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Effects of Continuation Electroconvulsive Therapy on Quality of Life in Elderly Depressed Patients: A Randomized Clinical Trial

W. Vaughn McCall, M.D., M.S.[a], **Sarah H. Lisanby, M.D.**[*,b], **Peter B. Rosenquist, M.D.**[a], **Mary Dooley, M.S.**[c], **Mustafa M. Husain, M.D.**[d], **Rebecca G. Knapp, Ph.D.**[c], **Georgios Petrides, M.D.**, **Matthew V. Rudorfer, M.D.**[b], **Robert C. Young, M.D.**[f], **Shawn M. McClintock, Ph.D., M.S.C.S.**[d], **Martina Mueller, Ph.D.**[c], **Joan Prudic, M.D.**[g], **Robert M. Greenberg, M.D.**[h], **Richard D. Weiner, M.D., PhD.**[i], **Samuel H. Bailine, M.D.**[j], **Nagy A. Youssef, M.D.**[a], **Laryssa McCloud, Ph.D.**[a], **Charles H. Kellner, M.D.**[k], and **the CORE/PRIDE Work Group**

[a]Department of Psychiatry and Health Behavior; Medical College of Georgia; Augusta University [b]National Institute of Mental Health, Bethesda, Maryland [c]Medical University of South Carolina, Charleston [d]University of Texas Southwestern Medical Center, Dallas [e]Hofstra Northwell School of Medicine, New York [f]New York Presbyterian/Weill Cornell Medical Center, New York [g]Department of Psychiatry, Columbia University, New York [h]New York University Langone Medical Center [i]Department of Psychiatry, Duke University School of Medicine, Durham [j]Zucker Hillside Hospital [k]Icahn School of Medicine at Mount Sinai, New York

Abstract

We examined whether electroconvulsive therapy (ECT) plus medications ("STABLE + PHARM" group) had superior HRQOL compared with medications alone ("PHARM" group) as continuation strategy after successful acute right unilateral ECT for major depressive disorder (MDD). We

Address correspondence to Dr. W Vaughn McCall; Department of Psychiatry and Health Behavior; Medical College of Georgia; Augusta University; 997 St Sebastian Way; Augusta, Georgia, 30912. Phone 706-721-6719. Fax 706-721-1793 (wmccall@augusta.edu).

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Conflict of Interest

Dr. McCall has been a scientific advisor for Merck, and Israeli Growth Partners, and a consultant to Luitpold Pharmaceuticals, Inc and Multiple Energy Technologies, LLC. Dr. Kellner receives honoraria from UpToDate, Psychiatric Times, and Northshore-LIJ Health System, and is a consultant to Luitpold Pharmaceuticals, Inc. Dr. Husain has received grant support from NIDA, NINDS, NIA, NARSD, Stanley Foundation, Cyberonics, Neuronetics, St. Jude medical (ANS), MagStim, Brainsway, NeoSync, Avanir, Alkermes, and has been a consultant to the Neurological Devices Panel of the Medical Devices Advisory Committee, Center for Devices and Radiological Health, Food and Drug Administration (FDA). Dr. Young is a consultant to the NIH. Dr. Lisanby has received grant support from NINDS, NIBIB, Brain and Behavior Research Foundation, Stanley Medical Research Foundation, Neosync, Nexstim, and Brainsway. Dr. Petrides has received research support from Amgen, Astra Zeneca, Corcept, Eli Lilly, Proteus, St. Jude Medical, and Sunovion, and he has served on an advisory panel for Corcept. Dr. McClintock has received grant support from the NIH/NIMH, honoraria from TMS Health Solutions and the US Department of Veteran Affairs, and is a consultant to Pearson. Dr. Nagy Youssef received grant support from the Department of Veterans Affairs, and CME honoraria form the Georgia Department of Behavioral Health and Developmental Disabilities. The other authors report no financial relationships with commercial interests.

hypothesized that scores from the Medical Outcomes Study Short Form-36 (SF-36) would be higher during continuation treatment in the “STABLE + PHARM” group versus the “PHARM” group. The overall study design was called “Prolonging Remission in Depressed Elderly” (PRIDE). Remitters to the acute course of ECT were re-consented to enter a 6 month RCT of “STABLE + PHARM” versus “PHARM”. Measures of depressive symptoms and cognitive function were completed by blind raters; SF-36 measurements were patient self-report every 4 weeks.

