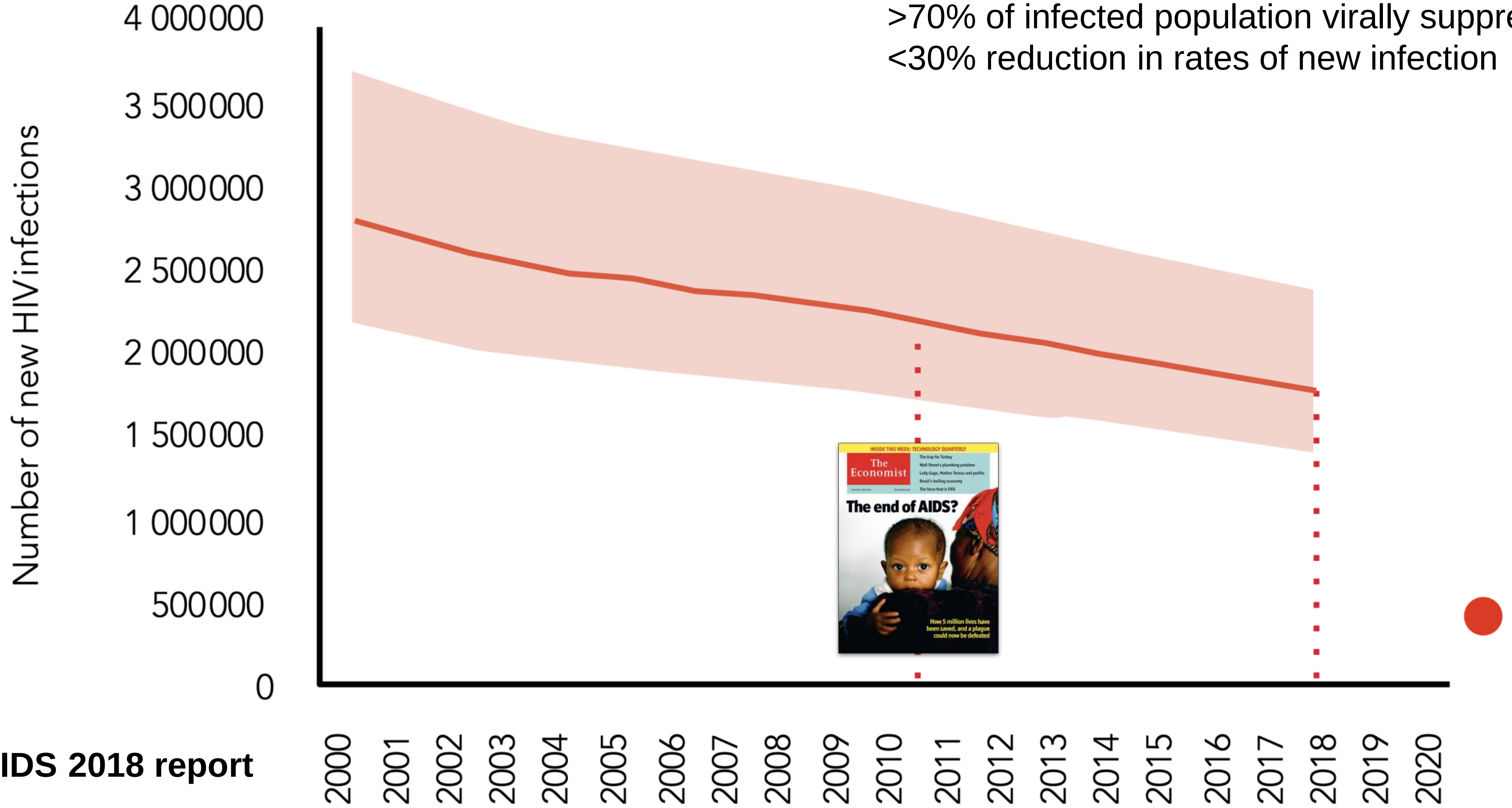
Understanding heterogeneities are crucial to achieve UNAIDS goals

