NNT and NNH for Acute Bipolar Depression Monotherapy*

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Pharmacotherapy	NNT		NNH				
	Response[a]	Remission[b]	Wt gain ≥7%	Sedation	Akathisia	Nausea	EPS
Quetiapine (IR/XR)[1] 300 or 600 mg/d	6	6	15	2	nr	nr	19
Lurasidone[2] 20 to 60 mg/d[c]	4	6	29	77	18	37	40
Lurasidone[2] 80 to 120 mg/d[d]	5	7	sp	13	12	10	15
OFC[3] 6/25, 6/50, or 12/50 mg/d)[e]	4	4	5	12	nr	36	15
Olanzapine[3,4] 5 to 20 mg/d[f]	11-12	11-12	5	6	nr	bp	nr
Lithium[5] (mean median serum conc: .61 mEq/L)[g]	15[h]	13[h]	bp	24	nr	12	nr
Lamotrigine[6] 100 to 400 mg/d[i]	12		nr	37	nr	bp	nr
Valproate[7] (mean serum conc: 430 - 568 µmol/L)	7	7	nr	nr	nr	6	nr
Aripiprazole[8] 5 to 30 mg/d[j]	44[h]		nr	33	5	12	nr

*N.B. Based on calculations from placebo-controlled studies only. Important limitations to these indirect comparisons include the fact that the study populations (Bipolar I with or without Bipolar II, with or without psychosis) and the durations (usually 6 or 8 weeks) differed.

In this table, NNT and NNH are rounded to the nearest whole number (i.e. rounded upwards only if the calculation ended in .5 or more).

The only treatments approved by Health Canada for the treatment of bipolar depression are Quetiapine and Lurasidone

Abbreviations:

NNT = number of patients needed to treat to achieve one extra responder or remitter in the treatment arm compared to the placebo arm of the trial
NNH = number of patients needed to treat to harm one extra person in the treatment arm with the undesired effect compared to the placebo arm
OFC = olanzapine-fluoxetine combination
mg/d = milligrams per day
nr = incidence of the side effect was not reported because it was below a certain frequency (usually < 5% or 10%) in treatment and placebo groups
sp = same as placebo (i.e. incidence of undesirable effect was identical in the treatment and placebo groups)
bp = below placebo (i.e. the incidence of the undesirable effect was less in the treatment group than in placebo group)
RPCT = Randomized placebo-controlled trial

Footnotes:

a	Defined as 50% improvement on Montgomery-Asberg Depression Rating Scale (MADRS) in most studies
b	Defined as ≤ 12 points on MADRS at end point in most studies
c	Mean daily dose = 31.8 mg (taken with ≥ 350 calories)
d	Mean daily dose = 82.0 mg (taken with ≥ 350 calories)
e	6/25 means olanzapine 6mg and fluoxetine 25 mg, etc. The mean daily doses were 7.4 mg/d for olanzapine and 39.3 mg/d for fluoxetine
f	The mean modal Olanzapine dose was 9.7 mg/d in Tohen M et al 2003[3] but not stated in Tohen M et al 2012[4]
g	35% of patients had median serum concentrations below 0.6 mEq/L; so this trial[5] was not probably not a fair test of lithium for bipolar depression
h	The improvement was not statistically significant versus placebo
i	The 50 mg dose was subtherapeutic, so not included in the analyses. Most other patients in the trials[6] were titrated to a fixed dose of 200 mg/d
j	In both studies[8], aripiprazole was flexibly dosed and the most common dose at end point was 10 mg/d

References:

1	NNT from reviews of 5 RPCTs: *Selle V et al Pharmacopsychiatry 2014;47:43-52* and *Chiesa A et al. Int Clin Psychopharmacol 2012;27(2):76-90* NNH calculated from data provided in *Citrome L. CNS Spectrums 2014:19:1-12* (based on three 8-week RPCTs)
2	PREVAIL 2: a 6-week RPCT (*Loebel A et al. Am J Psychiatry 2014;17(2):160-168)*
3	8-week RPCT of Olanzapine vs OFC vs placebo *(Tohen M et al. Arch Gen Psychiatry 2003;60(11):1079-88)*
4	6-week RPCT of Olanzapine vs placebo *(Tohen M et al. Br J Psychiatry 2012;201:376-382)*
5	EMBOLDEN I: an 8-week RPCT of Lithium vs Quetiapine vs placebo *(Young AH et al. J Clin Psychiatry 2010;71(2):150-162)*
6	NNT from an independent meta-analysis and meta-regression of individual patient data from 5 RPCTs with durations of 7 to 10 weeks. Although none of the individual trials reported a significant effect on the primary outcome, response rates with lamotrigine became statistically significant when data from the 5 trials were pooled. Although overall NNT = 12, in subgroup analyses response rate was significant only in those with severe (baseline HDRS > 24) depression (45.5% with Lam vs 30.1% with placebo, so NNT = 7; P = .001) but not in the less severely depressed subgroup (47.5% with Lam vs 44.6% with placebo, so NNT = 35; P = .4). *(Geddes JR et al. Br J Psychiatry 2009;194;4-9).* NNH values were calculated from data in *Calabrese JR et al. Bipolar Disorders 2008;10:323-333.* NNH for benign rash = 44. Serious rash: 1/1000 – 1/2000
7	Meta-analysis of 4 small RPCTs: durations (6 or 8 weeks), patients included (bipolar I or both I and II) and definitions of response and remission varied in the trials, and total sample size was small, so the evidence was termed "preliminary" (*Bond DJ et al. J Affect Disord 2010;124:228-234)*
8	NNT and NNH calculated from data in *Thase ME et al. J Clin Psychopharmacol 2008;28(1):13-20* (2 identically designed, 8-week RPCTs)