Participants were 120 patients ≥ 60 years old. Patients with dementia, schizophrenia, bipolar disorder, or substance abuse were excluded. The “PHARM” group received venlafaxine and lithium. The “STABLE + PHARM” received the same medications, plus 4 weekly outpatient ECT sessions, with additional ECT session as needed. Participants were mostly female (61.7%) with a mean age of 70.5 ± 7.2 years. “STABLE + PHARM” patients received 4.5 ± 2.5 ECT sessions during Phase 2. “STABLE + PHARM” group had 7 point advantage (3.5–10.4, 95% CI) for Physical Component Score of SF-36 (P <0.0001), and 8.2 point advantage (4.2–12.2, 95% CI) for Mental Component Score (P <0.0001). Additional ECT resulted in overall net health benefit. Consideration should be given to administration of additional ECT to prevent relapse during the continuation phase of treatment of MDD.

Keywords

Electroconvulsive therapy; quality of life; randomized controlled trial; major depressive disorder; continuation therapy

Introduction

Major Depressive Disorder (MDD) is a leading cause of poor health-related quality of life (HRQOL).(WHO Guidelines Approved by the Guidelines Review Committee, 2011) The HRQOL deficits increase with depression symptom severity.(McCall et al., 1999a) Age influences the HRQOL deficit patterns, with younger depressed patients reporting more problems with relationships and older depressed patients reporting more problems with daily living and role functioning.(McCall, Cohen, Reboussin, and Lawton, 1999a) A third of depressed patients do not respond to two or more sequential antidepressant medications, and are deemed to have treatment resistant depression (TRD).(Kubitz et al., 2013;McCall, 2007) TRD patients are candidates for electroconvulsive therapy (ECT), acknowledged as the most effective TRD treatment.(Lisanby, 2007)

HRQOL is exceptionally poor in MDD patients referred for ECT, and worse than that of unselected MDD patients in general outpatient settings,(McCall et al., 2013) and HRQOL is a factor in referral patterns for ECT.(McCall et al., 1999b) Naturalistic studies of MDD have shown that ECT results in improved HRQOL, with the degree of improvement greater for patients who received ECT as opposed to antidepressant medications.(McCall et al., 2001) Similarly, modern ECT randomized clinical trials (RCT) not including a non-ECT comparator arm also showed improvement in QOL.(McCall WV et al., 2011;McCall et al., 2004) Both in the naturalistic studies and the prior RCTs, improvement in HRQOL was best explained by improvement in depression symptoms, with little or no relationship to any

cognitive side effects. In naturalistic studies, improvement in HRQOL was sustained over 6-months after ECT in patients with sustained remission with HRQOL values indistinguishable from healthy population norms.(McCall, Reboussin, Prudic, Haskett, Isenberg, Olfson, Rosenquist PB, and Sackeim, 2013) In contrast, depressive relapse after ECT was associated with worsening in HRQOL.(McCall et al., 2006)

HRQOL is central to understanding the overall net risks and benefits of treatments, including those of ECT. While ECT results in remission of depressive symptoms, it also is associated with cognitive side effects. The issue of cognitive side effects is of particular concern for the elderly population who are more vulnerable for age-related cognitive problems.(Rizzi et al., 2014) Medical decision making regarding the risk/benefit ratio of ECT could be usefully informed by the study of health related quality of life measures. (Devanand et al., 1994;Scalia et al., 2007;Weiner, 1984) However, prior HRQOL studies in ECT have lacked randomized comparisons of ECT versus a non-ECT alternative group.

We present here the HRQOL outcomes as a secondary analysis from a randomized comparison of ECT combined with venlafaxine (VEN) and lithium (Li), versus VEN and Li without ECT, as continuation therapy after a successful ECT course for elderly adults with MDD.

Material and Methods

Design Overview

The *Prolonging Remission in Depressed Elderly (PRIDE)* study was a NIH-funded randomized, multi-center study that compared two post-acute-ECT continuation treatment strategies: (1) pharmacotherapy that combined venlafaxine (VEN) and lithium (Li) (*PHARM*); and (2) PHARM enhanced by the addition of an individualized, flexible, algorithm-based ECT schedule (**S**ymptom-**T**itrated, **A**lgorithm-**B**ased, **L**ongitudinal **E**CT, STABLE) (*STABLE + PHARM*).(Lisanby et al., 2008)

PRIDE consisted of two phases: in Phase 1, 240 patients, ≥ 60 years old with unipolar MDD received acute ECT 3 times per week in combination with oral VEN; in Phase 2, 120 remitters who were randomized to either PHARM or STABLE + PHARM comprised the intent-to-treat (ITT) sample. The primary efficacy outcome variable was the 24-item Hamilton Rating Scale for Depression ($HRSD_{24}$) total score measured longitudinally over 6-months. A priori secondary outcome variables included HRQOL. The results of Phase 1 have been previously reported for both antidepressant efficacy and HRQOL,(Kellner et al., 2016b;McCall et al., 2017) and the Phase 2 efficacy results have been reported.(Kellner et al., 2016a) The study was approved by the institutional review board at each study site, and the investigation was carried out in accordance with the latest version of the Declaration of Helsinki.