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



UNAIDS 2018 report

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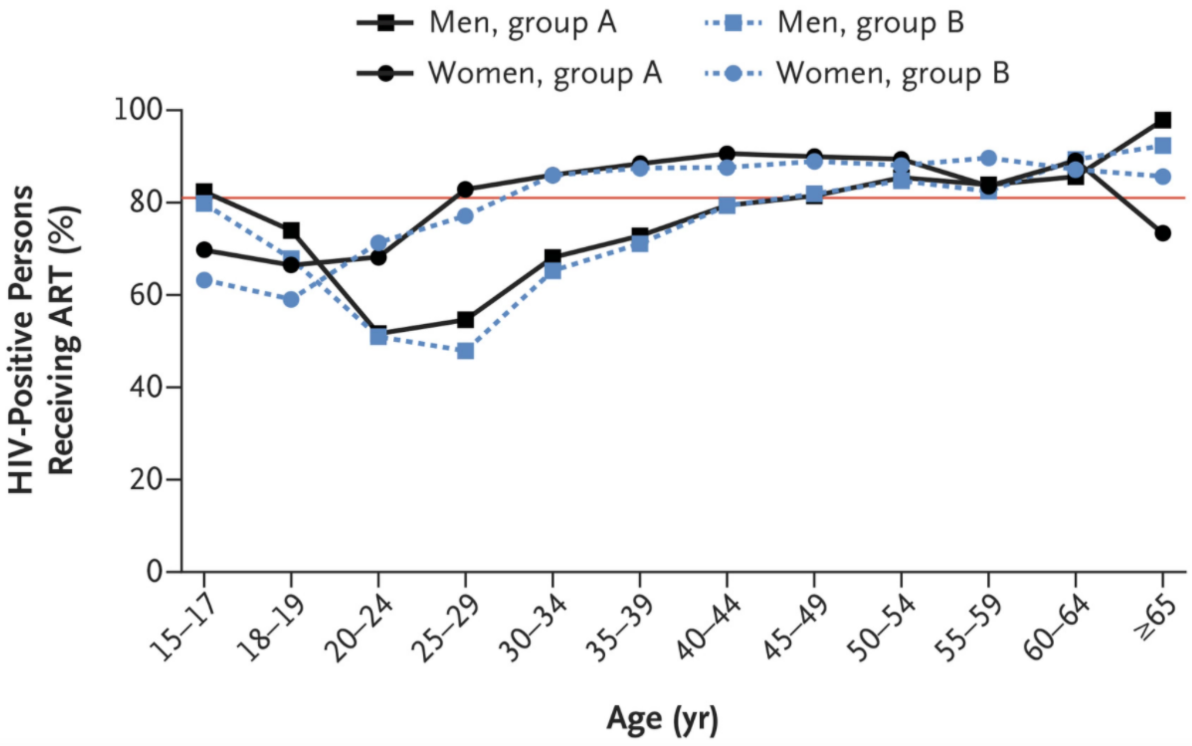
HPTN 071 (PopART)

