Efficacy of antimanic treatments: meta-analysis of randomized, controlled trials.

We conducted meta-analyses of findings from randomized, placebo-controlled, short-term trials for acute mania in manic or mixed states of DSM (III-IV) bipolar I disorder in 56 drug-placebo comparisons of 17 agents from 38 studies involving 10,800 patients. Of drugs tested, 13 (76%) were more effective than placebo: aripiprazole, asenapine, carbamazepine, cariprazine, haloperidol, lithium, olanzapine, paliperdone, quetiapine, risperidone, tamoxifen, valproate, and ziprasidone. Their pooled effect size for mania improvement (Hedges’ g in 48 trials) was 0.42 (confidence interval (CI): 0.36-0.48); pooled responder risk ratio (46 trials) was 1.52 (CI: 1.42-1.62); responder rate difference (RD) was 17% (drug: 48%, placebo: 31%), yielding an estimated number-needed-to-treat of 6 (all p<0.0001). In several direct comparisons, responses to various antipsychotics were somewhat greater or more rapid than lithium, valproate, or carbamazepine; lithium did not differ from valproate, nor did second generation antipsychotics differ from haloperidol. Meta-regression associated higher study site counts, as well as subject number with greater placebo (not drug) response; and higher baseline mania score with greater drug (not placebo) response. Most effective agents had moderate effect-sizes (Hedges’ g=0.26-0.46); limited data indicated large effect sizes (Hedges’ g=0.51-2.32) for: carbamazepine, cariprazine,
haloperidol, risperidone, and tamoxifen. The findings support the efficacy of most clinically used antimanic treatments, but encourage more head-to-head studies and development of agents with even greater efficacy.