

Protocol for a systematic review and meta-analysis of whole blood mycobacterial growth assays for assessing human tuberculosis susceptibility

Search strategy and selection criteria

PubMed and EMBASE will be searched to identify relevant studies using the following search terms: (“mycobacterial” or “mycobacterium” or “mycobacteria” or “tuberculosis” or “BCG”); (“growth inhibition” or “mycobacterial immunity” or “antimycobacterial immunity” or “MGIA”) and (“assay” or “in vitro” or “whole blood”). References cited by these publications will be searched to find other relevant articles.

For inclusion in this study, peer-reviewed, English-language publications will be selected that describe cross-sectional, case-control, or cohort studies using WBMGA to study mycobacterial growth in human blood samples in relation to: risk of TB infection; risk of TB disease; established or possible TB risk factors. All available literature will be studied without the limitation of any start date.

Two reviewers will independently review potentially relevant publication titles, then abstracts and finally full-text publications for eligibility, with discrepancies being resolved by discussion and potentially resolved by a third reviewer, if necessary. Quality of the included studies will independently be evaluated by two reviewers using a quality assessment tool from National Heart, Lung, and Blood Institute (NHLBI), leading to an overall rating for the quality of each study of “good”, “fair”, or “poor”. Disagreements will be resolved through discussion and potentially resolved by a third reviewer, if necessary.

Data analysis/synthesis of findings

WBMGA results, study characteristics and methodological characteristics will be extracted from each publication and categorized by factors known to decrease or likely to affect TB susceptibility by JB and CAE.

WBMGA results will be presented as statistically significant or not. Additionally, ratios of one study group versus the other will be calculated for each of the main findings of the publications, representing relative growth, and presented in a figure.

Meta-analyses will be performed by pooling relative growth ratios of studies that are deemed comparable and calculating the respective weighted means of these ratios, including weighted confidence intervals.

Heterogeneity of data will also be assessed.