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

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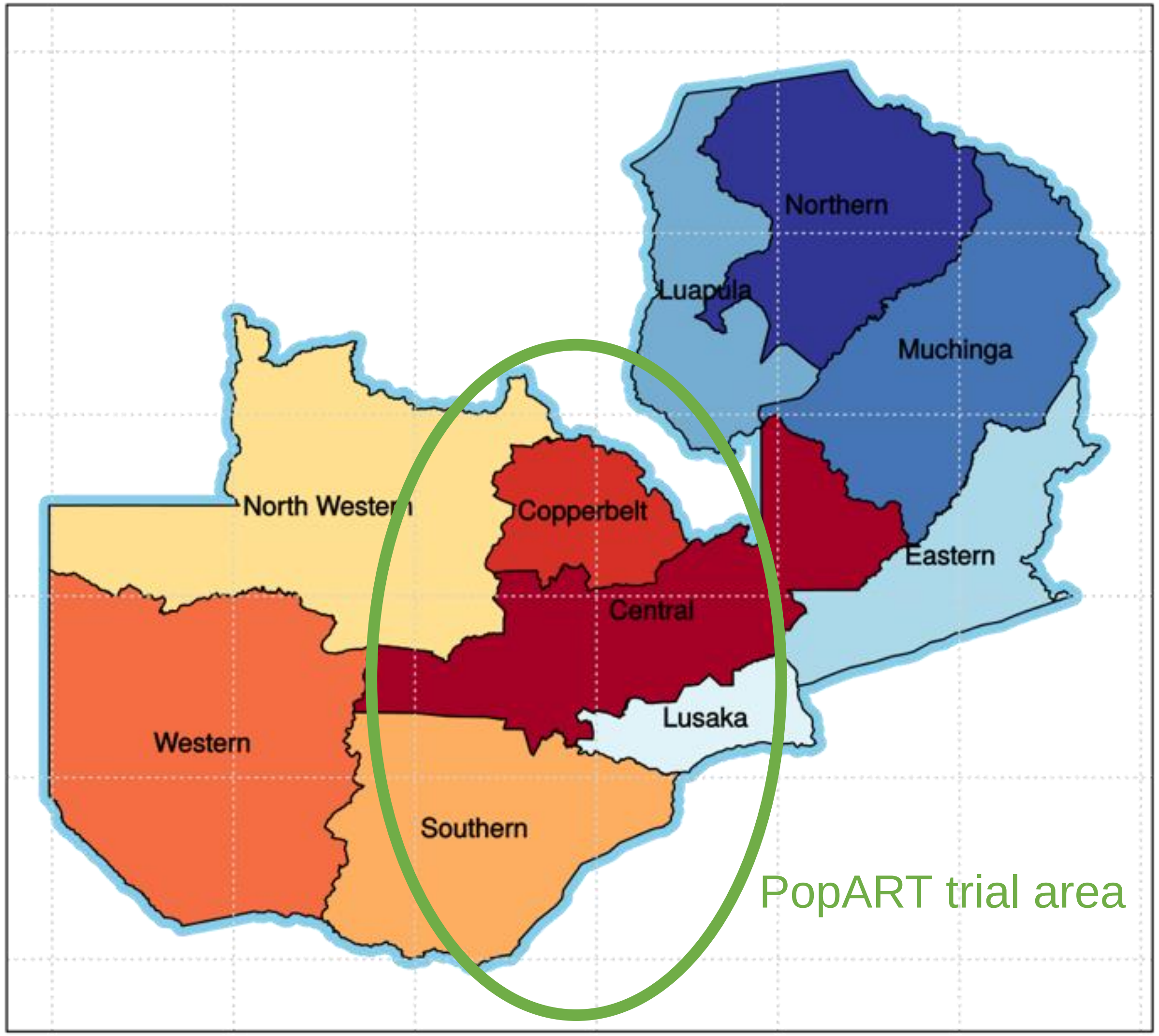
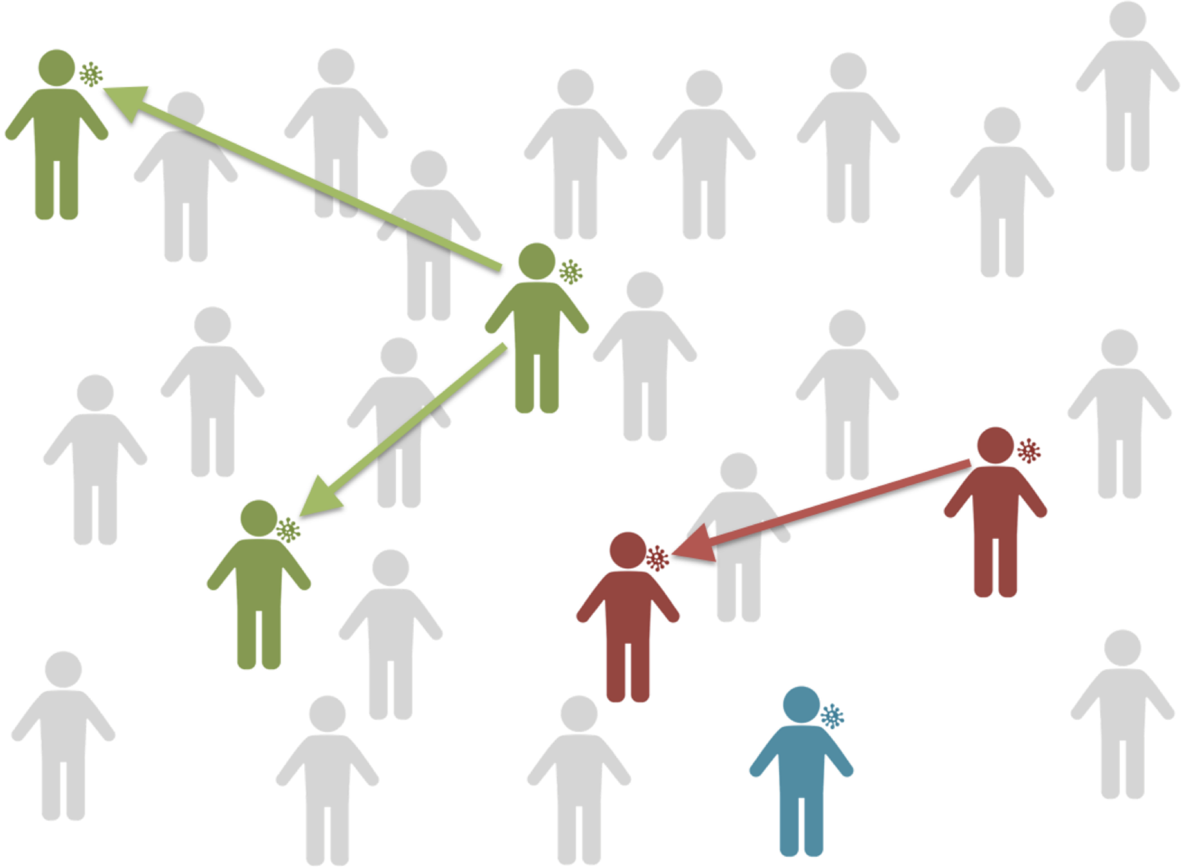
Participants

