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Title: A multicentric cohort analysis of culture conversion and reversion in multidrug resistant tuberculosis (MDRTB) patients

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Body: **BACKGROUND** Culture conversion is used to define the duration of the intensive phase of treatment for MDRTB. We have estimated the rates and predictors of culture conversion and reversion and described treatment outcomes according to culture conversion and reversion. **METHODS** Observational retrospective cohort analysis of MDRTB patients, with at least 12 months of follow-up in MSF supported projects in 5 countries. Culture conversion was defined by 2 consecutive negative cultures and reversion by 2 consecutive positive cultures after conversion. Favourable outcomes (cure or treatment completed) and unfavourable outcomes (death or failure) conformed with WHO case definitions. **RESULTS** From 1185 patients, 26% showed resistance to injectable second-line drugs (SLDs) and/or fluoroquinolones on baseline testing. The rate of culture conversion was 73% and the median time to conversion was 3.8 months. Out of 867 culture converted patients 11% reverted with a median time to reversion of 4.4 months after conversion. Previous treatment with SLDs and SLD resistance at baseline were independently associated with the absence of culture conversion at 12 months and culture reversion. Unfavourable outcomes were significantly higher among patients who reverted after initial conversion 41/54 (75.9%) compared to those who did not revert 21/403 (5.2%), $p < 0.001$. **DISCUSSION AND CONCLUSION** Like patients with documented resistance to SLD, patients with a history of treatment with SLDs are more likely to remain culture positive at 12 months of treatment or to present culture reversion after initial conversion.

Culture reversion should be considered in the definition of treatment failure.