Patient Sample

Patients enrolled in Phase 1 were aged 60 years and older referred for ECT for the treatment of unipolar MDD, without dementia, with or without psychosis, with a pretreatment $HRSD_{24}$ total score ≥ 21. Exclusion criteria included: bipolar disorder, schizoaffective

disorder, schizophrenia, dementia, delirium, intellectual disability, history of substance abuse in the past 6 months, or neurological conditions or active general conditions assumed to affect cognition or treatment response. Also, patients failing to respond to an adequate trial of Li+VEN or ECT in the current episode were excluded. Inclusion criteria for the randomized phase (Phase 2) were achievement of remission in Phase 1 defined as: (a) $HRSD_{24}$ total score ≤10 on two consecutive ratings, and (b) $HRSD_{24}$ total score did not increase > 3 points on the second consecutive $HRSD_{24}$ or remained ≤ 6. Written informed consent was obtained before entrance to Phase 1 and before randomization in Phase 2.

Treatments

Symptom-Titrated, Algorithm-Based Longitudinal ECT (STABLE)—STABLE featured an initial fixed, tapered, ECT treatment schedule followed by a symptom driven, flexible component, in addition to the same VEN + Li as in PHARM, and the combination is termed STABLE + PHARM. The initial fixed portion consisted of 4 ECT in one month, within specified treatment windows. Treatment frequency in the subsequent flexible component (weeks 5–24) was determined by application of the STABLE algorithm, which prescribed 0–2 ECT in a given week based upon a patient's $HRSD_{24}$ total scores, details of which have been previously reported.(Lisanby, Sampson, Husain, Petrides, Knapp, McCall, Young, Prudic, and Kellner, 2008)

ECT procedures—ECT was delivered with right unilateral electrode placement with a high-dose, ultrabrief pulse stimulus, (RUL-UBP) described in our earlier report.(Kellner, Husain, Knapp, McCall, Petrides, Rudorfer, Young, Sampson, McClintock, Mueller, Prudic, Greenberg, Weiner, Baline, Rosenquist, Raza, Kaliora, Latoussakis, Tobias, Briggs, Liebman, Geduldig, Teklehaimanot, Dooley, Lisanby, and CORE/PRIDE Work Group, 2016a) Continuation ECT in Phase 2 was administered at the same stimulus dose as the last treatment in Phase 1.

Medication Procedures—Open label VEN was started in Phase 1 at an initial dosage of 37.5 mg *po*, with a target dose of 225 mg qD by the end of Phase 1. This dosage was continued following randomization in Phase 2. Open label Li was started at 300 mg/day on the day of randomization in Phase 2, with a target level for most patients in the 0.4–0.6 mEq/L range. For VEN and Li dosing/procedures were identical for the PHARM arm and the STABLE + PHARM arm, except that Li was withheld the night before ECT in the STABLE + PHARM arm. The schedule of clinic and telephone ratings was identical for both the PHARM and STABLE + PHARM arms.

Assessments

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 acute ECT and again at the end of Phase 1/beginning of Phase 2. Thereafter, the SF36 was measured every 4 weeks during Phase 2. SF36 data were scored in terms of the 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 sum of the questions for that subscale,

transformed into a 0–100 scale. Lower scores define more disability. Individual scores were then transformed into T-scores, with means of 50 and standard deviations of 10. The 8 subscales were then aggregated into the two total scores: Physical Health Factor T-score (comprised of PF, RP, BP, and GH subscales) and Mental Health Factor T-score (comprised of the VT, SF, RE, and MH subscales) following the algorithm provided by Ware, Kosinski & Dewey, by weighing the 8 subscale scores by their respective physical and mental factor scores and summing over the physical and mental subscale scores.(Ware et al., 2000) In addition, there are two age- and sex-adjusted summary scores; physical component score (PCS) and mental component score (MCS).