- 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

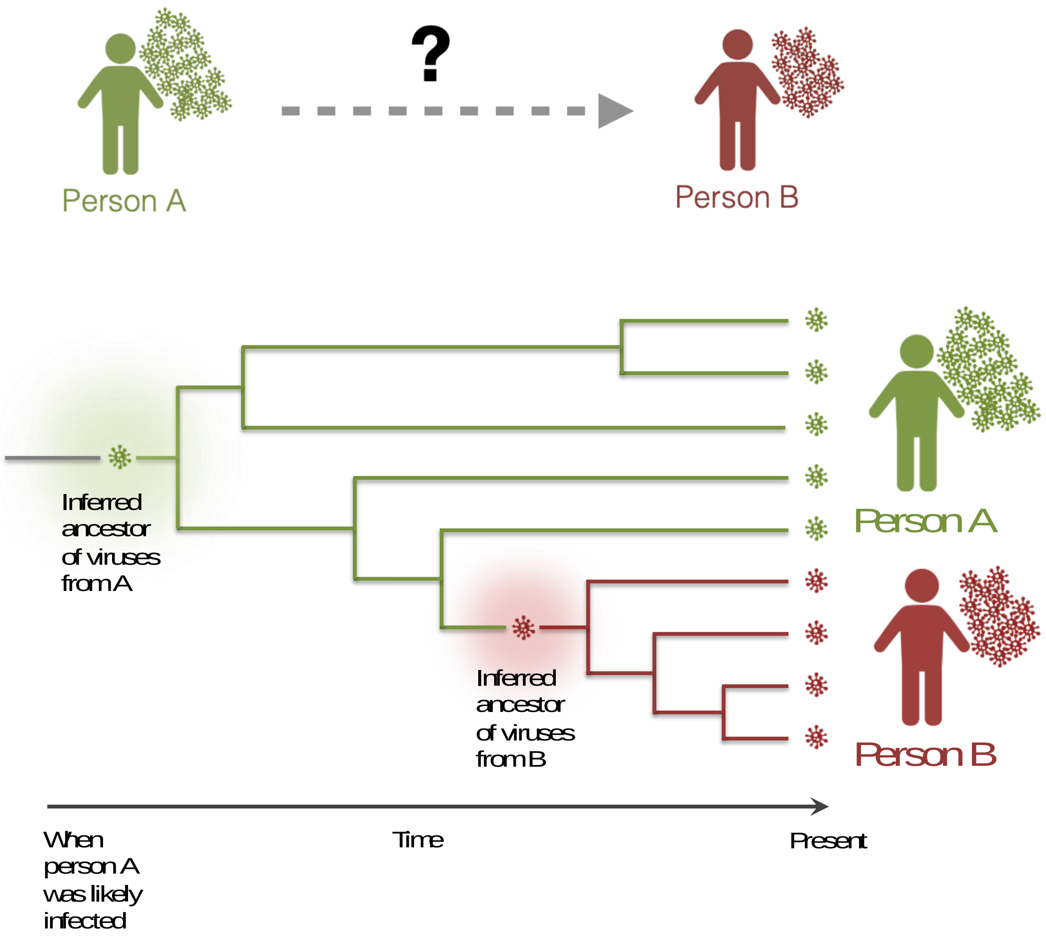


Source attribution

- 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



- Phylogenetics helps use 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

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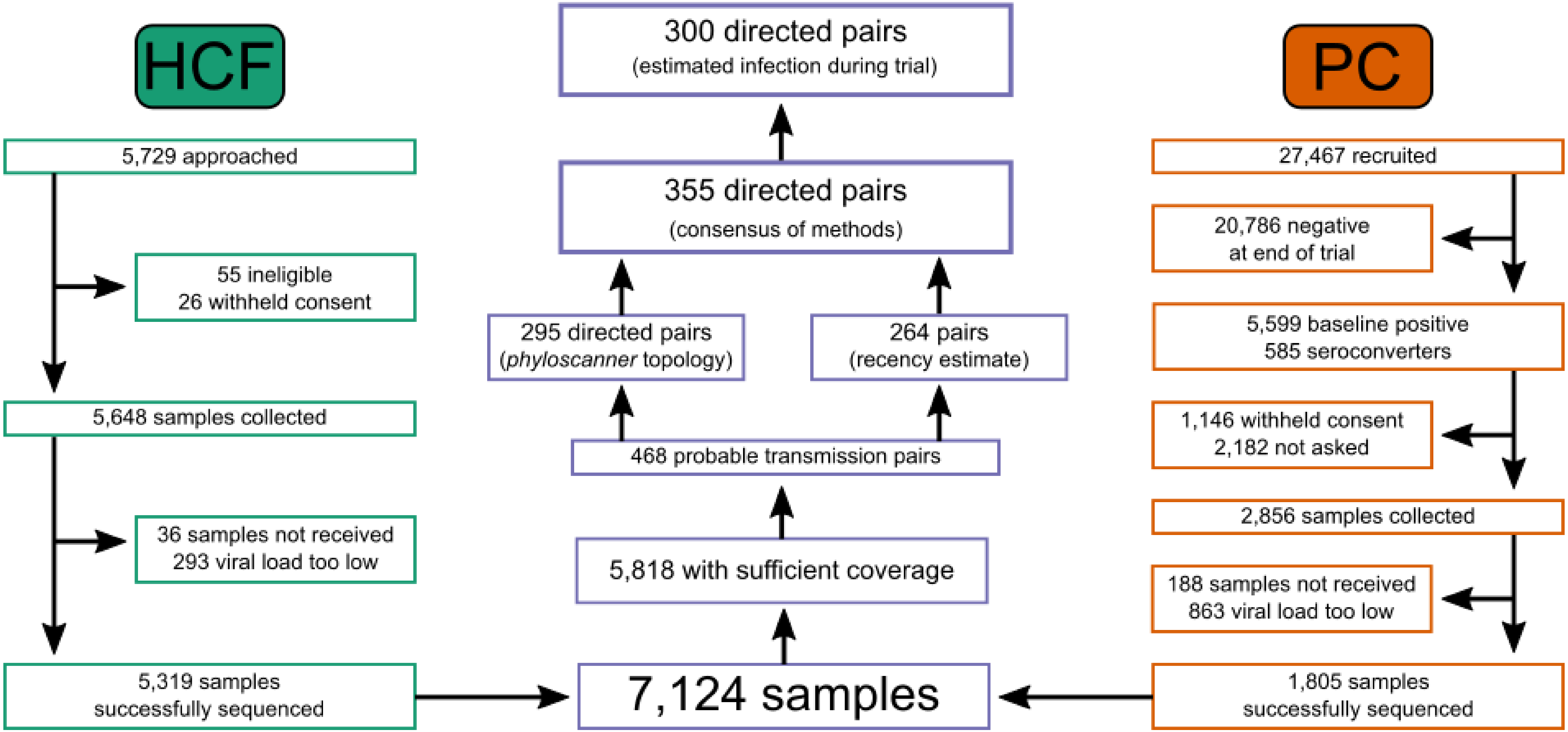
Summary of recruitment



