HHS Public Access

Author manuscript

Acta Psychiatr Scand. Author manuscript; available in PMC 2024 April 01.

Published in final edited form as:

Acta Psychiatr Scand. 2023 April ; 147(4): 322–332. doi:10.1111/acps.13537.

Factors Associated with Early and Late Response to Electroconvulsive Therapy

Kamber L. Hart, MS[a], **Thomas H. McCoy Jr, MD**[a,b], **Michael E. Henry, MD**[a,b], **Stephen J. Seiner, MD**[a,c], **James Luccarelli, MD, DPhil**[a,b]

[a]Harvard Medical School, 25 Shattuck Street, Boston MA

[b]Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Boston MA

[c]Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA

Abstract

Objective: Electroconvulsive therapy (ECT) is an effective treatment for severe depressive symptoms, yet more research is needed to examine predictors of treatment response, and factors associated with response in patients not initially improving with treatment. This study reports factors associated with time to response (early vs late) to ECT in a real-world setting.

Methods: This was a retrospective, single-center cohort study of patients endorsing moderate to severe depressive symptoms using the Quick Inventory of Depressive Symptomatology (QIDS; QIDS>10). Response was defined as 50% or greater decrease in QIDS score from baseline. We used logistic regression to predict response at treatment #5 (early response) as well as after treatment #5 (late response) and followed patients through ECT discontinuation or through treatment #20.

Results: Of the 1699 patients included in this study, 555 patients (32.7%) responded to ECT treatment at treatment #5 and 397 (23.4%) responded after treatment #5. Among patients who did not respond by treatment #5, those who switched to brief pulse width ECT from ultrabrief pulse ECT had increased odds of response after treatment #5 compared to patients only receiving ultrabrief pulse (aOR = 1.55, 95% CI: 1.16 – 2.07). Additionally, patients with less improvement in QIDS from baseline to treatment #5 had decreased odds of response after treatment #5 (aOR = 0.97, 95% CI = 0.97–0.98).

Conclusion: Among depressed patients treated with ECT, response occurred in 56.0% of patients by treatment #20. Patient receiving ultrabrief pulse ECT at baseline and who did not respond by treatment #5 had greater odds of subsequent response if switched to brief pulse ECT than if continued with ultrabrief pulse.

Corresponding Author: James Luccarelli, MD, DPhil, Address: Massachusetts General Hospital, 32 Fruit Street, Yawkey 6A, Boston MA 02114, jluccarelli@partners.org, Phone: 617-726-2000, Fax: 606-206-8090.

Conflicts of Interest

THM receives research funding from the Stanley Center at the Broad Institute, the Brain and Behavior Research Foundation, National Institute of Mental Health, National Human Genome Research Institute Home, and Telefonica Alfa. JL receives research funding from the National Institute of Mental Health and Harvard Medical School. He holds equity in Revival Therapeutics. The remaining authors have no disclosures to report.

Keywords

Affective disorders; Cohort studies; Electroconvulsive therapy; Real World Evidence

Introduction:

Electroconvulsive therapy (ECT) is an effective treatment for severe depressive symptoms, with reported remission rates ranging from 50–70% (Bahji et al., 2019; Dierckx et al., 2012). Given the cost and potential side effects of ECT, an improved understanding of predictors of ECT response would help guide referral for ECT treatment. Multiple prior studies have explored factors associated with response to ECT, with factors including older age, presence of psychotic symptoms, and increased severity of depression being associated with improved response (de Vreede et al., 2005; Medda et al., 2014; Spaans et al., 2016; Szegedi et al., 2009; Yao et al., 2019). These studies, however, have had limited sample size, and meta-analyses have been challenged by the heterogeneity of study design including variations in the definition of remission/response as well as the specific predictors included in the analysis (van Diermen et al., 2018). Additionally, many studies focus on predictors of short-term response to ECT over a few treatments, without examining predictors that predict response over a greater number of treatments (de Vreede et al., 2005; Nordenskjöld et al., 2012).

