

Data

- Retrospective study, data from individuals diagnosed with TB in Blantyre, Malawi, between January 1, 2015–December 31, 2019
- 717 whole-genome sequences (WGS) of culture-positive TB [n=3856]
- Participant data include
 - Demographics + socioeconomic variables
 - TB treatment outcome
 - Healthcare visit history
 - HIV infection/treatment status

Aims

Build methods to improve our understanding of **transmission** using **WGS data**:

1. **Estimate transmission flows** between different regions in Blantyre
 - a. Need to account for sampling differences among regions
2. Identify patient characteristics associated with **recent transmission**
 - a. Combinations of age, geographic location, socioeconomic status, and HIV infection could be associated with higher transmission
3. Reconstruct **person-to-person transmission networks** in closely-related clusters.
 - a. Need to account for unobserved cases contributing to transmission
 - b. Need to account for phylogenetic uncertainty

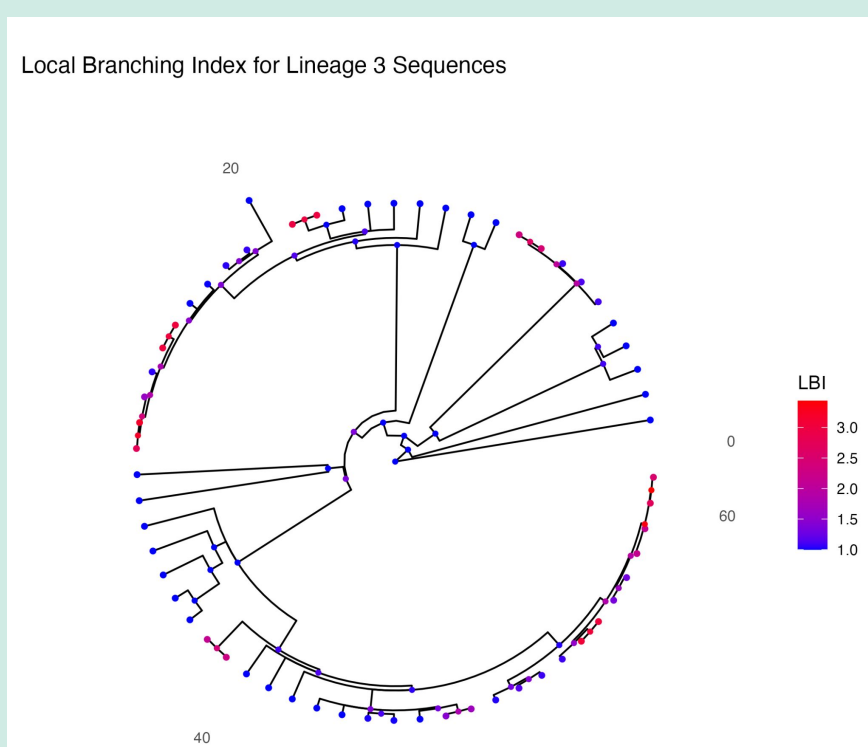
2. Using phylogenetic tree statistics to detect high fitness sequences

Local branching index (LBI): a proxy for fitness/transmission. Inverse-exponentially-weighted mean of distances from each vertex in the phylogeny. LBI is a measure of branching rate in the phylogenetic tree describing the 717 sequences.

Sequences (observed or inferred) with many closely-related other sequences have high LBI (similar to timed haplotype density)

Some characteristics of individuals correlate with transmission success as measured by LBI

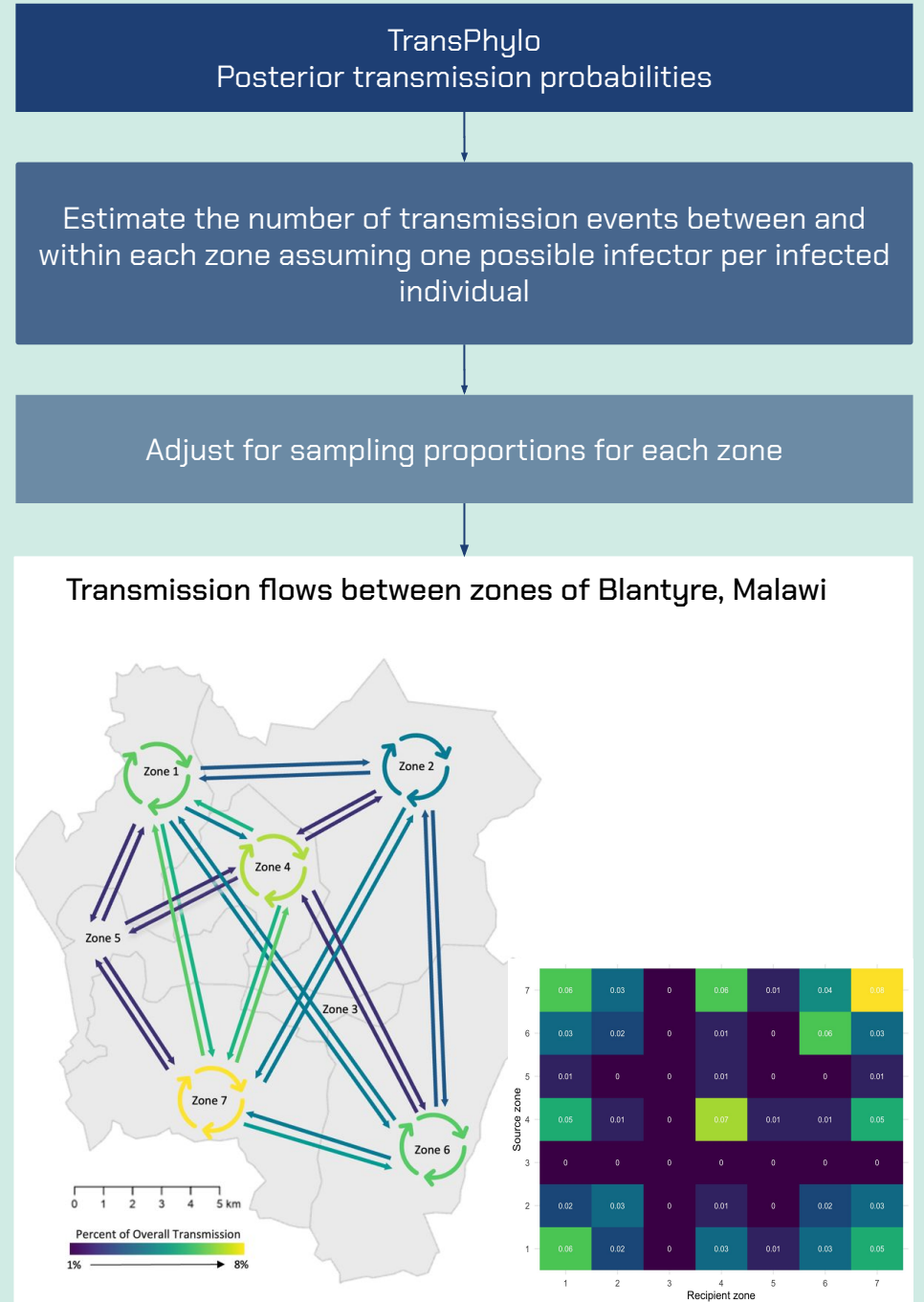
- Socioeconomic status
- HIV infection
- Location in Blantyre