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

7,124 samples

5,818 with sufficient coverage

468 probable transmission pairs

295 directed pairs (*phyloscanner* topology)

264 pairs (recency estimate)

355 directed pairs (consensus of methods)

300 directed pairs (estimated infection during trial)

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Results

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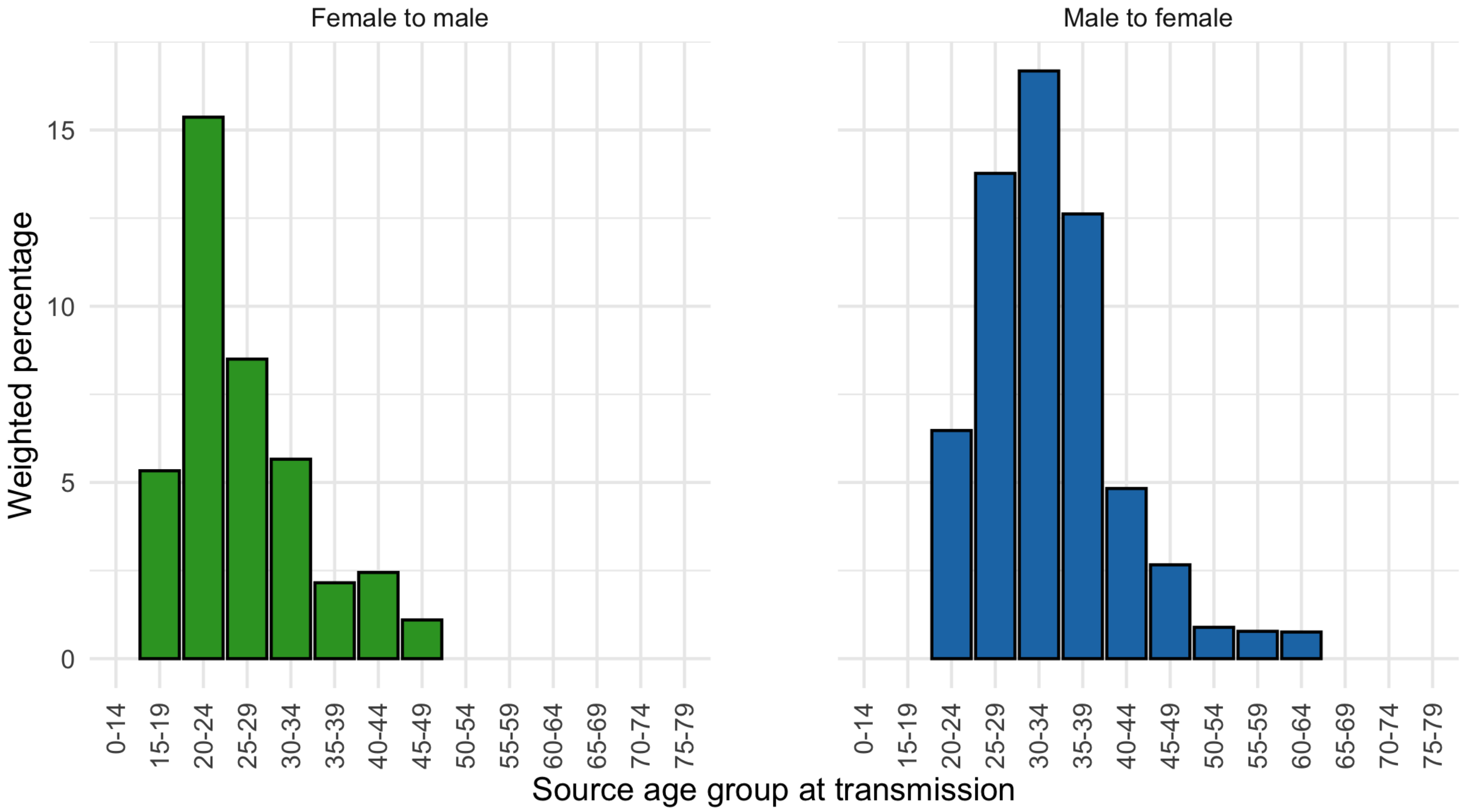
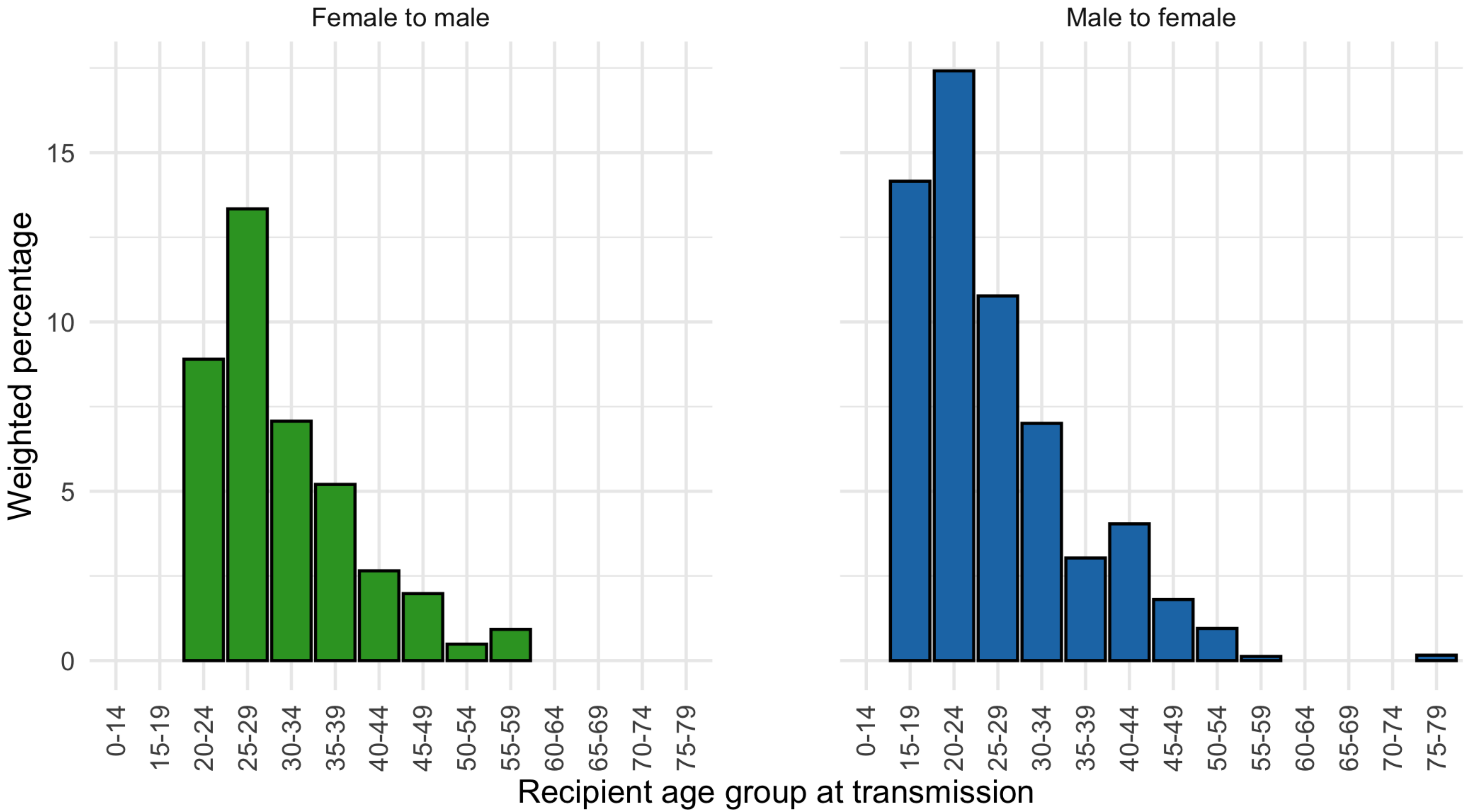

