Exploring early, culture-negative TB with ultrasensitive nucleic acid tests.

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Methods and Materials

- New highly-sensitive PCR tests such as GeneXpert Ultra are replacing the culture as reference standard for diagnosis.
- There has been an increasing observation of “False-positives” (Ultra positive and culture negative)

Hypothesis

- We proposed these symptomatic individuals are not “false-positives”, but actually have early or culture-negative TB

Substudy to a multicenter diagnostic accuracy evaluation of Ultra

- Adults with pulmonary TB signs/symptoms and without recent TB treatment in Uganda, Kenya and South Africa between July 2018 and May 2018.
- Sputum, blood and urine were collected on enrollment and follow up (over 12 months)
- Based on results participants were classified as “discordants”
- A negative control and positive control was also enrolled (Matched by age, sex HIV status, and previous TB history)

There was no statistical difference regarding distribution of gender, age, enrollment site and HIV status between discordants and non-discordants

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Results

- During follow up, almost half (49%) of discordants were started on TB treatment. Of the non-treated group, one participant grew MTB and 11 had persistent Ultra result that negativized during follow up without any intervention.

Conclusions

- We found microbiologic signals of TB during follow up of discordants (Persistent Ultra, positive TB culture, positive augmented TB culture) suggesting Ultra can identify culture-negative TB
- Ongoing evaluation of host and bacterial biomarkers from the substudy samples will help understand early or culture-negative TB