

Systematic review and meta-analysis comparing iTBS vs. TMS vs. sham in randomized controlled trials.

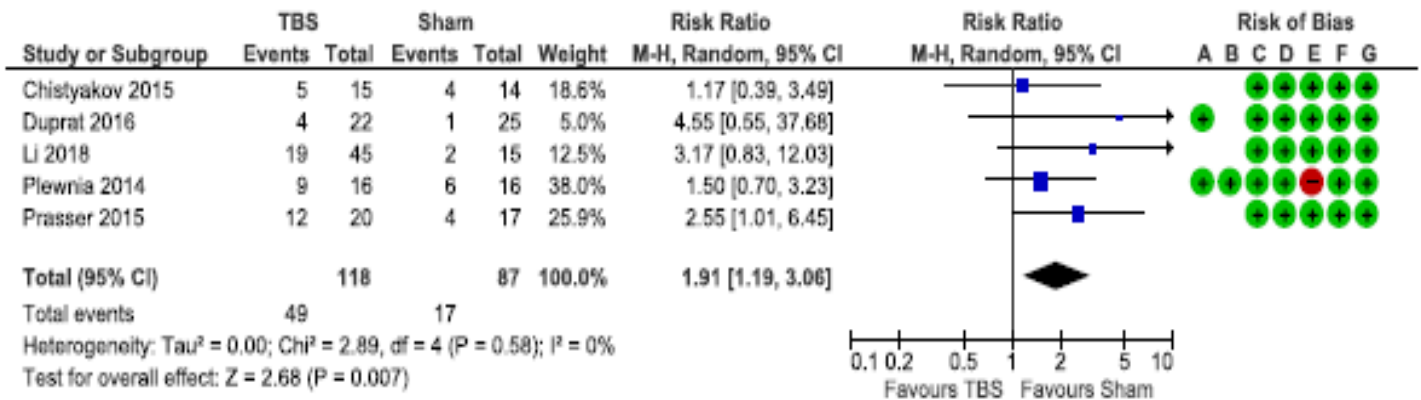
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Background: The objective was to evaluate the outcomes (response and safety/adverse events) of intermittent theta burst stimulation (iTBS) to repetitive transcranial magnetic stimulation (rTMS) and to sham (iTBS v. sham) when used in patients with major depressive disorder (MDD) in randomized controlled trials (RCTs).

Methods: The use of preferred reporting items for systematic reviews and meta-analyses guidelines (PRISMA) was utilized. The Cochrane methodology for evaluating RCTs was employed using risk of bias assessments, data synthesis, and statistical methods, including forest plots (risk ratio; M-H random effects; 95% CI). Eligibility criteria for study inclusion/exclusion were formulated a priori. Eligibility criteria included: primary diagnosis of MDD, reporting of outcome(s) [response of  $\geq 50\%$  reduction in HDRS score; yes/no],  $\geq 1$  week duration of therapy, manuscript only publication, and safety.

Results: A systematic review of the literature identified 270 records of which 8 manuscripts were used for qualitative and 7 for meta-analyses. Risk of bias demonstrated an overall low risk of bias (Fig 1; green, blank, red – low, unclear, high risk); forest plots of response rates of iTBS v sham (Fig 1; iTBS  $\geq 50\%$  response reduction v. sham; RR=1.91; 95% CI: 1.19-3.06;  $I^2=0\%$ ;  $P=0.007$ ); iTBS v. rTMS (no statistical difference on outcome of response;  $P=0.57$ ); and adverse events iTBS v. sham (no statistical difference v. sham).

Fig 1:



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Conclusions:

The response rates to iTBS v. sham were significantly improved; iTBS v. rTMS were statistically similar and adverse events no worse than sham. iTBS should be considered as an alternative to rTMS in those MDD patients where it is indicated.