**Reporting of outcomes in phase II studies of drug-sensitive tuberculosis**

**LJ Bonnett1.,2 & G Davies2**

1Department of Biostatistics, University of Liverpool

2Department of Clinical Infection, Microbiology & Immunology, University of Liverpool

**Background:** TB remains a major killer amongst infectious diseases and current treatment involves a four-drug regimen for at least six months.Clinical development of a single novel TB drug is expected to take at least six years, while a completely novel combination regimen would require twenty years or more. New drugs and regimens are required to shorten treatment duration, reduce toxicity and combat drug resistance but the optimal methodology to define the critical path for these regimens is not well-defined.

We reviewed historic phase II trials of pulmonary tuberculosis in newly diagnosed patients to quantify and rank the efficacy of combinations of seven drugs of interest – ethambutol (E), isoniazid (H), pyrazinamide (Z), rifampicin (R), streptomycin (S), thiacetazone (T), and para-aminosalicylic acid (P), according to endpoints reported in these trials.

**Methods:** Phase II trials of combinations of seven agents for drug sensitive individuals with tuberculosis were included in our review. Early clinical endpoints incorporated proportion culture negative at eight weeks and early bactericidal activity (EBA) over two, seven and 14 days. Pooled estimates were obtained via the generalised inverse variance method. In cases where a measure of spread was unavailable, we used the proportion of patients contributed by each study, per drug combination, to estimate a standard error.

**Results:** 49 phase II studies were identified presenting data on 24 drug combinations. 18 studies contributed to the eight week culture negativity results with most evidence being available for the combination EHRZ - nearly 80% of patients will achieve culture negativity by eight weeks according to solid culture results. This is the highest result for any combination considered. 63 studies contributed to the EBA 0-2 day results with most evidence being available for patients on H monotherapy. The pooled result in this case is approximately 0.4 log10CFU/ml/sputum although it was difficult to rank the combinations due to the relatively low number of trials. Only eight studies contributed to the EBA 0-7 results and to the EBA 0-14 results and the quality of reporting in these studies was poor.

**Conclusion:** Due to the poor quality of reporting and limited data on the drug combinations of interest, in the absence of individual participant data (IPD), this is the best summary currently available. However, requests for IPD are ongoing and an update with more precise and accurate estimates can be expected in the near future.