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Effects of a right unilateral ultrabrief pulse electroconvulsive therapy course on health related quality of life in elderly depressed patients[☆]

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Abstract

Introduction—Patients with Major Depressive Disorder (MDD) referred for electroconvulsive therapy (ECT) have poorer Health Related Quality of Life (HRQOL), compared with other

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patients with MDD, but ECT is associated with significant and durable improvement in HRQOL. However, no prior research has focused exclusively on elderly patients with MDD receiving ECT.

Methods—HRQOL data from 240 depressed patients over the age of 60 was measured with the Medical Outcomes Study Short Form 36 (SF-36). The SF-36 was measured before and after a course of acute ECT. Predictors of change in HRQOL scores were identified by generalized linear modeling.

Results—At baseline, participants showed very poor HRQOL. After treatment with ECT, the full sample showed marked and significant improvement across all SF-36 measures, with the largest gains seen in dimensions of mental health. Across all participants, the Physical Component Summary (PCS) score improved by 2.1 standardized points (95% CI, 0.61,3.56), while the Mental Component Summary (MCS) score improved by 12.5 points (95% CI, 7.2,10.8) Compared with non-remitters, remitters showed a trend toward greater improvement in the PCS summary score of 2.7 points (95%CI, -0.45, 5.9), while the improvement in the MCS summary score was significantly greater (8.5 points, 95% CI, 4.6,12.3) in the remitters than non-remitters. Post-ECT SF-36 measurements were consistently and positively related to baseline scores and remitter/non-remitter status or change in depression severity from baseline. Objective measures of cognitive function had no significant relationships to changes in SF-36 scores.

Limitations—This study's limitations include that it was an open label study with no comparison group, and generalizability is limited to elderly patients.

Discussion—ECT providers and elderly patients with MDD treated with ECT can be confident that ECT will result in improved HRQOL in the short-term. Attaining remission is a key factor in the improvement of HRQOL. Acute changes in select cognitive functions were outweighed by improvement in depressive symptoms in determining the short term HRQOL of the participants treated with ECT.

Keywords

ECT; quality of life; major depressive disorder; elderly

Introduction

While world-wide progress is being made in reducing the mortality due to common infectious diseases and dietary deficiency,(Lozano et al., 2012) there is little evidence of progress in reducing the morbidity due to mental illness. The World Health Organization has predicted that major depressive disorder (MDD) will become a leading cause of world-wide disability. (WHO Guidelines Approved by the Guidelines Review Committee, 2011) The relationship of MDD to disability is dependent upon the age of the patient.(McCall et al., 1999a) Young patients with MDD are more likely to report problems with relationships, while older patients with MDD are more likely to report problems with managing the demands of everyday life. For the purposes of this paper, we will use the term 'function' to describe observable behaviors such as activities of daily living (ADLs) and instrumental activities of daily living (IADLs), while the term 'health-related quality of life' (HRQOL) is reserved to describe self-reports of health dimensions (e.g., pain, fatigue, competence in performing an emotional role). Patients are generally able to accurately describe their level

of functional activity, even after a course of electroconvulsive therapy (ECT). (McCall et al., 2002)