ECT administration can involve multiple different electrode placements (unilateral, bitemporal, bifrontal) and electrical pulse widths (ultrabrief pulse or brief pulse), which may vary in efficacy and tolerability. While many prospective research studies specify these ECT parameters *a priori* (de Vreede et al., 2005; Medda et al., 2014; Spaans et al., 2016), in clinical practice there is greater heterogeneity in ECT parameter utilization, and clinicians may make changes to a patient's ECT regimen over the course of a treatment series. Despite this common practice, the effects of changes in ECT parameters during a treatment course has been little explored, and there have not been prospective trials comparing changes in ECT parameters among patients who do not initially respond to treatment. For these reasons, more research is needed to examine predictors of both early and late response to ECT, as well as to examine the role of changing ECT parameters within larger, real-world cohorts.

Aims of the Study

This study sought to identify demographic or clinical factors that predicted a patient's response to ECT treatment in a large, single site cohort. We also sought to identify factors that were associated with a more rapid response to ECT, and factors associated with response over a longer series of treatments among patients who do not initially respond to treatment.

Methods:

ECT Treatment:

This retrospective cohort study included patients receiving ECT at a single freestanding psychiatric hospital between May 2011 and March 2020. Patients received ECT using

a Mecta Sepctrum 5000Q (Tualatin, OR), and their individualized seizure threshold was determined at first treatment (Luccarelli et al., 2020b, 2021b). By default, treatments were given 3 times weekly; modifications to both dosing and electrode placement were determined by the clinical judgement of the treating psychiatrist. Methohexital was the default anesthetic, and succinylcholine muscle relaxant was used for all patients. Demographic data is from patient self-report; diagnosis was extracted from the patient's clinical record at the time of their first treatment. The cohort was limited to patients with major depressive disorder (MDD) or bipolar disorder (BPAD). Prior work has described additional cohort data and description of treatment methodologies (Hart et al., 2022; Luccarelli et al., 2021a, 2021c). Since some patients received multiple courses of ECT over the study period, only the index treatment series was included in this analysis. To ensure that assessments captured a single treatment series, patients were excluded from analysis if their 5th treatment within a series was more than 30 days from their initial treatment, if their 10th treatment was more than 60 days from their initial treatment, or if their 15th treatment was more than 150 days from their initial treatment.

Outcome Measure:

The primary symptom scale used in this study was the Quick Inventory of Depressive Symptomatology – Self Report 16 item scale (QIDS)(Rush et al., 2003). The QIDS was administered as part of routine clinical care prior to the first treatment and after treatment #5, #10, #15, and #20. Due to variability in clinical care, a QIDS conducted within one treatment of each primary timepoint was included as data for the major timepoints; for example, a QIDS conducted after treatments #4–6 were included as data for treatment #5. The distribution of assessment timepoints included in each primary time point is presented in Supplemental Table 1. To focus our analyses on the effect of ECT on depressive symptoms, our cohort was limited to patients experiencing moderate to severe symptoms of depression at baseline (QIDS >10). A QIDS score of 6–10 indicates mild depression, 11–15 indicates moderate severity, 16–20 indicates severe depression symptomatology, and >=21 indicates very severe depressive symptoms (Rush et al., 2003).Treatment response was defined as a decrease in QIDS composite score of greater than or equal to 50% from baseline. Patients who responded to ECT by treatment #5 were classified as early responders, while those who responded at a subsequent time point were classified as late responders. Remission was defined as QIDS < 6. Patients were excluded from analysis if they did not provide a baseline QIDS, or if they lacked any QIDS follow-up data. Individuals were followed until drop out from ECT treatment or until treatment #20.

Statistical Analysis:

Our first aim was to identify baseline factors that predicted response at treatment #5. Therefore, we constructed a logistic regression model including baseline demographic data (age, sex, diagnosis), baseline treatment location (inpatient vs. outpatient) and baseline QIDS score. We also included two variables to capture baseline ECT parameters: 1) pulse width, stratified into brief pulse (pulse width >0.37 ms) and ultrabrief pulse (pulse width 0.3 or 0.37 ms), and 2) electrode placement, stratified as unilateral or bilateral (defined as bitemporal or bifrontal).