Female to male
Male to female
Weighted percentage
0
5
10
15
0-14
15-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
75-79
Source age group at transmission


Female to male
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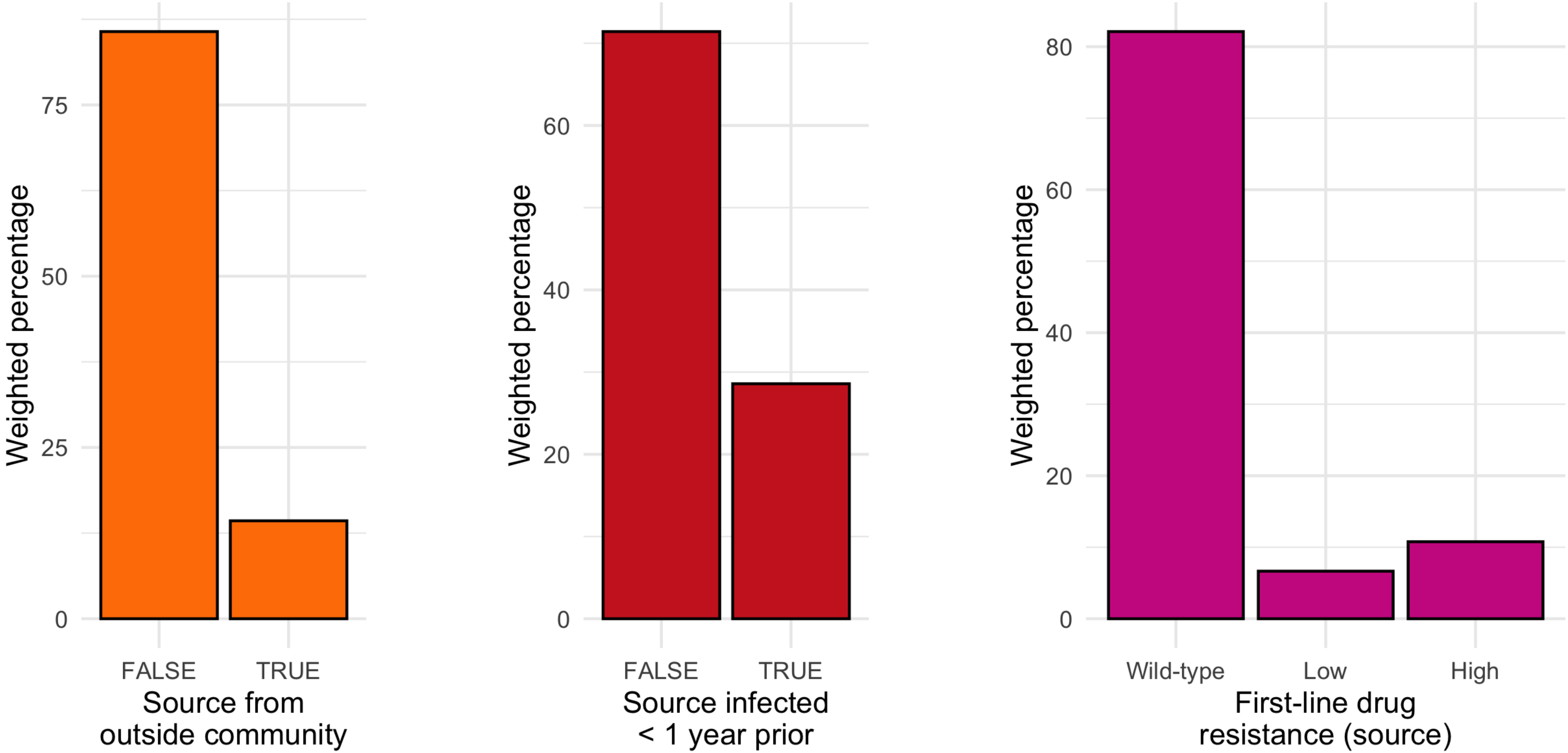
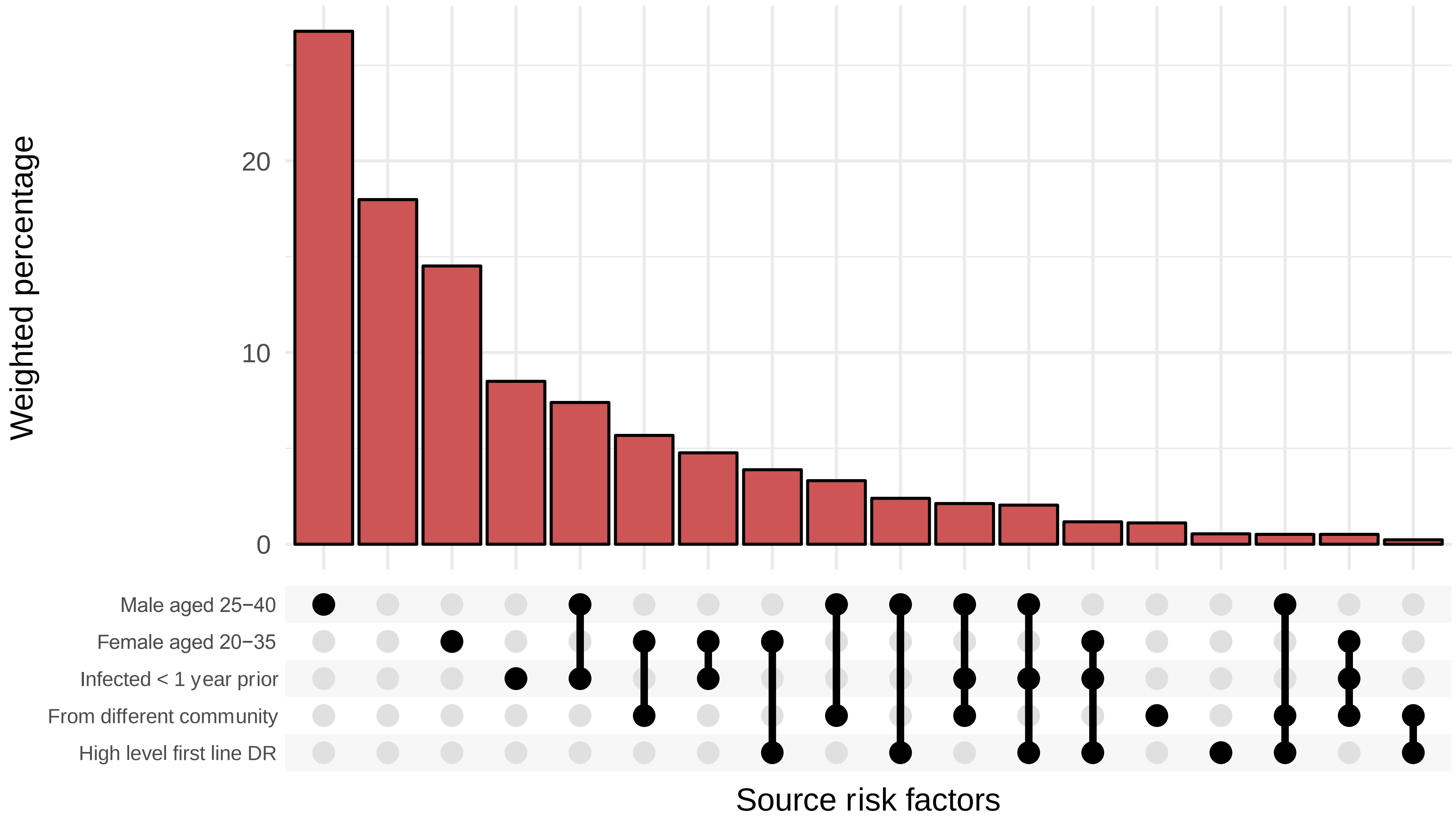
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
75-79
Recipient age group at transmission