Depression severity and remission/relapse status—Depressive symptom severity was measured using the $HRSD_{24}$, and was treated as a continuous variable for the purposes of the relationship between HRQOL and depression severity.(Hamilton, 1960) However, participants left Phase 2 of the study if they relapsed, which was defined as two consecutive $HRSD_{24}$ scores ≥ 21, or the need for psychiatric hospitalization, or becoming suicidal. (Kellner, Husain, Knapp, McCall, Petrides, Rudorfer, Young, Sampson, McClintock, Mueller, Prudic, Greenberg, Weiner, Baline, Rosenquist, Raza, Kaliora, Latoussakis, Tobias, Briggs, Liebman, Geduldig, Teklehaimanot, Dooley, Lisanby, and CORE/PRIDE Work Group, 2016a)

Cognitive Function—The Wechsler Test of Adult Reading (WTAR) was administered once at Phase 1 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 delayed recall of verbal information, expressed as '% retention.'(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) The MMSE was measured every two weeks, CVLT-II monthly, and DRS-2 I/P was measured at midpoint and end of the study period.

Randomization and Masking of Treatment Assignment

The permuted block method of randomization was used, stratified by site. Block size was varied to minimize the likelihood of unmasking. Clinical raters and neuropsychological technicians were masked to treatment assignment.

Statistical Analysis

All statistical analyses were done by the authors (RGK, MM, and MD). Analysis was conducted on an intent-to-treat (ITT) sample using SAS 9.4. Longitudinal analyses were conducted using mixed effect models (MEM) to examine change in SF-36 sub-scores over a 24-week period. Simple models were analyzed for both the 2 SF-36 component and total scores, as well as the 8 sub-scores, with the total scores/subscores as the dependent variable and with fixed effects for the independent variables treatment (STABLE vs. PHARM), time (even weeks), and the time-by-treatment interaction. Expanded models adjusted the simple models for clinical site as a stratification variable, psychosis, WTAR, and time varying effect of CVLT-II retention, DRS-2 I/P, and MMSE. All available data for these variables collected

during Phase 2 were used in these models. Treatment interactions for age and psychosis were tested for significance. Additionally, expanded models for the total scores and subscores were adjusted for age and gender, whereas, the PCS and the MCS were calculated as age- and gender-adjusted scores and therefore did not need further adjustment. Furthermore, expanded models were adjusted for the time varying effect of $HRSD_{24}$, except for those subscores that included questions that were similar to those of $HRSD_{24}$ (MCS, Mental Health Factor T-Score, and MH). To account for random effects of subjects, random intercepts were used in all models and random slopes were used in models where the G-matrix was positive definite.

RESULTS

120 patients were randomized to PHARM (n=59) and STABLE + PHARM (n=61). Patients entering into Phase 2 had a mean $HRSD_{24}$ total score of 6.1; the majority were female (61.7%) and white (95%), with a mean age of 70.5 ± 7.2 years. The patients assigned to STABLE + PHARM received an average of 4.5 ± 2.5 continuation ECT sessions during Phase 2.

The time and group adjusted SF-36 mean score difference at 24-weeks was statistically significant between PHARM and STABLE + PHARM for PCS, MCS, total scores and all of the subscores (all $p<0.02$) except the BP subscore ($p=0.078$). Patients randomized to STABLE + PHARM had significantly higher quality of life scores at the 24-week visit compared to patients in the PHARM group. All SF-36 subscores as well as PCS and MCS showed a statistically significant time-by-treatment interaction in the simple models (all $p<0.04$, Table 1) indicating that the effect of time on quality of life depended on the treatment arm.

When the simple models were adjusted for additional covariates, all models except for the SF-36 subscores SF, RP, and RE resulted in statistically significant adjusted mean subscore differences at 24-weeks (all $p<0.04$, results not shown). $HRSD_{24}$ was statistically significantly associated with SF-36 PCS and subscores in all models where it was included except for Physical Health Factor T-Score (Table 2). Group assignment to STABLE + PHARM versus PHARM did not significantly contribute to the model after accounting for the effects of $HRSD_{24}$ (Table 2). For models that did not include $HRSD_{24}$, time was statistically significantly associated with both SF-36 MCS and Mental Health Factor T Score (all $p<0.02$) but not MH subscore ($p=0.09$). Age was statistically significantly associated with SF-36 subscores Physical Health Factor T-Score, PF, and RP (Table 2). Of particular note, cognitive variables had modest associations to HRQOL variables. (Table 2)