Our second aim was to identify factors associated response after treatment #5, or late response to ECT. Therefore, we limited the cohort to those not responding at treatment #5 and repeated the logistic regression including the same demographic variables (baseline age, sex, diagnosis) and treatment location at treatment #5. To capture change in symptom severity and ECT parameters during treatment, we included percent change in QIDS score from baseline to treatment #5, as well as 2 variables to capture ECT parameters. ECT parameters were summarized into the following variables: 1) pulse width, stratified into patients that only received ultrabrief pulse, patients that started with ultrabrief pulse and switched to brief pulse during their treatment series, or patients only receiving brief pulse; 2) receipt of bilateral ECT at any point in the study period. Since patients progressed through treatment series over different time courses, we performed a sensitivity analysis by repeating the logistic regression assessing for response after treatment #5 and adding time to endpoint (either response or final treatment) to the analysis as a covariate.

To assess for factors associated with dropout between assessment points, we constructed logistic regression models to predict if a patient would still be receiving treatment at treatment #10, treatment #15, and treatment #20. Each model included demographic data (age, sex, and diagnosis) as well as treatment location (inpatient or outpatient) at the prior assessment timepoint, percent change in QIDS score from baseline to the prior treatment timepoint, and ECT parameters at the prior timepoint. ECT parameters were pulse width (stratified to ultrabrief pulse or brief pulse), and laterality (unilateral vs bilateral electrode placement). Patients that met criteria for response at a prior treatment timepoint were not included in the analyses.

This study was reviewed by the Mass General Brigham Institutional Review Board and approved with a waiver of informed consent. All analyses were completed in R (version 4.1.0).

Results:

1699 patients met inclusion criteria by having baseline QIDS >10 and at least one follow-up QIDS measurement. Of these, 555 patients (32.7%) responded to ECT treatment at treatment #5 (early responders) and 397 (23.4%) responded after treatment #5 (late responders; treatment #10 (N = 242), treatment #15 (N = 109), and treatment #20 (N = 46)); that is, 952 (56.0%) of the 1699 patients who began treatment achieved QIDS defined response at or before treatment #20 (Supplemental Figure 1). 38.6% (214/555) of patients responding at treatment #5 achieved remission of depressive symptoms (QIDS<6) and 35.0% (139/397) of patients responding after treatment #5 achieved remission.

The remaining 747 patients (44.0% of the original cohort) were classified as non-responders as they did not meet QIDS response criteria at any time point. Table 1 shows baseline demographics for the entire cohort, and for the overall responder and non-responder subgroups. Patients were mostly white (91.8%) and female (59.6%). Clinical diagnosis was MDD in 78.8% of patients and BPAD in 21.3%. Most patients received ultrabrief pulse, unilateral ECT at baseline (ultrabrief pulse: 94.1%, unilateral: 97.2%). The distribution of pulse widths at each treatment timepoint is presented in Supplemental Figure 2). Looking

across all treatment timepoints 30.0% of bilateral ECT treatments were bifrontal electrode placement and 70.0% were bitemporal.

The 555 early responders had an average percent decrease in their overall QIDS score of 65.4% (SD = 11.7) from baseline to treatment #5. The 1,144 non-responders at treatment #5 had an average percent decrease in their overall QIDS score from baseline of 20.1% (SD = 19.0). Supplemental Table 2 shows the baseline demographics stratified by response at treatment #5. Figure 1 shows the composite QIDS score at baseline and treatment #5 separated by response status at treatment #5. In a logistic model of the outcome of response vs. non-response at treatment #5, older age at baseline was associated with increased odds of response (aOR = 1.01, 95% CI: 1.00 – 1.01), while outpatient treatment at baseline was associated with decreased odds of response (aOR = 0.49, 95% CI: 0.39 – 0.62; Table 2). Patient sex, clinical diagnosis, baseline QIDS, and ECT parameters were not significantly associated with response at treatment #5. Results were similar in an analysis limited to patients with assessment only at the primary treatment timepoint (treatment #5; data not shown).