Patients with MDD who are referred for ECT have poorer scores on measures of HRQOL relative to unselected outpatients with MDD.(McCall et al., 2013) Naturalistic observation of a mixed-age sample of 88 inpatients with MDD who received ECT showed greater improvement in HRQOL as measured by the Daily Living and Role Functioning of the Basis-32, with an effect size advantage >1.0 at one month after hospitalization, as compared with inpatients with MDD who did not receive ECT.(McCall et al., 2001) Antunes and Fleck reported on the change in HRQOL using the Basis –32 and the World Health Organization Quality of Life scale, and reported a large effect size improvement of approximately 1.0. (Antunes et al., 2009) In a mixed-age sample of 77 patients with MDD (mean age 57.3 years), impairments in HRQOL were improved by a factor of about 50% 2 weeks and 4 weeks after an ECT course. Improvement in HRQOL was explained by reduction in depression symptom severity, while improvement in IADLs was related to improved cognitive function after ECT.(McCall et al., 2004) In another study, 184 mixed-aged adults (mean age 47.6) received a course of bilateral (BL) or right unilateral (RUL) ECT to treat MDD, and were followed for 6 months. HRQOL was exceptionally poor before ECT, and improved immediately after the ECT course. Remission from MDD was associated with greater gains in HRQOL than non-remission. Interestingly, continued gains in HRQOL over 6 months was related to both sustained remission over 6-months and to electrode placement, as participants assigned to RUL relative to BL electrode placement had better HRQOL outcomes. In this study, HRQOL was unrelated to changes in cognitive function.(McCall WV et al., 2011) The ECT Services study included 283 mixed-age participants with MDD (mean age 55.4 years) treated with ECT according to provider preference and HRQOL was measured with the Medical Outcomes Study Short Form 36 (SF-36). In this study, improvement was seen widespread, with 87% of participants showing improved scores, with remitters showing approximately an effect size of 1.0, and non-remitters had an improvement effect size of approximately 0.5. The gains were sustained for up to 6 months, with those participants showing the greatest improvement in measures of global cognitive function also showing the greatest improvement in HRQOL.(McCall et al., 2006) Increasing age in this study was associated with greater improvement in the HRQOL domains of mental health and social function, but less improvement in the physical function domain.

While the accumulated evidence suggests that patients with MDD treated with ECT have poorer baseline HRQOL, compared with other patients with MDD, and that they experience significant improvement in HRQOL that persists for months after ECT, no prior research has focused exclusively on elderly adult patients with MDD receiving ECT. Specific examination of the effects of ECT on elderly patients with MDD would be valuable for several reasons: (1) elderly patients with MDD are disproportionately represented among patients with MDD treated with ECT,(McCall et al., 1999b) (2) concerns about pre-ECT and post-ECT cognitive status of elderly patients with MDD raises questions about the impact of ECT on HRQOL,(McCall et al., 2003) (3) as elderly patients with MDD treated with ECT have better antidepressant response to ECT than younger patients, it raises the possibility of an enhanced effect on HRQOL,(Rhebergen et al., 2015;Tew et al., 1999) and (4) the differential impact of depression on IADLs and HRQOL in depressed elderly relative to

younger patients with MDD.(McCall, Cohen, Reboussin, and Lawton, 1999a) To address this knowledge gap, we undertook a secondary analysis of the “Prolonging Remission in Depressed Elderly” (PRIDE) study data acquired in Phase 1 in which elderly adults with MDD were treated with a combination of right unilateral ultra-brief pulse ECT and venlafaxine.

Methods

Patients

Full details of the methods of Phase 1 of the PRIDE study can be found elsewhere.(Kellner et al., 2016) Recruitment occurred at multiple sites, and approval for the study was obtained from the institutional review board (IRB) at each study site. Participants provided their own, written, informed consent. Briefly, participants were in- or outpatients, age 60, with a diagnosis of unipolar MDD, and a Hamilton Rating Scale for Depression-24 item (HRSD₂₄) total score 21. (Hamilton, 1960) All participants received venlafaxine (VLF) during both the acute ECT course and during continuation therapy after acute ECT, while all participants who proceed from the acute ECT course to the randomized second phase of treatment (not considered in this paper) received lithium (Li). Hence, all participants had to be candidates to receive both VLF and Li in Phase 1. Exclusion criteria were bipolar disorder, schizoaffective disorder, dementia, substance abuse/dependence in last 6 months, contraindications to Li or VLF, or prior failure to respond to an adequate trial of Li + VLF in the index episode, or any ECT in the current episode. Also participants with a history of active general medical or neurological conditions that would have affected cognition or treatment response, such as Parkinson’s Disease, stroke, or multiple sclerosis, were excluded. The participants’ severity of general medical conditions was measured with the Cumulative Illness Rating Scale – geriatric (CIRS-G).(Linn et al., 1986)

Procedures

Medication Washout and Concomitant Medications—Psychotropic medications were discontinued within 1 week of starting Phase 1, except for venlafaxine as described below. Rescue medication for agitation, anxiety, or insomnia was limited to lorazepam up to 3 mg/day, or equivalent.

