Does HIV infection reduce the probability of transmission of pulmonary tuberculosis?

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Introduction

HIV positive patients with pulmonary TB are thought to be less likely to transmit *M.tuberculosis* than HIV negative patients, even accounting for smear status, because they have a shorter duration of disease.

Whole genome sequencing of *M.tuberculosis* can identify who transmits to whom, and provides a new method to test this hypothesis.

Methods

Setting: Karonga District, northern Malawi

Patients: All patients with culture-confirmed TB diagnosed 1996-2010. Asked about prior contacts. 8% of HIV+ on ART before TB diagnosis.

Transmission defined using number of single nucleotide polymorphisms (SNPs) from whole genome sequencing:

1) Define appropriate cut-off no. of SNPs using repeat specimens in individuals (Fig 1)[1]

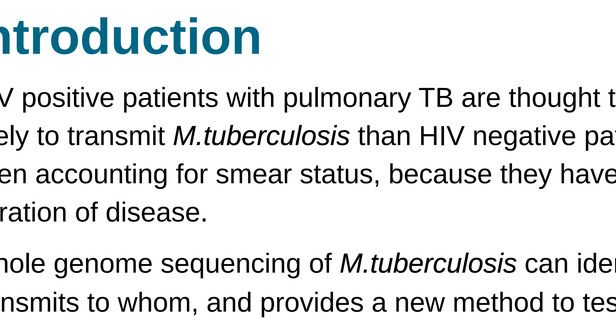


Fig. 1 Number of SNPs between pairs of samples from individuals from this population, suggesting cut-off at ~ 10 SNPs

2) Compare epidemiologically-linked pairs

3) Construct transmission networks using SeqTrack

4) Compare transmission from HIV+ and HIV- TB patients, controlling for other factors

Results

1687 high quality sequences (72% of all culture-positive patients in this period).

Epidemiologically-linked pairs

Sequences available for 187 pairs (Fig 2):

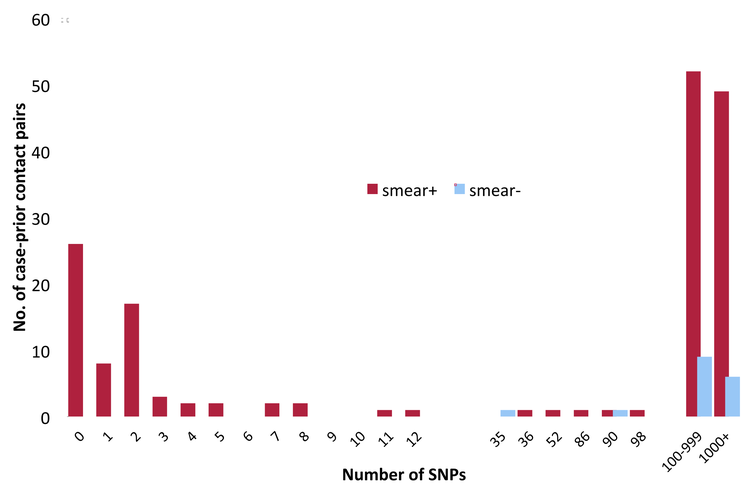


Fig. 2 Number of SNPs between epidemiologically linked pairs

Using cut-off of ≤10 SNPs, no transmission from 17 smear negative patients. Those with 11-99 SNPs excluded as uncertain. Among those with smear positive prior contact transmission confirmed in:

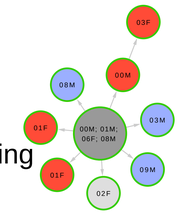
Table 2: Proportion of transmissions confirmed from HIV+ and HIV- smear positive named source contacts

	Transmission confirmed		Relative risk	Adjusted for closeness of contact
HIV +	38.0%	22/71	0.83 (0.5-1.2)	0.78 (0.54-1.1)
HIV-	46.0%	29/63	1	1

In population, ~ 60% smear+ TB cases are HIV+. If transmission reduced by 22%, would account for 47% of transmissions resulting in disease.

Results

Network analysis[2]



Allow up to 10 SNPs.

Exclude data from last 3 years (except for measuring transmissions).

32% (431/1346) of patients identified as source of transmission to at least one more patient (and up to 12 others).

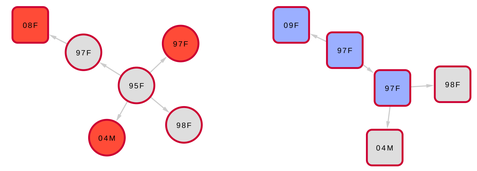


Table 2: Transmissions from HIV+ and HIV- pulmonary TB patients in whole population

	Transmission		Odds ratio from ordered logistic regression	Adjusted for age, sex, year, smear status, lineage
HIV +	30.8%	181/588	1.1 (0.81-1.5)	1.2 (0.82-1.6)
HIV-	28.6%	91/318	1	1

Conclusions

Transmission of *M.tuberculosis* from smear+ TB patients resulting in disease in other patients is only slightly reduced, if at all, in HIV positive patients compared to HIV negative patients.

Where a high proportion of TB patients are HIV positive, they may be the major source of transmission resulting in TB disease.

References

[1]Guerra-Assunção JA et al. J Infect Dis 2014 PMID 2533729

[2]Guerra-Assunção JA et al. eLife 2015 (in press)

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