References

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3:e03568.
3. Didelot X, Fraser C, Gardy J, and Colijn C. (2017) Genomic
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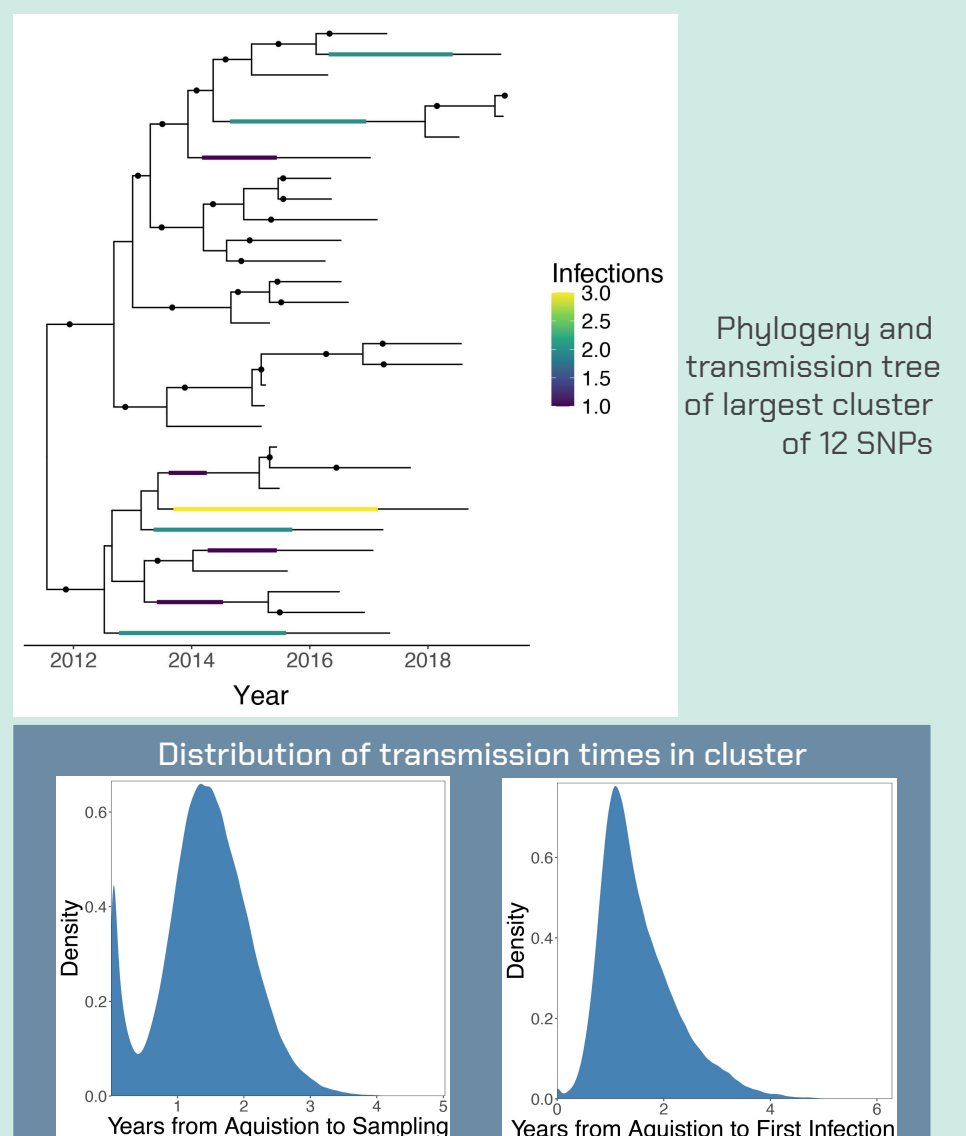
1. Estimating transmission flows



3. Simultaneous inference of phylogeny and transmission tree

We applied the Bayesian software BREATH to estimate transmission and evolutionary history of small TB clusters

BREATH constructs the phylogenetic tree and the transmission tree simultaneously.



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