ECT—ECT procedures were standardized as follows: 3x weekly, standard RUL placement (D’Elia placement)(D’Elia et al., 1975) with ultrabrief (UB) pulse (0.3 ms) stimuli. A dose titration procedure to determine seizure threshold was carried out at the initial session, and subsequent sessions were administered at 6x seizure threshold. Seizure adequacy criterion was a motor seizure 15 s, with restimulation, if needed. If the HRSD₂₄ demonstrated <25% drop from baseline by treatment 6, the stimulus dose was increased by 50%. If the HRSD₂₄ demonstrated <25% drop from baseline by treatment 9, the stimulus dose was increased again by 50%.

Medication—VLF was started 1–5 days prior to ECT or up to 2 days after the first treatment at an initial dosage of 37.5 mg *po*, increased by 37.5 mg every 3 days or as tolerated, with a target dose of 225 mg *qD*.

Assessments

Diagnostic, Demographic and Baseline Clinical Assessments—Baseline assessments were obtained for eligible participants who provided informed consent. Diagnosis was established using either the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)(Spitzer et al., 1992) (study years 1–2) or the Mini-International Neuropsychiatric Interview (MINI)(Sheehan et al., 1998) (years 3–6). The change to the MINI as a diagnostic instrument was made to minimize patient burden at the baseline assessment. As the SCID-I and the MINI have similar diagnostic accuracy (Sheehan et al., 1997; Sheehan et al., 1998; Kotwicky & Harvey, 2013),(Kotwicky et al., 2013;Sheehan et al., 1997;Sheehan, Lecrubier, Harnett-Sheehan, Amorim, Janavs, Weiller, Hergueta, Baker, and Dunbar, 1998) we did not account for the change in diagnostic tool in the statistical analysis. The change from the SCID to the MINI at year 3 was approved by the Data Safety and Monitoring Board (DSMB).

These instruments were further used to specify the melancholic, atypical, and psychotic subtypes of Major Depressive Disorder.

Depression outcome measures—The HRSD₂₄ was administered three times per week, before each ECT. The primary outcomes in Phase 1 were remission status and the longitudinal trajectory of HRSD₂₄ total scores. Participants were classified as *remitters* based on: (a) HRSD₂₄ ≤ 10 on two consecutive ratings, and (b) HRSD₂₄ did not increase > 3 points on the second consecutive HRSD₂₄, or remained ≤ 6, consistent with other ECT clinical trials in MDD.(Sackeim et al., 2009) The minimum number of ECT required for remission was 2, but there was no maximum. *Non-remitters*: (a) did not meet the above remission criteria, (b) had at least 12 treatments, and (c) reached a plateau defined as no clinical improvement (< 3 point decrease in HRSD₂₄ after last 2 consecutive treatments).

Cognitive Function—The Wechsler Test of Adult Reading (WTAR) was administered only at baseline as an estimate of pre-morbid intellectual functioning.(Wechsler, 2001) Global cognitive function was measured with the Mini Mental State Examination (MMSE). (Folstein et al., 1975) The second edition of the California Verbal Learning Test (CVLT-II) was used to assess verbal learning and memory.(Delis et al., 2000;Woods et al., 2006) The Dementia Rating Scale 2nd edition Initiation/Perseveration Index (DRS-2 I/P) was used to measure executive function.(Lezak et al., 2004)

HRQOL—HRQOL was measured with the Medical Outcomes Study Short Form 36 (SF-36).(Ware, Jr. et al., 1992;Ware et al., 2003) The SF-36 was measured at baseline prior to ECT, and again at the end of Phase 1 acute ECT. SF-36 data were scored in terms of 8 standard subscales: Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH). The score for each subscale is the weighted sums of the questions for that subscale, transformed into a 0–100 scale. Lower scores define greater disability. Individual scores were then transformed into “T scores” (i.e., standardized scores), with a mean of 50 and standard deviation of 10. The 8 subscales were also aggregated into two total scores – the Physical Component Summary T score (PCS) and the Mental Component

Summary T score (MCS). Both total scores were obtained summing over all eight subscales scores weighed by their respective physical and mental factor score coefficient following the algorithm provided by Ware, Kosinski & Dewey)(Ware et al., 2000).

