Mycobacterium tuberculosis infection decreases the HIV-1 antibody response

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BACKGROUND

Hypothesis: MTB infection influences HIV-1 antibody responses

- Majority of MTB exposed do not develop active disease
  - 1.7 billion infected
- HIV-1 infection heightens risk of active tuberculosis
- MTB infection
  - enhances HIV-1 control (Kusejko 2020 PLoS Biol.)
  - elevates non-communicable diseases
  - may boost unrelated antibody responses

METHODS

Population: People with HIV from the Swiss HIV Cohort Study

Exposure: MTB infection

- Infected (cross sectional) (n=129)
- Active TB (>180 days post outcome measure) (n=16)

Control: MTB uninfected (n=1,940)

Outcome: Change in HIV-1 antigen binding/neutralization

- Swiss 4.5k study
  (Rusert 2016 Nature Med.; Kadelka 2018 J. Exp. Med.)
- 8 HIV-1 virus neutralization panel (score from 0 to 24)
- 13 HIV-1 antigen binding panel (relative binding 0 to 1)

Covariables:

- Sex, Age, Time since infection (years off ART), Ethnicity (White, Black, Other), HIV RNA viral load, CD4 T cell count, HIV diversity

Statistical methodology:

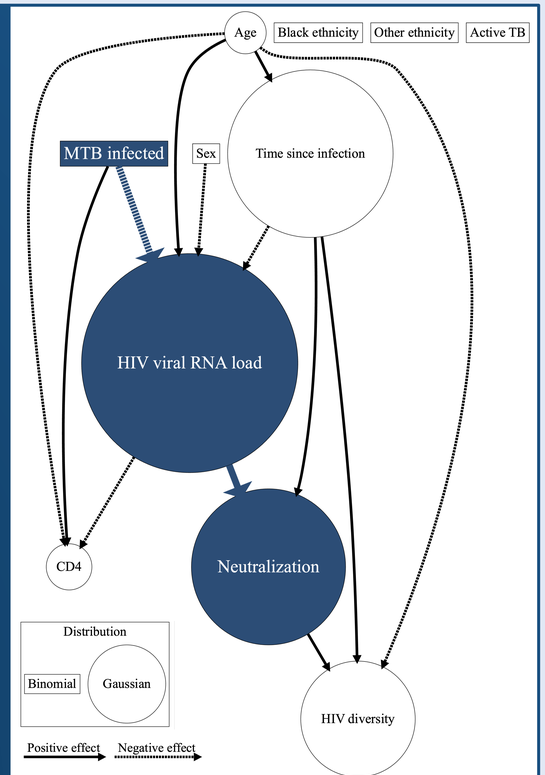
- Linear/Tobit Regression & Bayesian networks

RESULTS

MTB infection **lowers HIV-1 viral load**

Reduces HIV-1 **antigen** exposure

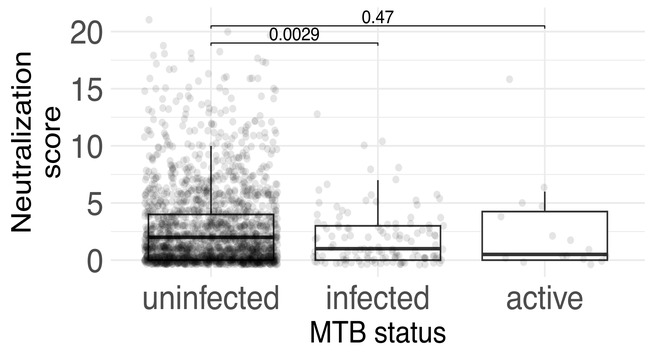
Impedes (neutralizing) HIV-1 **antibody development**



