

SUPPLEMENTARY FILE 14: Comparison to Menzies reviews

Menzies *et al.* published two systematic reviews in 2009, one of which sought to determine the effectiveness of the WHO recommended retreatment regimen at that time (2 months of INH EMB RIF STM PZA followed by one of INH EMB RIF PZA and then five of INH EMB RIF) in previously treated patients or those with INH monoresistance.[1] The second looked at the impact of the duration and intermittency of RIF, stratifying by different resistance patterns, including INH monoresistance and INH-STM resistance.[2]

Although we considered all the studies from both Menzies publications for inclusion in our review, the final list of publications differed substantially between our work and theirs, largely due to three criteria- 1) the temporal (1965-June 2008) and language (English, French, Spanish) inclusion criteria put in place by Menzies, 2) their exclusion of studies that utilised rifapentine or rifabutin, or regimens dosed once weekly or of a single drug alone, 3) our exclusion of studies where the INH monoresistant population was not considered sufficiently 'pure'. We agree with Menzies that regimens dosed once weekly or of a single drug alone are likely to be inadequate, but they added statistical strength to our data network, even if they would not be used in clinical practice. Our more up-to-date search also identified two extra studies [3, 4] and one study update [5] since June 2008. Indeed, in our review we included 32 extra studies versus the first Menzies paper,[1] and 38 versus the second when studies of INH monoresistance or non-MDR poly drug resistance were described.[2] Five studies included by the first Menzies paper were not considered eligible for our review (one did not break down treatment outcomes by regimen, one included a number of patients with MDR disease imbalanced between treatment arms whose outcomes could not be separated from those with INH monoresistant disease, and three were not randomised by treatment regimen or randomisation was broken during the trial)[6-10] and nine included by the second (five did not report treatment outcomes for patients with INH monoresistant strains by treatment regimen, three were either not randomised by treatment regimen or randomisation was broken during the trial, one did not report baseline resistance patterns),[8, 10-18] with two in common.

Unlike with meta-regression, our analysis technique additionally involved the loss of a number of studies from the final network due to all treatment arms having the same regimen under our grouping system (and a few were additionally lost due to having no events in any arm). However, the Menzies studies used models treating each study arm as an independent cohort, breaking within-study comparisons. Therefore if certain treatments were given to higher/lower incidence populations the resulting estimates of treatment differences could be biased (a limitation admitted by the authors). There is therefore a trade-off between

the inclusion of studies numbers and methodological rigour.

References

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