Statistical Analysis—For continuous and categorical group comparisons, independent sample t-tests and chi-square tests were used respectively. All analyses were conducted using SAS 9.4.

Multiple imputation was used to handle missing data. Missingness was assessed at baseline and post assessment measurement for putative predictors; each missing baseline and post assessment measurement SF-36 subscale and summary score was imputed 100 times using SAS Proc MI with the Markov Chain Monte Carlo (MCMC) method. Following imputation, standard statistical methods were used and results were combined across imputations using SAS Proc MIAnalyze which accounts for the variability between imputed values in the 100 datasets. Models were assessed using available standard methods such as imputation model residuals to confirm Gaussian distribution assumptions are met and autocorrelation plots to verify that imputation converged. Each imputation model for the individual subscale and summary scores included remission status, study site, age, gender, psychosis, education, CIRSG severity, WTAR baseline Full Scale IQ, MMSE baseline raw score, HRSD₂₄ baseline and post assessment total score, CVLT-II delayed recall and percent retention scores, and DRS-2 I/P scaled score. For calculation of CIRSG severity score the rating of psychiatric impairment was excluded due the otential for multicollinearity with other measures including HRSD₂₄.

To evaluate significant change from baseline to post assessment for the total sample for each SF-36 subscale and summary score for the imputed data set, paired t-tests were used to test the difference from zero for the total sample. Pooled t-tests were used to compare the difference in mean change from baseline between remitters and non-remitters.

To evaluate the predictors of change from baseline in quality of life subscale and summary scores, generalized linear models (GLM) were used. Post assessment SF-36 subscale and summary scores were used separately as the outcome measure (dependent variable); all models contained baseline SF-36 subscale or summary score, baseline premorbid intellectual ability (WTAR), change from baseline in MMSE, delayed recall and percent retention (CVLT-II), and the DRS-2 I/P. Furthermore, remission status was included for subscale and summary scores related to mental health and change in the HRSD₂₄ total score was included for subscale and summary scores related to physical functioning. In addition, potential covariates (age, gender, psychosis, education, and CIRSG severity) were assessed for significance in bivariate models and included in the full model if the p-value was <0.20. The full model was assessed and the covariate with the highest p-value was subsequently removed and the model rerun. This was repeated until only statistically significant covariates remained.

Results

Two-hundred and forty patients contributed to the analyses. The sample was mostly female and White, with severe depressive symptoms and intact global cognitive function at baseline (Table 1). Baseline demographic and clinical features were similar between remitters and non-remitters with remission status determined based on the post HRSD₂₄ score. At baseline, participants showed very poor HRQOL on each subscale and the 2 summary scores, with the exception of the PCS and the BP subscale that approached a normative mean value of 50 (Table 2). The HRSD baseline for patients diagnosed with SCID versus MINI were very similar, (MINI: 31.6 $\pm$ 7.4 vs SCID: 30.3 $\pm$ 7.1; difference: -1.2/ $\pm$ 7.3; $p=0.258$) supporting the idea that SCID and MINI are equivalent in detecting major depressive disorder.

Participants received a mean of 7.4 $\pm$ 3.5 ECT sessions (median: 7; range: 1–16). At the conclusion of ECT, the full sample showed marked and significant improvement across all SF-36 subscales and summary scores, with the biggest gains seen in dimensions of mental health (Table 2). Compared with non-remitters, remitters showed greater improvement in SF-36 scores pertaining to dimensions of mental health. No HRQOL subscales declined after ECT in either the remitter or the non-remitter groups (Table 3).

