

In the Eye of the Beholdee: The Impact of Adjunctive Antidepressants vs Placebo on Quality of Life in the Aftermath of Bipolar I Depression

Shannon Reid¹, Leanne Hui¹, Chithra Pream Raju¹, Nazlin Walji¹, & Lakshmi Yatham¹

¹Department of Psychiatry, University of British Columbia

email: shannon.reid@ubc.ca

Introduction

- An important indicator of overall health and wellbeing, quality of life (QoL) represents an individual's satisfaction in various domains of life, including physical health, social relationships, and occupational functioning.
- Even during periods of remission, people with bipolar disorder frequently experience subsyndromal depressive symptoms and report markedly impaired QoL (1, 2).
- Despite their widespread use to treat bipolar I depression (3), few studies have examined QoL as an outcome in randomized controlled trials (RCTs) of adjunctive antidepressant maintenance therapy in bipolar I disorder.

Objective

To assess the impact of adjunctive antidepressant maintenance therapy on QoL for 52 weeks after remission from a bipolar I depressive episode.

Methods

- In this double-blind, multi-site RCT, participants entered from an open-label phase in which escitalopram 10-30mg/day or bupropion XL 150-450mg/day was used to treat an episode of bipolar I depression along with a stable dose of mood stabilizers, second-generation antipsychotics (SGAs), or both.
- 178 participants, aged 18 to 65, were randomized in a 1:1 ratio to maintain antidepressant therapy for 52 weeks following remission, or switch to placebo at 8 weeks.
- 139 participants were included in a modified intent-to-treat dataset of participants who had at least one post-baseline Q-LES-Q.
- QoL was assessed with the Quality of Life Enjoyment and Life Satisfaction Questionnaire (Q-LES-Q) at baseline, week 24, and week 52 or final visit. Participants who were withdrawn from the study for any reason completed a Q-LES-Q at the time of withdrawal.
- Last observation carried forward (LOCF) imputation was used whereby early termination data were carried forward to the next visit.

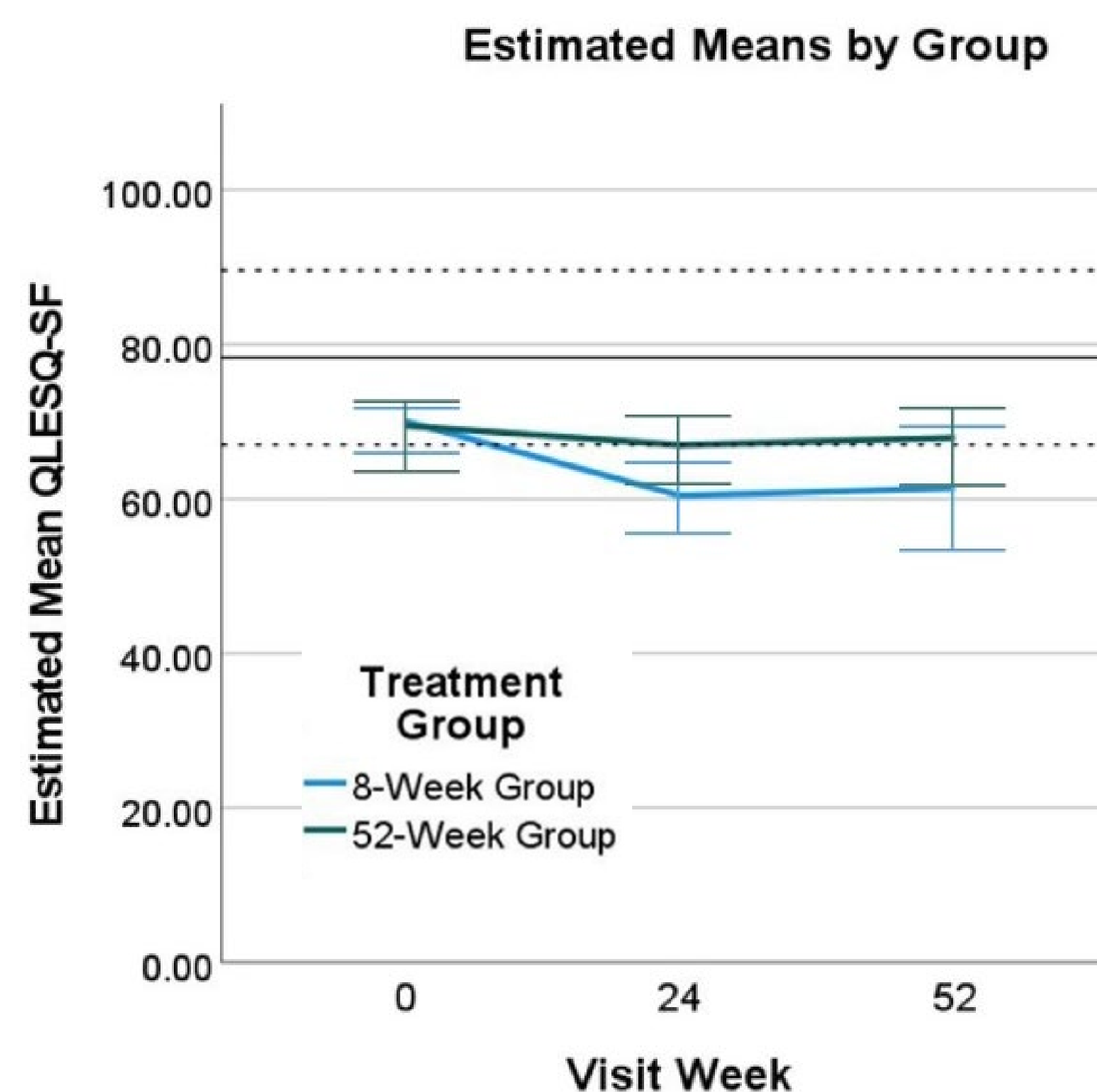
- Q-LES-Q scores are expressed as a percent-maximum value and community samples have an average of 78.3 (SD = 11.3); scores below 1 SD (i.e. 55.7 - 67) are considered mild-to-moderately impaired QoL (4).
- A longitudinal linear mixed-effects model was fit with the Q-LES-Q scores as the outcome variable, accounting for the baseline score.
- Fixed effects included age, sex, baseline Montgomery-Asberg Depression Rating Scale (MADRS) score, study visit, treatment, and treatment-by-visit interaction. Random intercepts were included to account for dependencies between repeated measures on the same participants.
- Time was modelled categorically to allow for an arbitrary trajectory over time; an autoregressive (order 1) covariance structure was specified to model the within-subject errors.
- Analyses were conducted with IBM SPSS version 28.0.