Following treatment #5, an additional 397 patients responded to ECT and were classified as late responders. This represents 23.4% of overall patients, or 44.7% of the 889 non-responders at treatment #5 who continue in ECT through at least treatment #10. Figure 2 shows the composite QIDS score at treatment #5-#20 among patients not meeting criteria for response at treatment #5 stratified by response after treatment #5. Late responders had a mean percent decrease in QIDS from baseline of 64.7% (SD = 11.3) at the time of treatment response, while never-responders had a mean percent change in QIDS of 20.4% (SD = 20.2) at the time of last treatment. At treatment #20, 172 patients continued in ECT treatment who did not meet response criteria based on QIDS score.

To explore factors more generally associated with later response to ECT, we performed a logistic regression on the binary outcome of response beyond treatment #5 vs. no observed response, with age, sex, diagnosis, location of treatment #5 (inpatient vs. outpatient), percent change in QIDS from baseline to treatment #5, as well as 2 variables summarizing changes in ECT parameters. Among 1144 patients not responding by treatment #5, 545 (47.6%) patients had a change in their ECT parameters from those used at baseline. Patients who started with ultrabrief pulse treatments and were switched to brief pulse ECT during their treatment had increased odds of response as compared to patients only receiving ultrabrief pulse (aOR = 1.55, 95% CI: 1.16 – 2.07). Patients receiving bilateral ECT at any point during the treatment period had decreased odds of response as compared to patients never receiving bilateral ECT treatment (aOR = 0.60, 95% CI: 0.42 – 0.85). Additionally, patients with less improvement in QIDS from baseline to treatment #5 had decreased odds of response after treatment #5 (aOR = 0.97, 95% CI = 0.97–0.98) and older patients had significantly increased odds of response (aOR = 1.01, 95% CI: 1.00 – 1.02). Patient sex, diagnosis, and treatment location at treatment #5 were not significantly associated with response after treatment #5 (Table 3). Results were similar in an analysis limited to patients with assessment only at the primary treatment timepoints (treatment #10, #15 and #20; data not shown).

A sensitivity analysis including days to treatment endpoint (either response or last treatment) as a covariate, yielded quantitatively similar results (Supplemental Table 3). Days to treatment endpoint was not significantly associated with response after treatment #5. Supplemental Table 4 shows the ECT parameters at each treatment point stratified by overall response to treatment.

Late responders had, on average, a 25.6% decrease in QIDS from baseline to treatment #5 (SD = 16.4), and never-responders had an average decrease in QIDS from baseline to treatment #5 of 17.3% (SD = 19.7). Among 196 patients with no improvement in QIDS from baseline to treatment #5 (defined as a QIDS score at treatment #5 that was equal to or greater than the QIDS score at baseline) 20.0% (39/196) eventually responded to treatment.

Since treatment location (inpatient vs outpatient) was significantly associated with response at treatment #5, we performed a sensitivity analysis to assess predictors of response among patients that never received inpatient care (n = 489). Within this cohort, treatment with ultrabrief pulse at baseline was associated with decreased odds of response at treatment #5 as compared to those receiving brief pulse ECT at baseline (aOR = 0.34, 95% CI: 0.14 – 0.84). After further limiting to patients not responding by treatment #5 (N = 378), switching from ultrabrief to brief pulse ECT was associated with increased odds of response after treatment #5 (aOR = 1.84, 95% CI: 1.09 – 3.11) and treatment with bilateral ECT at any point during the treatment series was associated with decreased odds of response (aOR 0.36, 95% CI: 0.19 – 0.66). Patients receiving bilateral ECT treatment at any point in the treatment series had a smaller percent change in QIDS from baseline to treatment #5 (mean = −11.5, SD = 19.1) as compared to patients never receiving bilateral ECT treatment (mean = −19.9, SD = 18.7). Patients with less improvement in QIDS score from baseline to treatment #5 had decreased odds of response after treatment #5 (aOR = 0.97, 95% CI: 0.96 – 0.98). These findings are consistent with our primary model. Treatment with only brief pulse ECT was associated with increased odds of response as compared to patients only receiving ultrabrief pulse ECT (aOR = 5.15, 95% CI: 1.54 – 18.26). There was not a significant effect of age on response after treatment #5. These findings differ from our primary model. Results are presented in supplemental Table 5 and 6.