The post-ECT SF-36 measurements were consistently and positively related to baseline scores and remitter/non-remitter status or change in HRSD₂₄ total score from baseline. The post-ECT SF-36 General Health measurement was positively related to age, while the Physical Functioning subscale was negatively related to age. The presence of psychotic symptoms was positively related to the post-ECT Physical Component Summary score and the Physical Functioning Subscale, but psychosis was negatively related to the Social Functioning Subscale. There were no statistically significant relationships between post-ECT SF-36 subscales or summary scores and estimates of premorbid intellectual ability, change in global cognitive function, or change from baseline in delayed recall or retention of verbal information (Table 4). The change in the DRS-2 I/P score was collinear with the MMSE and thus was removed from the analytic models.

Discussion

The main overall finding of this analysis is that the acute effects of an ECT course, when combined with venlafaxine, produces a marked improvement in HRQOL in elderly patients with MDD that is similar to what has been described in mixed-age samples. Participants had very poor HRQOL at baseline, and improved HRQOL was seen immediately at the conclusion of an ECT course combined with venlafaxine. Participants who remitted showed greater improvement in HRQOL. Notably, in this study, no decline in HRQOL was observed in any group. Final HRQOL status was closely related to both baseline HRQOL and remission/non-remission status, but was unrelated to cognitive function. The finding of superior physical health and physical functioning after ECT in those participants with baseline psychotic symptoms is consistent with earlier reports from our team that found that psychotic symptoms in the setting of MDD were a good prognostic factor for remission with ECT. (Petrides et al., 2001) In contrast, the finding of poorer social functioning after ECT in

those participants with pre-ECT psychotic symptoms is not entirely unexpected and suggests that psychotic symptoms are related to more enduring impairment of social relationships even after successful ECT.

This report is subject to a number of limitations. First, the generalizability of the findings are limited to elderly adults with MDD who were taking concomitant venlafaxine and low dose, as-needed lorazepam in the context of treatment with RUL UB ECT. Other forms of ECT, higher doses of benzodiazepines, or different concomitant psychotropic medications could have produced different results. Second, as this was an open label study with no comparison group, the improvement in HRQOL group could be related to regression to the mean, but this seems unlikely as the effect was so closely related to improvement in depression status. Finally, this report does not address longer term effects of ECT on HRQOL in the elderly. Longer term effects of ECT in HRQOL in elderly patients will be the subject of a later report.

There are several clinical implications of these findings. First, ECT providers and elderly patients with MDD treated with ECT can be confident that ECT will result in short-term improved HRQOL. Second, attainment of remission is the key to improving HRQOL. Third, any acute change in select cognitive functions may be unrelated to short-term change in HRQOL.

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Highlights

- Health-related quality of life (HRQOL) is poor in elderly patients with major depressive disorder (MDD) who are referred for electroconvulsive therapy (ECT).
- An acute course of high dose, right unilateral, ultrabrief pulse ECT is associated with improvements in HRQOL in elderly MDD patients immediately after the course of ECT.
- Changes in HRQOL in elderly MDD patients after ECT are best explained by the antidepressant effect of ECT, and are not related to the cognitive side effects of ECT.

Table 1
Demographic and clinical characteristics at baseline for total sample and by remitter status