Discussion

This is the first report of the HRQOL effects in a randomized comparison of a treatment strategy that included ECT combined with medication versus medication alone. Participants who received ECT in the STABLE + PHARM group had better HRQOL on every dimension of the SF-36 across 6-months of follow up compared with the patients in the PHARM group. The HRQOL benefits were best explained by superior control of depressive symptoms in the

STABLE + PHARM group, with negligible contribution of cognitive function variables. The results of this study are especially meaningful since the elderly participants with severe MDD may be viewed as a particularly vulnerable population who are referred for ECT. (McCall, Cohen, Reboussin, and Lawton, 1999b;McCall et al., 2003) These results provide strong evidence that ECT produces an overall net health benefit. Strengths of this study included a well-controlled design, use of standardized clinical neuropsychological variables to assess cognitive function, use of standardized psychometrically sounds measures of HRQOL, and an accounting of other confounding variables. However, as this study was designed to examine prevention of depressive relapse and was not designed to examine acute antidepressant effects, caution is warranted in drawing conclusions about HRQOL effects of ECT during acute treatment of depression in which the ECT treatments would be given more frequently than was done in this relapse prevention intervention.

The current report has some limitations. First, the measure of HRQOL was completed by patient self-report, and we did not include any measures of clinician-rated or third party observers, but in prior work we showed that ECT patients' assessment of their functional status closely matched the assessments of observers.(McCall et al., 2002) Second, lithium, venlafaxine, and as-needed lorazepam were the only medications examined in this study, while RUL UB ECT was the only form of ECT. Other medication regimens and other ECT treatment approaches may have produced different results. Indeed, different electrode placements have been shown to have differential effects on HRQOL, with RUL having superior HRQOL outcomes as compared with bilateral electrode placement.(Galvez et al., 2016;McCall WV, Rosenquist PB, Kimball, Haskett R, Isenberg, Prudic, Lasater, and Sackeim, 2011) Finally, the number of ECT treatments in the STABLE arm was low in comparison to a typical acute course of ECT, however it is remarkable that a low number of ECTs were sufficient to enhance HRQOL over a 6 month period.

The present report adds to the literature on the beneficial effects of ECT on HRQOL and the overall net health benefits. Our findings should assure patients, families, and caregivers of depressed elderly patients that ECT is a medically appropriate choice for elderly adults with MDD and is likely to produce improvement in HRQOL that can be sustained during the continuation phase of treatment by employing combined ECT and medication to support remission. The PRIDE study results support the merit of continuing ECT as a means of staving off depressive symptoms. Our findings substantiate that for elderly adults with MDD, ECT can be a quality-of-life-enhancing treatment when used as a continuation strategy in combination with medication to prolong remission.

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Drs. Knapp and Mueller had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis

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Table 1

"Basic Model SF-36 Total and Subscales at week-24, by Treatment adjusted for Time, and Treatment-by-Time interaction".

