Auld, AF; Fielding, KL; Gupta-Wright, A; Lawn, SD (2016) Xpert MTB/RIF - why the lack of morbidity and mortality impact in intervention trials? Transactions of the Royal Society of Tropical Medicine and Hygiene, 110 (8). pp. 432-44. ISSN 0035-9203 DOI: https://doi.org/10.1093/trstmh/trw056

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The percentage of rifampicin resistant (RR) TB patients with missing information on RR treatment initiation declined from 52.4% in the baseline phase to 31.0% in the Xpert phase, p<0.001. No differences in the percentage of enrollees documented to be LTFU before RR treatment (0.9% pre- vs. 2.3% post-Xpert, p=0.30), or documented to be dead before RR treatment (2.4% pre- vs. 1.0% post-Xpert, p=0.50) were noted.

Abbreviations: TB, tuberculosis; LTFU, loss to follow-up; KPS, Karnofsky Performance Score; NA, not available; BMI, body mass index; NS, not statistically significant; SS, statistically significant on the basis of an odds ratio with 95% confidence interval excluding 1 (p-value not provided); m, month; ART, antiretroviral treatment; ICU, intensive care unit; OR, odds ratio; CI, confidence interval; SA, South Africa

a Both median TB score (2 vs. 2, p=0.85), and median Karnofsky Performance Score (KPS) (80 vs. 90, p=0.23) in culture-positive patients, who had started TB treatment, did not differ at 2 months post randomization, or at 6 months.

b In XTEND, the percentages reported here represent those not starting TB treatment by 28 days after bacteriological TB confirmation.

c Composite poor outcome was death, LTFU, and treatment failure.

d Composite poor outcome was death, LTFU, and treatment failure.

e Heterogeneous confidence intervals.

f P-value was not provided. Instead, the 95% confidence interval was provided and included 1: 29.6% versus 31.7%. OR=0.93; 95% CI=0.79-1.08

g P-value was not provided. In the text, the paper states “loss to follow-up was not changed by the intervention (16.2% vs. 15.9%)”.

h No p-value was provided. The text states that “Adjusted for HIV status, age group and city, the intervention resulted in a 35% decrease in TB-attributed deaths (OR=0.65, 95%CI=0.44-0.97)”

i The percentage of rifampicin resistant (RR) TB patients with missing information on RR treatment initiation declined from 52.4% in the baseline phase to 31.0% in the Xpert phase, p<0.001. No differences in the percentage of enrollees documented to be LTFU before RR treatment (0.9% pre- vs. 2.3% post-Xpert, p=0.30), or documented to be dead before RR treatment (2.4% pre- vs. 1.0% post-Xpert, p=0.50) were noted.

Table 3: Treatment Outcomes Assessed in Clinical Trials Designed to Estimate Xpert Impact on Patient Outcomes

<table>
<thead>
<tr>
<th>Study, author, date</th>
<th>LTFU before TB treatment among Microbiologically-Confirmed TB Patients</th>
<th>TB Treatment Outcomes</th>
<th>LTFU and Mortality among all Study Enrollees</th>
<th>Mortality predictors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Micro Xpert p</td>
<td>2m TB scorea 2m KPSa</td>
<td>2m Mortality 3m Mortality Micro Xpert p</td>
<td></td>
</tr>
<tr>
<td>TB-NEAT⁹</td>
<td>15% 8% 0.03</td>
<td>32% 29% 0.55</td>
<td>32% 8% 8% 0.71</td>
<td></td>
</tr>
<tr>
<td>XTEND[10,20,21]</td>
<td>14.9% 17% 0.91</td>
<td>Compositec 12.5% 11.7% 0.8</td>
<td>6m Mortality 5.0% 3.9% 0.43</td>
<td></td>
</tr>
<tr>
<td>Brazil Stepped Wedge[12,21]</td>
<td>NA NA NA</td>
<td>Composite⁴ 31.7% 29.6% NS⁵</td>
<td>NA NA NA NA NA NA NA</td>
<td></td>
</tr>
<tr>
<td>Zimbabwe RCT¹⁴</td>
<td>NA NA NA</td>
<td>Composite⁵ 12.5% 12.7% 0.750</td>
<td>6m Mortality 3.8% 3.4% 0.52</td>
<td></td>
</tr>
<tr>
<td>South Africa Single Clinic CRT[12]</td>
<td>NA NA NA</td>
<td>2m Mortality 17% 14% 0.80</td>
<td>2m Mortality 17% 17% 0.96</td>
<td></td>
</tr>
<tr>
<td>Uganda Pre-post Trial[13]</td>
<td>NA NA NA</td>
<td>2m LTDF 10% 2% &lt;0.001</td>
<td>1m Mortality 34% 27% 0.26</td>
<td></td>
</tr>
<tr>
<td>SA ICU RCT[15]</td>
<td>NA NA NA</td>
<td>3m Mortality 42% 32% 0.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indonesia Pre-trial[18]</td>
<td>52.4% 31.0% &lt;0.001</td>
<td>NA NA NA NA NA NA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- HIV-positive vs. HIV-negative
- Lower baseline TB score.
- Known HIV-positive and not on ART vs. HIV-negative
- Not knowing HIV status vs. HIV-negative
- BMI <18.5 vs. 18.5-24.9
- Age <30 vs. ≥50 years
- Higher number of TB symptoms
- Male sex
- HIV positive vs. HIV-negative
- HIV unknown vs. HIV-negative
- Rio vs. Manaus
- Male sex
- Low CD4 count (<100) vs. >100
- TB diagnosed at enrollment before ART start.

Mortality predictors among all ICU enrollees (N=341), not just those randomized:
- Age 24-39 vs. <24 years
- HIV-positive and ART unknown vs. HIV-positive not on ART.
- APACHE-II score >25 vs. <20.

Multivariable analysis: Mortality predictors for unfavorable TB treatment outcome:
- Male sex
- HIV positive vs. HIV-negative
- HIV unknown vs. HIV-negative
- Rio vs. Manaus
- Male sex
- Low CD4 count (<100) vs. >100
- TB diagnosed at enrollment before ART start.

Multivariable analysis:
- APACHE-II score >25 vs. <20.

Multivariable analysis:
- HIV-positive vs. HIV-negative
- Lower baseline TB score.