Characteristic	Total Sample		Non-remitter		Remitter		p-value
	N	n	n	n	n	n	
DEMOGRAPHICS							
Age (y)	240	69.9 ± 7.6 (68.5)	92	68.8 ± 7.8 (66.5)	148	70.6 ± 7.3 (70.0)	0.077
Education (y)	239	14.5 ± 3.3 (14.0)	91	14.5 ± 3.3 (14.0)	148	14.5 ± 3.3 (14.0)	0.998
Female	240	46 (57.5%)	92	46 (50.0%)	148	92 (62.2%)	0.064
White	240	228 (95.0%)	92	87 (94.6%)	148	141 (95.3%)	0.807
Hispanic	240	9 (3.8%)	92	3 (3.3%)	148	6 (4.1%)	-
BASELINE CLINICAL CHARACTERISTICS							
Recurrent Episode	240	210 (87.5%)	92	82 (89.1%)	148	128 (86.5%)	0.547
Psychosis	240	28 (11.7%)	92	8 (8.7%)	148	20 (13.5%)	0.258
Melancholia	239	141 (59.0%)	91	58 (63.7%)	148	83 (56.1%)	0.243
Atypical	239	5 (2.1%)	91	1 (1.1%)	148	4 (2.7%)	-
Psychiatric Hospitalizations	229	2.4 ± 3.4 (2.0)	86	2.7 ± 4.9 (1.0)	143	2.2 ± 2.0 (2.0)	0.367
HRSD ₂₄ Baseline	240	31.2 ± 7.3 (30.0)	92	31.8 ± 7.1 (31.0)	148	30.9 ± 7.4 (30.0)	0.320
MMSE Baseline (raw)	239	27.5 ± 2.4 (28.0)	91	27.5 ± 2.6 (28.0)	148	27.5 ± 2.2 (28.0)	0.803
CIRS-G Severity Index [†]	223	1.5 ± 0.4 (1.5)	88	1.5 ± 0.4 (1.5)	135	1.4 ± 0.4 (1.4)	0.292
WTAR IQ Score	208	106.0 ± 10.2 (108.0)	74	105.9 ± 9.9 (108.0)	134	106.1 ± 10.5 (108.0)	0.928
DRS-2 L/P AMSS Score	222	8.0 ± 3.2 (8.0)	81	8.4 ± 2.9 (10.0)	141	7.8 ± 3.3 (8.0)	0.141
DEMOGRAPHICS							
CVLT % Retention	200	68.9 ± 35.9 (75.0)	73	69.8 ± 36.1 (75.0)	127	68.0 ± 35.8 (80.0)	0.735
CVLT Long delay free recall standard score	203	-1.0 ± 1.2 (-1.0)	73	-0.9 ± 1.3 (-1.0)	130	-1.0 ± 1.2 (-1.0)	0.559
FAMILY HISTORY OF MENTAL DISORDERS							
Psychiatric Illness	233	160 (68.7%)	89	60 (67.4%)	144	100 (69.4%)	0.746
Mood Disorder	231	143 (61.9%)	88	56 (63.6%)	143	87 (60.8%)	0.671
Major Depressive Disorder	230	136 (59.1%)	88	55 (62.5%)	142	81 (57.0%)	0.413
Bipolar Disorder	231	33 (14.3%)	88	12 (13.6%)	143	21 (14.7%)	0.825

Data are represented as mean ± SD (median) for continuous variables and number (%) for categorical.

[†]Psychiatric item removed

Table 2

Mean difference from baseline in SF-36 subscale and summary T scores for total sample

TOTAL SAMPLE				
SF-36 T scores	Baseline Mean (SE)	Last Mean (SE)	Difference ^I Mean (95% CI)	P-Value
<i>Physical Factors</i>				
Physical Component Summary (PCS)	45.76 (.81)	47.84 (.75)	2.09 (0.61, 3.56)	0.0058
Bodily Pain (BP)	44.68 (.89)	47.71 (.84)	3.03 (1.24, 4.82)	0.0009
Role Physical (RP)	32.97 (.83)	39.05 (.84)	6.07 (4.24, 7.90)	<0.0001
General Health (GH)	39.61 (.74)	45.65 (.70)	6.04 (4.55, 7.53)	<0.0001
Physical Functioning (PF)	37.28 (.82)	41.33 (.80)	4.05 (2.43, 5.67)	<0.0001
<i>Mental Factors</i>				
Mental Component Summary (MCS)	18.30 (.69)	30.79 (.93)	12.49 (10.61, 14.38)	<0.0001
Mental Health (MH)	21.55 (.67)	34.48 (.81)	12.93 (11.21, 14.65)	<0.0001
Role Emotional (RE)	21.38 (.68)	29.84 (.89)	8.46 (6.38, 10.54)	<0.0001
Vitality (VT)	31.67 (.64)	41.26 (.75)	9.59 (7.88, 11.30)	<0.0001
Social Functioning (SF)	24.05 (.67)	33.05 (.84)	9.00 (7.18, 10.82)	<0.0001

^IDifference = Post minus Baseline score

Table 3

Mean Baseline, Post, and Difference from baseline in SF-36 subscale and summary T-scores by outcome status.

