Impact of GeneXpert MTB/RIF on Triage of Respiratory Isolation Rooms for Inpatients with Presumed TB: A Hypothetical Trial.

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Background:

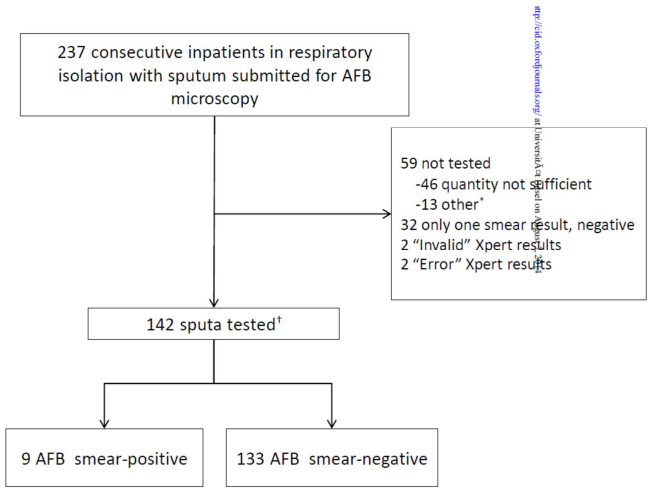
- Evaluation of individuals with presumed tuberculosis (Tb) is time- and resource-intensive, as sensitivity of sputum smear-microscopy is rather poor for the diagnosis of Tb and culture may require weeks.
- Transmission of TB in health-care setting poses a risk to patients and health-care workers.
- CDC guidelines (1994): screening, personal respiratory protection devices AND respiratory isolation until three serial respiratory samples (8-24 hours apart) are smear-negative for acid-fast bacilli.
- CDC guidelines (2009): PCR testing on at least one respiratory specimen.
- Effective but inefficient in low-burden setting: requires several days, can delay tests and procedures, is expensive (isolation), may have a negative impact on employment of the patients….AND unnecessary for most patients in a low-burden setting, as only a small proportion of patients placed in isolation actually have TB!
- GeneXpert MTB/RIF has a high sensitivity and specificity for smear-positive TB (100%), and a moderate sensitivity for smear-negative Tb (50-70%); short turn-around time (3-4 hours).
- **Study objective**: To analyze the impact of GeneXpert testing on respiratory isolation usage in a low-burden country.

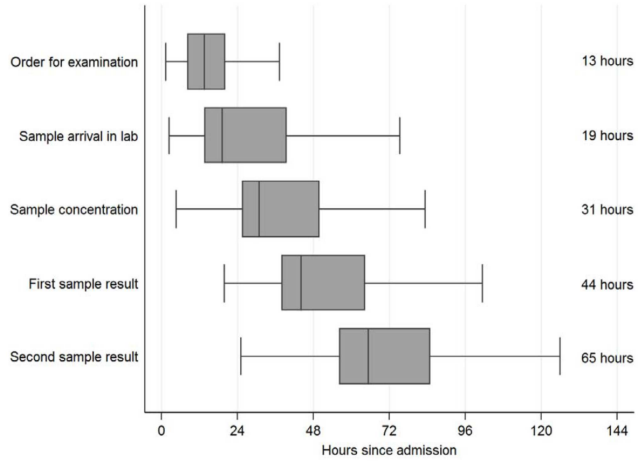
Methods:

- Prospective, observational, hypothetical single-centre study (San Francisco).
  - Included patients: consecutive patients admitted to the medical service for evaluation for pulmonary Tb between 3/2012 and 3/2013.
  - Patients were placed in respiratory isolation, submitted at least **two** sputa for microscopy.
  - Discharge from isolation after **two negative, concentrated sputum smears**. All patients submitted a **third** sputum sample afterwards.
- Exclusion criteria : patients with only one sputum sample examined.
- Procedures:
  - Sputum concentration/decontamination; auramine-rhodamine staining; liquid/solid media culture
  - Xpert testing on residual sputum pellet after concentration of the first sputum sample.
  - Smear results were reported before Xpert testing was done; Xpert results were **NOT** reported.
- Statistical analysis:
  - Calculation of diagnostic accuracy of smear microscopy and Xpert testing in reference to the gold standard (positive culture among first THREE sputum samples). Positive/negative smear was defined as positive/negative result on the first **TWO** sputum samples collected.
  - Calculation of median time from hospital admission to processing, reporting and discharge from hospital.
  - Hypothetical time from admission to first Xpert result: performed on concentration (once daily at 4pm after sputum concentration) vs. performed on unconcentrated sputum sample (around the clock). Turn-around time of three hours.

Results:

- Figure 1 (Study enrollment): 142/237 inpatient admissions were included.





- Table 1 (Clinical characteristics): 30% HIV-positive, >90% sputa (expectorated or induced).
- Table 2/3 (Diagnostic accuracy): 9 culture-positive patients; 8/9 smear-positive and Xpert-positive, 1/9 smear- and Xpert-negative (false-negative, same patient). 1 smear "false-positive" sample as culture grew M. abcessus. Sensitivity 89%, negative-predictive value 99% for both tests.
- Figure 2 (Median time): 44 hours from admission to report of first smear result, 65 hours until final smear diagnosis (positive/negative) and 66 hours until final negative smear diagnosis.
- Table 4 (Time saved with Xpert strategy): respiratory isolation reduced by a median of 35 hours per patient or 159 days during one year. Even greater reduction with Xpert testing before concentration (45 hours, 258 days).

Discussion:

- Single sputum Xpert test to guide inpatient isolation management decisions could reduce the median duration of time in isolation by nearly **2 days** (and even more if three sputa are performed!!).
- Attractive and **safe** (NPV of 99%) in low-burden setting (6% of inpatients undergoing evaluation for pulmonary Tb were culture-positive) with the potential of significant cost-savings (even more in the case of a three-sputa strategy).
- Limitations:
  - Sputum quality of first sputum and smear positivity of subsequent sputa?
  - Utility of a second Xpert test (but low-yield of a second test in low-burden setting; number needed to test 200!)?
  - Low number of Tb cases; Exclusions of a significant number of cases.
  - Unconcentrated strategy not tested.
  - No data about time from admission to discharge from isolation.
  - Not an intervention study (physician judgement? How would the result be used in reality?)
  - GeneXpert testing still not widely available (costly!) AND still imperfect compared to culture!
  - In-house data about duration and efficiency of isolation (how many isolated patients are diagnosed with Tb? Impact of timely bronchoscopy?)
  - Suggested strategy: discharge from isolation after a single smear- and Xpert-negative sputum (or BAL) BUT collection of two additional sputum samples afterwards?

Conclusion: Implementing Xpert testing for inpatients with possible pulmonary Tb has the potential to reduce duration of respiratory isolation of patients unlikely to have TB in low-burden settings.