To explore factors associated with discontinuation of ECT treatment, we performed logistic regressions on the outcome of continuing in ECT treatment through treatment #10, #15, and #20. Patients receiving outpatient treatment at treatment #10 were more likely to reach treatment #15 (aOR 1.84, 95% CI: 1.35 – 2.51 and (aOR 1.01, 95% CI: 1.00 – 1.02, respectively). There were no covariates that significantly predicted which patients would continue receiving ECT at treatment #5 or treatment #20 (Supplemental Table 7).

Discussion:

In a large, single-center cohort of routine clinical care, covering 1699 patients with moderate to severe depressive symptoms receiving ECT treatment, 32.7% met criteria for early ECT response by having a 50% or greater reduction in QIDS score by treatment #5. An additional 397 (23.4% of the original cohort) met criteria for late response by responding to treatment between treatments #10 and #20, for an overall response rate of 56.0% across treatment

time points. Of the 1699 patients who began treatment, 575 discontinued treatment prior to QIDS defined response or treatment #20 for a dropout rate of 33.8%. Consistent with prior results, the majority of ECT response occurred during the earliest phase of treatment. The two largest prospective trials of ECT, the CORE and PRIDE trials, both indicate that the mean number of treatments required to reach remission of depression is 7.3 (Kellner et al., 2006a, 2016), and that close to 90% of patients that will reach remission from ECT do so by their 9th treatment (Kellner et al., 2010, 2006b). The treatment of those patients who do not initially respond to ECT remains a key therapeutic dilemma, and this study adds to the evidence based for continuing ECT treatment in select individuals who do not show an early response.

In this cohort, older age was associated with increased response to ECT which is consistent with prior literature (Nordenskjöld et al., 2012; O'Connor et al., 2001; van Diermen et al., 2018) and the more frequent use of ECT in old age depression (Luccarelli et al., 2020a). The magnitude of this effect was, however, small. Our results also suggest that outpatients were less likely to respond to ECT at treatment #5 as compared to inpatients, which is consistent with prior findings (Nordenskjöld et al., 2012). This may be reflective of the other therapeutic interventions available to inpatients such as increased frequency of psychotherapy, medication changes, general therapeutic milieu, etc. Baseline depression severity, as measured by the QIDS, was not associated with treatment response. This is consistent with data from the Prolonging Remission in Depressed Elderly prospective trial, in which baseline depression severity was not associated with response rate, but discordant with results from a 2018 meta-analysis finding a small but significant association between increased depression severity and higher odds of response (but not remission)(Kellner et al., 2016; van Diermen et al., 2018). Overall, these baseline demographic and symptoms severity predictors explained only a small minority of the variance in response at treatment #5, and so further research is needed into other predictors of short-term response to ECT.

The second aim of this study was to identify factors, including treatment parameter changes, that were associated with late response to ECT. Among the 889 patients not meeting criteria for response at treatment #5 that continued to receive treatment at treatment #10, a total of 397 went on to achieve response at a later point, for an overall response rate of 56.0% of the starting 1699 patients. Notably, however, 255 non-responders at treatment #5 dropped out of treatment prior to treatment #10 (15.0% of the original cohort) and an additional 320 (18.8%) dropped out prior to treatment #20.

Patients with greater improvement at treatment #5 were more likely to eventually meet criteria for response. This is consistent with prior work (Husain et al., 2004; Kho et al., 2004; Pinna et al., 2018). Notably, however, minimal response by treatment #5 was not a marker of futility of further ECT, as even among those patients who showed no reduction in depressive symptoms by treatment #5, 20% eventually met criteria for response. Additionally, duration of treatment (time from baseline treatment to either response or final treatment) was not significantly associated with response. That is, patients that are followed for longer periods of time are not more likely to respond to ECT. This suggests that improvement within this cohort is not simply being driven by mean reversion over time.