SF-36 T-scores	Remitter Mean (SE)	Non-remitter Mean (SE)	Difference (Remitter minus Non-Remitter) Mean (95% CI)	p-value
Physical Component Summary (PCS)				
Baseline	45.9 (0.95)	45.5 (1.49)	0.42 (-2.94, 3.78)	0.8083
Post	49.1 (0.85)	45.9 (1.38)	3.15 (0.00, 6.30)	0.0497
Difference (Post-Baseline)	3.13 (1.51, 4.75)	0.40 (-2.42, 3.22)	2.73 (-0.45, 5.91)	0.0919
p-value	0.0002	0.7806		
Bodily Pain (BP)				
Baseline	45.0 (1.07)	44.1 (1.55)	0.93 (-2.72, 4.57)	0.6182
Post	48.8 (0.94)	46.0 (1.59)	2.83 (-0.73, 6.39)	0.1188
Difference (Post-Baseline)	3.76 (1.74, 5.78)	1.86 (-1.43, 5.14)	1.91 (-1.88, 5.70)	0.3236
p-value	0.0003	0.2683		
Role Physical (RP)				
Baseline	32.5 (1.00)	33.8 (1.45)	-1.30 (-4.69, 2.10)	0.4539
Post	41.0 (0.92)	35.9 (1.57)	5.16 (1.66, 8.67)	0.0039
Difference (Post-Baseline)	8.55 (6.51, 10.59)	2.09 (-1.17, 5.35)	6.46 (2.68, 10.24)	0.0008
p-value	<.0001	0.2088		
General Health (GH)				
Baseline	40.6 (0.91)	38.1 (1.25)	2.47 (-0.55, 5.49)	0.1085
Post	49.4 (0.68)	39.6 (1.24)	9.80 (7.15, 12.45)	<.0001
Difference (Post-Baseline)	8.85 (-10.58, -7.28)	1.52 (-4.09, 1.23)	7.33 (4.30, 10.35)	<.0001
p-value	<.0001	0.2551		
Physical Functioning (PF)				
Baseline	37.8 (0.99)	36.4 (1.42)	1.47 (-1.88, 4.81)	0.3896
Post	42.9 (0.93)	38.8 (1.43)	4.07 (0.73, 7.40)	0.0170
Difference (Post-Baseline)	5.05 (3.20, 6.89)	2.45 (-0.53, 5.42)	2.60 (-0.85, 6.05)	0.1395
p-value	<.0001	0.1067		
Mental Component Summary (MCS)				