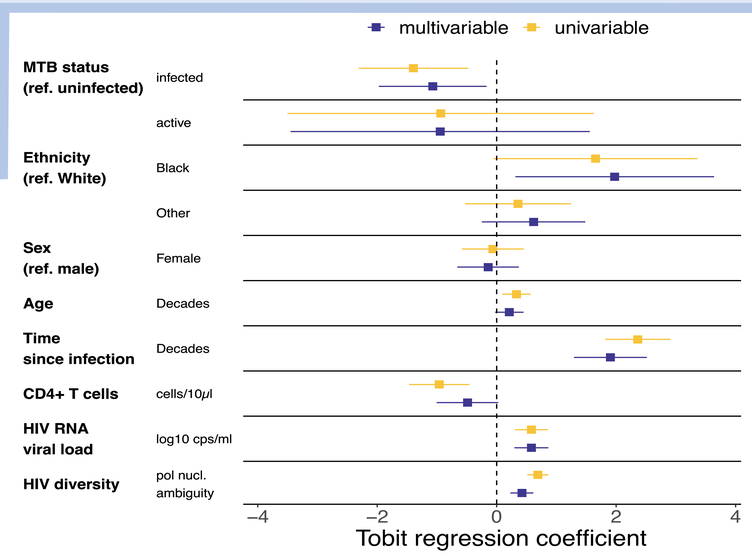
Additive Bayesian network of MTB status, HIV neutralization, and demographic characteristics.

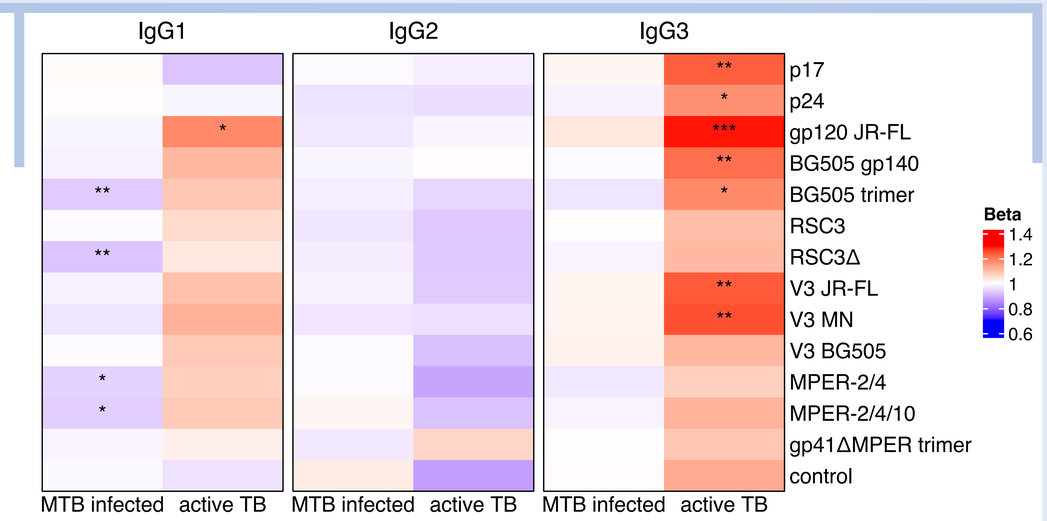
CONCLUSION

- **MTB infection in PWH is associated with:**
  - **Decreased HIV immune response**
  - **Lower HIV-1 neutralization**
  - **Lower HIV-1 IgG1 binding response**
- **Pathway most likely indirect**
  - **MTB reduces HIV-1 viral load**
  - **Reduces antigen exposure required for antibody development**
- **Additive Bayesian networks allow to identify associations and pathways between clinical and immunological variables**
- **Active TB >180d post antibody measure in PWH is associated with:**
  - **Increased IgG3 binding response**
  - **Potential value for diagnostic biomarker**



Neutralization score in dependence of MTB status, adjusted for demographic characteristics.





Association of MTB status (ref. uninfected) with **relative antibody binding** against HIV antigens, adjusted for demographic characteristics.

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