In our sample, over 90% of patients received unilateral, ultrabrief pulse ECT at baseline. Over the course of the treatment, the most common changes in ECT parameters within this cohort was from unilateral, ultrabrief pulse to unilateral, brief pulse. Our analyses suggest that changing from ultrabrief pulse ECT to brief pulse ECT was associated with increased odds of late response to ECT among patients not showing response by treatment #5 as compared to patients continuing to receive ultrabrief pulse ECT. Prior work has suggested that brief pulse ECT is associated with higher rates of remission and faster response as compared to ultrabrief pulse ECT, but may be associated with greater cognitive side effects (Bahji et al., 2019; Tor et al., 2015). This suggests that patients not responding to ultrabrief pulse ECT by the 5^{th} treatment may benefit from a change to brief pulse ECT. However, additional prospective studies are needed to replicate this finding.

Our results also showed that bilateral ECT treatment at any point during the treatment series was associated with decreased odds of response. This is not consistent with prior work, which found similar rates of initial response between patients receiving unilateral ECT and bitemporal ECT(Semkovska et al., 2016). Unilateral electrode placement is often preferred for initial treatment as it has been shown to have less of an adverse effect on cognition and memory (Kellner et al., 2010). However, bitemporal electrode placement may have a more rapid reduction in symptoms as compared to unilateral electrode placement(Kellner et al., 2010). In our cohort, patients receiving bilateral ECT treatment at any point in the treatment series had a smaller percent change in QIDS from baseline to treatment #5 as compared to patients never receiving bilateral ECT treatment. While our dataset does not include information on clinical decision making, this may suggest that our finding that bilateral ECT treatment was associated with decreased odds of response is due to confounding by indication, or in other words, sicker patients that are not responding to unilateral treatment are transitioned to bilateral ECT, despite the increased risk of side effects. We chose to combine bitemporal and bifrontal electrode placement because of the overall low rates of bilateral electrode placement, especially at the beginning of treatment (Supplemental Table 4). Future work, including prospective trials, is needed to better identify subsets of patients that respond to different ECT treatment parameters and to better elucidate criteria for changing ECT treatment parameters.

In this study, we chose to use response (50% or greater reduction in symptoms from baseline) as opposed to remission (complete resolution of depressive symptoms) as our primary outcome since prior work has demonstrated high rates of residual depressive symptoms after treatment (Fava, 2020). We found that 38.6% of patients responding at treatment #5 achieved remission of depressive symptoms and 35.0% of patients responding after treatment #5 achieved remission. This shows that there are similar rates of remission among early and late responders and suggests that there are high rates of residual symptoms even among patients with a significant clinical response to ECT. The rate of response in this study is lower than the rate of response found in prior randomized trials of ECT(Bahji et al., 2019). As our results draw from real-world clinical practice, as opposed to prospective clinical trials, further research is required to assess the generalizability of findings, and the actual response rate derived in real-world clinical practice in diverse settings, especially since these data are drawn from a tertiary referral center. Additional research is needed

to better understand the frequency the residual symptoms after ECT treatment, and to determine which symptom domains have the highest rates of residual symptoms.

Limitations:

These data are drawn from an existing clinical cohort and represent the administration of ECT in a real world, clinical setting. However, all the standard limitations of observational data apply as well as those of longitudinal analysis with imperfect follow up. For example, these data rely on clinical diagnoses extracted from the medical record instead of diagnoses from a structured clinical interview and these data do not contain the reason for ECT treatment or other psychiatric symptomatology (e.g., depression, depression with psychotic features, mania, psychosis, etc.) nor does it include information on length of current depressive episode. We have attempted to address this limitation by limiting our analyses to patients with moderate to severe depression at baseline. It is also important to note that these data do not contain information on clinical rationale for changes in ECT parameters and include a heterogenous sequence of parameter changes. While this is reflective of real-world administration of ECT, in which there is little clinical trials evidence to guide dose escalation or changes in parameters following initial non-response, this variance makes it more challenging to interpret the effect of changes in ECT parameters and dosing regimens on outcomes. Additionally, the majority of patients in this sample began with ultrabrief pulse width and right unilateral electrode placement, and so these results provide less data on patients who begin with bilateral or brief pulse stimuli, which may be preferred at baseline for patients with the most severe illness. Moreover, we are unable to assess the effects of baseline medications, medication changes, or psychotherapeutic changes which may have co-occurred with ECT treatment.