SF-36 T-scores	Remitter Mean (SE)		Non-remitter Mean (SE)		Difference (Remitter minus Non-Remitter) Mean (95% CI)		p-value
Baseline	19.2	(0.87)	16.9	(1.13)	2.27	(-0.54, 5.08)	0.1128
Post	34.9	(0.98)	24.2	(1.62)	10.73	(7.07, 14.39)	<.0001
Difference (Post-Baseline)	15.74	(13.72, 17.76)	7.28	(3.88, 10.68)	8.46	(4.58, 12.34)	<.0001
p-value	<.0001		<.0001				
Mental Health (MH)							
Baseline	22.6	(0.86)	19.9	(1.03)	2.70	(-0.01, 5.41)	0.0508
Post	38.4	(0.81)	28.2	(1.44)	10.1	(6.97, 13.27)	<.0001
Difference (Post-Baseline)	15.78	(13.82, 17.73)	8.35	(5.40, 11.31)	7.42	(3.88, 10.96)	<.0001
p-value	<.0001		<.0001				
Role Emotional (RE)							
Baseline	21.6	(0.83)	21.1	(1.18)	0.46	(-2.33, 3.25)	0.7472
Post	33.6	(0.97)	23.9	(1.56)	9.71	(6.08, 13.33)	<.0001
Difference (Post-Baseline)	12.01	(9.70, 14.31)	2.76	(-0.89, 6.40)	9.25	(4.98, 13.51)	<.0001
p-value	<.0001		0.1377				
Vitality (VT)							
Baseline	32.8	(0.82)	29.8	(0.99)	2.96	(0.38, 5.54)	0.0243
Post	44.6	(0.75)	35.9	(1.39)	8.67	(5.68, 11.67)	<.0001
Difference (Post-Baseline)	11.78	(9.93, 13.63)	6.07	(2.88, 9.25)	5.71	(2.13, 9.29)	0.0018
p-value	<.0001		0.0002				
Social Functioning (SF)							
Baseline	24.2	(0.81)	23.8	(1.16)	0.38	(-2.36, 3.12)	0.7852
Post	35.5	(0.90)	29.0	(1.55)	6.51	(3.05, 9.97)	0.0002
Difference (Post-Baseline)	11.35	(9.40, 13.30)	5.22	(1.80, 8.64)	6.13	(2.29, 9.97)	0.0018
p-value	<.0001		0.0028				

¹ Standard Error (SE) reported for means at Baseline and Post, 95% Confidence Interval (CI) reported for Difference from Baseline scores.

Table 4

Beta coefficients from linear regression investigating potential predictors of quality of life (SF-36 subscale and summary scores) by remitter status

OUTCOME		β-coefficients							
SF-36 T-SCORE	Baseline Score	Remitter	HRSD ^I	MMSE ^I	WTAR	Delayed Recall ^I	% Retention ^I	Age	Psychosis
Physical Factors									
Physical Component Summary (PCS)	0.59 ^{*****}	NA	-0.15 [*]	0.19	0.02	0.64	-0.00		4.50 [*]
Bodily Pain (BP)	0.51 ^{*****}	NA	-0.22 ^{**}	0.39	0.02	0.31	-0.01		
Role Physical (RP)	0.51 ^{*****}	NA	-0.22 ^{**}	-0.03	0.02	0.40	-0.00		
General Health (GH)	0.52 ^{*****}	NA	-0.41 ^{*****}	0.15	0.01	0.60	-0.00	0.18 [*]	
Physical Functioning (PF)	0.55 ^{*****}	NA	-0.14 [*]	-0.05	0.04	0.76	-0.00	-0.23 [*]	5.41 [*]
Mental Factors									
Mental Component Summary (MCS)	0.46 ^{*****}	9.66 ^{*****}	NA	-0.26	-0.10	0.09	-0.00		
Mental Health (MH)	0.35 ^{*****}	9.19 ^{*****}	NA	-0.26	-0.04	0.51	-0.00		
Role Emotional (RE)	0.30 ^{**}	NA	-0.32 ^{***}	-0.18	-0.00	-0.49	-0.01		
Vitality (VT)	0.30 ^{***}	7.16 ^{*****}	NA	-0.00	-0.07	1.22	-0.00		
Social Functioning (SF)	0.50 [*]	NA	-0.25 ^{**}	-0.06	-0.10	0.21	-0.01		-5.28 [*]

HRSD was not used in factors with questions related to depression, instead, Remitter status was used

Baseline score, Remitter status or HRSD, MMSE, WTAR, Delayed Recall, and Percent Retention remained in model regardless of covariate p-value significance.

Age and/or Psychosis only remained in the model if covariate p-value was significant (<0.05).

^I Change from baseline score (Last minus Baseline score)

* p-value <0.05;

** p-value <0.01,

*** p-value <0.001,

**** p-value <0.0001