Results

Table 1. Characteristics of patients at baseline			
Characteristic	8-Wk Group (n = 75)	52-Wk Group (n = 64)	Total (n = 139)
Site of enrollment – no. (%)			
Canada	9 (12)	9 (14)	18 (13)
India	65 (87)	53 (83)	118 (85)
Korea	1 (1)	2 (3)	3 (2)
Female sex – no. (%)			
Age (years)	42.76 ± 11.04	40.77 ± 11.33	41.84 ± 11.18
Race – no. (%)			
Asian	65 (87)	55 (86)	120 (86)
Black	1 (1)	0	1 (1)
White	9 (12)	8 (13)	17 (12)
Other	0	1 (2)	1 (1)
Drug combination – no. (%)			
Bupropion XL + mood stabilizer (MS)	13 (17)	10 (16)	23 (17)
Bupropion XL + MS + SGA	13 (17)	12 (19)	25 (18)
Bupropion XL + SGA	1 (1)	2 (3)	3 (2)
Escitalopram + MS	19 (25)	17 (27)	36 (26)
Escitalopram + MS + SGA	25 (33)	19 (30)	44 (32)
Escitalopram + SGA	4 (5)	4 (6)	8 (6)
Post-baseline Q-LES-Q – no. (%)			
Week 24 Q-LES-Q	73 (97)	64 (100)	137 (97)
Week 52 Q-LES-Q	47 (63)	46 (72)	93 (66)

- 72 participants (27 in the 52-week group and 45 in the 8-week group) discontinued the trial: 1 in the 8-week group was withdrawn for nonadherence, 2 in the 52-week group and 6 in the 8-week group withdrew informed consent, and 6 in the 52-week group and 3 in the 8-week group lost to follow up. Participants were also withdrawn from the trial (19 in the 52-week group and 35 in the 8-week group) if they experienced any mood episode.
- The 52-week and 8-week groups had similar baseline Q-LES-Q scores, ranging from 68.38 to 68.73 respectively ($p = .85$), within normal range (i.e. ≥ 67) of QoL.
- Overall, QoL declined significantly over time, dropping -9.65 points from baseline at week 24 (95% CI, -15.21 to -4.08; $p < .001$) and -9.47 points from baseline at week 52 (95% CI, -17.94 to -1.00; $p = .034$).
- The effect of treatment was significant at 24 weeks ($\beta = 7.10$, 95% CI, 0.19 to 14.01; $p = .041$), but not significant at 52 weeks ($\beta = 7.56$, 95% CI, -2.00 to 17.12; $p = .089$).

Figure 1. Estimated Means by Treatment Group



Discussion

- Antidepressant maintenance treatment preserves QoL in bipolar I patients until 6 months after remission of depression.
- However, beyond 6 months, the buoying effect of treatment on QoL dissipates, which may be attributed to the high attrition rate beyond this point.
- These findings align with those of the primary analysis of this study (5), in which a sensitivity analysis of outcomes after 6 weeks found a significant difference in time to relapse of any mood episode while on adjunctive antidepressant maintenance therapy.

References

1. Deckersbach, T., Nierenberg, A. A., Kessler, R., Lund, H. G., Ametrano, R. M., Sachs, G., Rauch, S. L., & Dougherty, D. (2010). RESEARCH: Cognitive rehabilitation for bipolar disorder: An open trial for employed patients with residual depressive symptoms. *CNS neuroscience & therapeutics*, 16(5), 298–307.
2. Michalak, E. E., Yatham, L. N., & Lam, R. W. (2005). Quality of life in bipolar disorder: a review of the literature. *Health and quality of life outcomes*, 3, 72.
3. Rhee TG, Olfson M, Nierenberg AA, Wilkinson ST. 20-Year trends in the pharmacologic treatment of bipolar disorder by psychiatrists in outpatient care settings. *Am J Psychiatry* 2020; 177: 706-15.
4. Schechter, D., Endicott, J., & Nee, J. (2007). Quality of life of 'normal' controls: association with lifetime history of mental illness. *Psychiatry research*, 152(1), 45–54.
5. Yatham, L. N., Arumugham, S. S., Kesavan, M., Ramachandran, K., Murthy, N. S., Saraf, G., Ouyang, Y., Bond, D. J., Schaffer, A., Ravindran, A., Ravindran, N., Frey, B. N., Daigneault, A., Beaulieu, S., Lam, R. W., Kondapuram, N., Reddy, M. S., Bhandary, R. P., Ashok, M. V., Ha, K., ... BEAM-BD Trial Group (2023). Duration of Adjunctive Antidepressant Maintenance in Bipolar I Depression. *The New England journal of medicine*, 389(5), 430–440.

Acknowledgement

Many thanks to the research team members, clinicians, and investigators who supported data collection and cleaning throughout the study.

