

Bayesian latent class analysis versus composite reference standards for estimating tuberculosis meningitis diagnostic test accuracy

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Background: Tuberculosis meningitis (TBM) represents 2-5% of the global annual TB burden, or 0.2-0.5 million cases^[1], a highly uncertain prevalence estimate as there is no reliable gold standard to definitively classify it. Despite recognition of the imperfect nature of employed reference standards, naïve methods used to evaluate accuracy of new TBM tests, e.g. composite reference standards (CRS), do not account for the uncertainty in their accuracy. Consequently, estimates of TBM diagnostic test sensitivity and specificity based on such methods may be biased.

Aims: We used Bayesian latent class analysis to estimate Xpert MTB/RIF (Xpert) accuracies for diagnosing TBM and compared these to estimates from multiple CRSs.

Methods: An existing dataset of all adults presenting to a tertiary care hospital with suspected extrapulmonary tuberculosis in New Delhi, India, in 2012 was analysed. We selected individuals undergoing investigation for TBM with valid results for bacterial culture, smear microscopy, cytopathology/histopathology, and Xpert. A heuristic model was created to understand relationships between latent classes and tests, with a random effect to denote bacterial burden (Figure). A Bayesian approach was used to estimate the latent class model. Multiple CRSs were defined by increasing numbers of positive component tests. Analyses were performed using RJAGS (Version 4-8) through R-studio (3.5.2).

Results: Using 224 patients with suspected TBM, Xpert sensitivity and specificity were 51.2% (95%CrI:34.2-71.0) and 99.6% (95%CrI:97.7-100). Xpert sensitivity varied dramatically by CRS definition: sensitivity was 33% (95%CI:98-100) with a CRS of any one positive test result, increasing to 52% (95%CI:34-69) with two positive results, and reaching 100% (95%CI:48-100) with all four positive results.

Conclusions: Unlike CRSs, Bayesian latent class analysis produces estimated test accuracies that incorporate reference standard uncertainty and conditional dependence for TBM, the most severe form of tuberculosis.

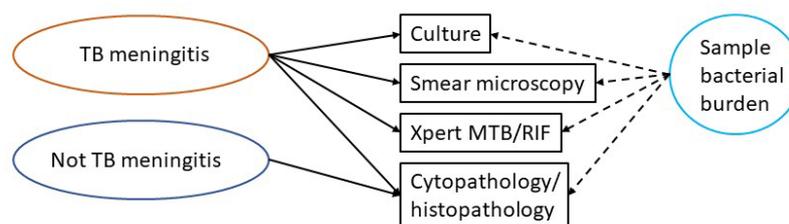


Figure: Heuristic model for TBM showing assumed relationships between latent classes (ovals), diagnostic test results (rectangles), and random effect (circle).

Keywords

Latent class analysis, diagnostics, tuberculosis meningitis, composite reference standards

References

^[1]World Health Organization, *Global tuberculosis report, 2019*, Geneva: World Health Organization.