Weighted percentage
75
50
25
0
FALSE
TRUE
Source from outside community
Weighted percentage
60
40
20
0
FALSE
TRUE
Source infected < 1 year prior
Weighted percentage
80
60
40
20
0
Wild-type
Low
High
First-line drug resistance (source)



Weighted percentage
20
10
0
Male aged 25−40
Female aged 20−35
Infected < 1 year prior
From different community
High level first line DR
Source risk factors

Conclusions

4

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

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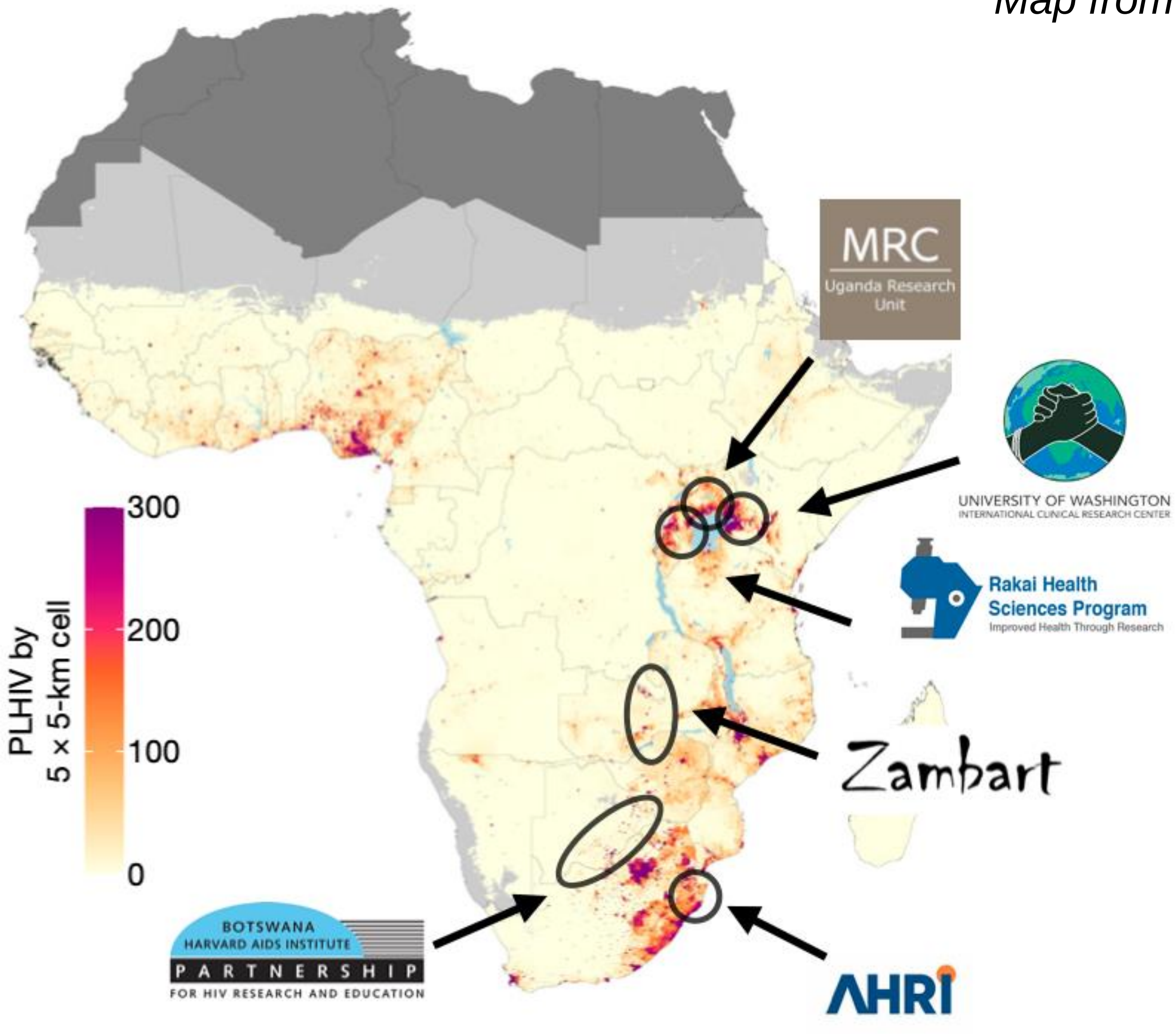
> HIV transmission is driven by “typical” sexual interactions and control strategies must take this into account

The PANGEA-HIV consortium

Map from Dwyer-Lindgren et al., 2019



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All PANGEA researchers, staff and study participants

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