		WEEK 24 ADJUSTED							BASELINE				
	Treatment *Time	PHARM		STABLE + PHARM		DIFFERENCE			PHARM		STABLE + PHARM		DIFFERENCE
SF-36 T-SCORE	p-value	Mean	(SE)	Mean	(SE)	Mean	(95% CI)	p-value	Mean	(SE)	Mean	(SE)	Mean (95% CI)
PHYSICAL													
Physical Component Score (PCS)[1]	<.0001	44.4	(1.2)	51.3	(1.2)	−7.0	(−10.4, −3.5)	0.0001	45.3	(0.8)	44.5	(1.1)	0.8 (−1.8,3.4)
Physical Health Factor T Score	0.0127	44.1	(1.4)	49.0	(1.3)	−4.9	(−8.7, (−1.1)	0.0125	49.1	(1.2)	48.5	(1.4)	0.7 (−3.0,4.3)
Bodily Pain (BP)	0.0361	48.4	(1.5)	52.1	(1.4)	−3.7	(−7.9, 0.4)	0.0777	49.4	(1.2)	48.4	(1.5)	1.1 (−2.8,4.9)
General Health (GH)	0.0006	43.9	(1.6)	52.3	(1.5)	−8.4	(−12.7, (−4.1)	0.0002	48.8	(1.0)	49.3	(1.0)	−0.5 (−3.3,2.3)
Role Physical (RP)	<.0001	40.9	(1.5)	49.6	(1.4)	−8.7	(−12.7, −4.6)	<.0001	42.3	(1.2)	39.2	(1.5)	3.1 (−0.8,6.9)
Physical Functioning (PF)	0.0057	41.0	(1.6)	46.7	(1.6)	−5.7	(−10.1, −1.2)	0.0133	43.2	(1.3)	42.4	(1.7)	0.9 (−3.2,5.1)
MENTAL													
Mental Component Score (MCS)[1]	<.0001	45.3	(1.5)	53.5	(1.4)	−8.2	(−12.2, −4.2)	0.0001	41.3	(0.9)	40.5	(1.0)	0.8 (−1.9,3.6)
Mental Health Factor T Score	0.0292	47.6	(2.0)	54.4	(1.9)	−6.7	(−12.3, −1.2)	0.0174	35.6	(1.5)	34.5	(1.5)	1.1 (−3.2,5.3)
Mental Health (MH)	0.0086	47.0	(1.6)	54.2	(1.6)	−7.2	(−11.6, −2.7)	0.0017	39.7	(1.2)	37.4	(1.2)	2.3 (−1.1,5.7)
Role Emotional (RE)	0.0006	42.8	(1.7)	50.4	(1.6)	−7.6	(−12.3, −3.0)	0.0016	35.0	(1.4)	32.1	(1.6)	2.9 (−1.3,7.1)
Vitality (VT)	0.0108	47.8	(1.7)	54.5	(1.7)	−6.7	(−11.4, −2.0)	0.0061	44.3	(1.1)	45.0	(1.2)	−0.6 (−3.8,2.5)
Social Functioning (SF)	0.0051	44.7	(1.5)	53.3	(1.4)	−8.6	(−12.7, −4.5)	<.0001	35.1	(1.4)	36.4	(1.4)	−1.2 (−5.2,2.7)

[1] Subscale scores are age and gender adjusted; higher scores are better

Table 2

"Regression coefficients for predictors of SF-36 Total and Subscales over 24 weeks for STABLE+PHARM"

OUTCOME	**β-coefficients**								
SF-36 T-SCORE	**STABLE+ PHARM**	**HRSD**	**MMSE**	**WTAR**	**% Retention**	**DRS**	**Psychosis**	**Age**	**Female**
Physical Factors									
Physical Component Score (PCS)[1]	1.90	−0.63****	−0.05	0.09	0.01	−0.13	−0.15	NA[1]	NA[1]
Physical Health Factor T Score	1.76	−0.09	−0.06	0.10	0.02	−0.13	3.91	−0.30*	−3.07
Bodily Pain (BP)	2.14	−0.42**	0.02	0.07	0.02	−0.04	4.50	−0.27	0.04
General Health (GH)	3.20	−0.57****	0.02	−0.10	0.04	−0.28	−1.53	−0.04	0.87
Role Physical (RP)	2.88	−0.67****	−0.03	0.23*	−0.02	0.07	2.09	−0.42**	−1.98
Physical Functioning (PF)	1.15	−0.29*	−0.03	0.24*	0.04	−0.39	−1.48	−0.39*	−5.77**
Mental Factors									
Mental Component Score (MCS)[1]	1.23	NA[2]	−0.05	−0.02	0.01	0.05	2.88	NA[1]	NA[1]
Mental Health Factor T Score	−1.62	NA[2]	−0.03	−0.08	−0.02	0.01	5.99	0.32	−2.17
Mental Health (MH)	2.89	NA[2]	−0.10	−0.10	0.04	0.38	5.29	0.33	−3.87
Role Emotional (RE)	1.21	−1.23****	0.02	0.15	−0.03	−0.10	−5.39	−0.15	−0.27
Vitality (VT)	2.95	−1.23****	0.04	0.08	−0.04	−0.23	2.13	−0.14	−0.93
Social Functioning (SF)	2.34	−1.05****	0.08	0.11	−0.01	−0.34	1.04	−0.22	0.49

[1] Subscale scores are age and gender adjusted

[2] Subscale scores included questions that were similar to those of $HRSD_{24}$ therefore excluded $HRSD_{24}$ from model

* p-value <0.05;

** p-value <0.01,

*** p-value <0.001,

**** p-value <0.0001

SF-36: Short-Form 36

STABLE: Symptom-Titrated, Algorithm-Based Longitudinal ECT
HRSD: 24-item Hamilton rating Scale for Depression
MMSE: Mini Mental State Examination
WTAR: Wechsler Test of Adult Reading
% Retention: delayed recall from the second edition of the California Verbal Learning Test (CVLT-II)
DRS: The Dementia Rating Scale-2nd Edition Initiation/Perseveration Index