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Supplementary Material

Article Title: Effectiveness of Supplementary Cognitive-Behavioral Therapy for Pharmacotherapy-Resistant Depression: A Randomized Controlled Trial

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Supplementary Material

Supplement to: Effectiveness of Supplementary Cognitive Behavioral Therapy for
Pharmacotherapy-resistant Depression: A Randomized Controlled Trial

Supplementary eTable 1. Type and dose of antidepressant medication prescribed at baseline, n (%)

Antidepressant medication	Dose (mg)	CBT (n=40)	TAU (n=40)	
SSRI total		21 (52.5%)	19 (47.5%)	
Sertraline	50-100	7 (17.5%)	12 (30.0%)	
Paroxetine	20-40	9 (22.5%)	3 (7.5%)	
Fluvoxamine	100-200	4 (10.0%)	5 (12.5%)	
Escitalopram	20	1 (2.5%)	0 (0.0%)	
SNRI total		5 (12.5%)	10 (25.0%)	
Duloxetine	40-60	2 (5.0%)	6 (15.0%)	
Milnacipran	75-150	3 (7.5%)	4 (10.0%)	
TCA total		9 (22.5%)	6 (15.0%)	
Amoxapine	60-150	5 (12.5%)	0 (0.0%)	
Clomipramine	75-150	1 (2.5%)	2 (5.0%)	
Nortriptyline	75-150	2 (5.0%)	1 (2.5%)	
Amitriptyline	75	1 (2.5%)	0 (0.0%)	
Other total		5 (12.5%)	9 (22.5%)	
Mirtazapine	30-45	3 (7.5%)	7 (17.5%)	
Sulpiride	250-300	2 (5.0%)	0 (0.0%)	
Trazodone	100	0 (0.0%)	2 (5.0%)	
Medication used for combination/augmentation therapy ^a	Dose (mg)	CBT (n=40)	TAU (n=40)	
Sertraline	SSRI	50	1 (2.5%)	2 (5.0%)
Fluvoxamine	SSRI	100	1 (2.5%)	0 (0.0%)
Duloxetine	SNRI	40	1 (2.5%)	0 (0.0%)
Milnacipran	SNRI	50	0 (0.0%)	1 (2.5%)
Amoxapine	TCA	50	0 (0.0%)	1 (2.5%)
Clomipramine	TCA	20	0 (0.0%)	1 (2.5%)
Nortriptyline	TCA	75	0 (0.0%)	1 (2.5%)
Amitriptyline	TCA	30-50	2 (5.0%)	1 (2.5%)
Imipramine	TCA	20-50	2 (5.0%)	0 (0.0%)
Nortriptyline	TCA	75	0 (0.0%)	1 (2.5%)
Mirtazapine	Other	15-30	3 (7.5%)	3 (7.5%)
Sulpiride	Other	100-200	7 (17.5%)	3 (7.5%)
Trazodone	Other	25-150	4 (10.0%)	3 (7.5%)
Aripiprazole	SGA	3-6	1 (2.5%)	5 (12.5%)
Olanzapine	SGA	5-10	1 (2.5%)	3 (7.5%)
Quetiapine	SGA	25-75	3 (7.5%)	2 (5.0%)
Lithium	Mood stabilizer	200-1200	2 (5.0%)	3 (7.5%)
Lamotrigine	Mood stabilizer	25-75	0 (0.0%)	2 (5.0%)
Sodium valproate	Mood stabilizer	200-800	3 (7.5%)	4 (10.0%)

^aSome patients received more than two medications as part of combination/augmentation therapy.

Abbreviations: SGA= second generation antipsychotic, SNRI=serotonin and norepinephrine reuptake inhibitor, SSRI=selective serotonin reuptake inhibitor, TCA=tricyclic antidepressant.

Supplementary eTable 2. Between-group mean difference in GRID-HAMD change scores (ITT population, n=40 in each group; last-observation-carried-forward analysis)

	CBT	TAU	Difference in Mean Change Scores ^{a,b} (95% CI)	P Value
	Mean (SD)	Mean (SD)		
GRID-HAMD score				
0 week (baseline)	20.9 (3.4)	20.8 (3.4)	-	-
8 weeks	12.1 (5.2)	14.2 (6.0)	-2.15 (-4.59 to 0.29)	0.08
16 weeks	8.2 (4.7)	13.2 (6.9)	-5.33 (-7.92 to -2.74)	<0.001
28 weeks (3-month follow-up)	7.8 (5.2)	11.3 (7.2)	-3.78 (-6.42 to -1.13)	0.006
40 weeks (6-month follow-up)	6.1 (4.5)	9.3 (6.9)	-3.48 (-6.02 to -0.94)	0.008
64 weeks (12-month follow-up)	5.4 (5.9)	10.1 (8.4)	-4.28 (-7.50 to -1.07)	0.001

Data are mean (SD).

^aDifference in mean change scores is the between-group difference in the least squares mean treatment change score from baseline to the datapoint from the last observation carried forward analysis.

^bBetween-group difference is the CBT group value minus the TAU group value.

Abbreviations: CBT=cognitive behavioral therapy, GRID-HAMD=17-item GRID-Hamilton Depression Rating Scale, ITT=intention to treat, TAU=treatment as usual.

Supplementary eTable 3. Sensitivity analyses for between-group difference in GRID-HAMD change scores at 12 months using pattern-mixture models (comparison of five imputation strategies)

Imputation Strategy	Difference in Mean Change Scores ^{a,b} (95%CI)	P Value
Randomized arm missing at random	-4.15 (-7.57 to -0.73)	0.018
Jump to control	-4.07 (-7.47 to -0.67)	0.02
Last mean carried forward	-4.15 (-7.59 to -0.71)	0.019
Copy increment in control	-4.29 (-7.67 to -0.91)	0.014
Copy control	-4.26 (-7.64 to -0.88)	0.014

^aDifference in mean change scores is the between-group difference in the least squares mean treatment change score from baseline to 12 months from the mixed-effects model for repeated measurement analysis.

^bBetween-group difference is the CBT group value minus TAU group value.

Abbreviations: GRID-HAMD=17-item GRID-Hamilton Depression Rating Scale.