Another limitation is the timing of symptom severity assessments, as patients may exit treatment between assessment timepoints. We are unable to assess symptom severity or reason for dropout in these patients, and so some patients who went on to achieve response and discontinued treatment between the assessment points may be erroneously classified as non-responders. However, while outpatients at treatment #10 were more likely to treatment #15, change in QIDS score did not significantly predict dropout at any of the timepoints. Furthermore, there were no significant predictors of patients continuing treatment at treatment #20. Patients continued to achieve response at treatment #20, and prior work has indicated that among patients who remain in prolonged maintenance ECT there is ongoing clinical improvement through 50–100 treatments (Luccarelli et al., 2020c), and so we are unable to assess how many patients may have achieved response if followed through later time points. While the QIDS 16 self-report has not been specifically validated in ECT treatment, prior work has shown that patient self-reported scores and clinician reported scores(Bernstein et al., 2007; Rush et al., 2006).

It is important to note that the patients in this cohort are predominantly white and received care at a private psychiatric hospital. While this is consistent with norms on ECT administration across the United States, we must consider how this affects the generalizability of these results as well recognize disparities in the availability of ECT (Case et al., 2012; Luccarelli et al., 2020a).

Conclusion:

Among 1699 patients with moderate to severe depressive symptoms receiving ECT treatment, 56.0% responded to ECT treatment with 32.7% of patients meeting criteria for response by treatment #5. Older age and treatment while inpatient were associated with increased odds of response to ECT. Among those not responding by treatment #5, a greater decrease in depressive symptoms at treatment #5 was associated with increased the odds of response after treatment #5. Patients who started with ultrabrief pulse treatments and were switched to brief pulse ECT during their treatment had increased odds of response as compared to patients only receiving ultrabrief pulse treatments.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding

This work was supported by the National Institute of Mental Health (T32MH112485, JL; R01MH120991, THM; 5R01MH112737-03, MEH) The sponsors had no role in study design, writing of the report, or data collection, analysis, or interpretation.

Data Availability Statement:

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References:

Bahji A, Hawken ER, Sepehry AA, Cabrera CA, Vazquez G, 2019. ECT beyond unipolar major depression: systematic review and meta-analysis of electroconvulsive therapy in bipolar depression. Acta Psychiatr. Scand 139, 214–226. 10.1111/acps.12994 [PubMed: 30506992]

Bernstein IH, Rush AJ, Carmody TJ, Woo A, Trivedi MH, 2007. Clinical vs. self-report versions of the quick inventory of depressive symptomatology in a public sector sample. J. Psychiatr. Res 41, 239–246. 10.1016/j.jpsychires.2006.04.001 [PubMed: 16716351]

Case BG, Bertollo DN, Laska EM, Siegel CE, Wanderling JA, Olfson M, 2012. Racial differences in the availability and use of electroconvulsive therapy for recurrent major depression. J. Affect. Disord 136, 359–365. 10.1016/j.jad.2011.11.026 [PubMed: 22169249]

de Vreede IM, Burger H, van Vliet IM, 2005. Prediction of response to ECT with routinely collected data in major depression. J. Affect. Disord 86, 323–327. 10.1016/j.jad.2005.03.008 [PubMed: 15935255]

Dierckx B, Heijnen WT, van den Broek WW, Birkenhäger TK, 2012. Efficacy of electroconvulsive therapy in bipolar versus unipolar major depression: a meta-analysis. Bipolar Disord. 14, 146–150. 10.1111/j.1399-5618.2012.00997.x [PubMed: 22420590]

Fava M, 2020. Pharmacological strategies for targeting residual symptoms in depression, in: Trivedi MH. (Ed.), Depression, Primer On. Oxford University Press, New York, NY.

Hart KL, Henry ME, McCoy TH, Seiner SJ, Luccarelli J, 2022. Individual response to electroconvulsive therapy is not correlated between multiple treatment courses. J. Affect. Disord 298, 256–261. 10.1016/j.jad.2021.11.002 [PubMed: 34742999]

Husain MM, Rush AJ, Fink M, Knapp R, Petrides G, Rummans T, Biggs MM, O'Connor K, Rasmussen K, Litle M, Zhao W, Bernstein HJ, Smith G, Mueller M, McClintock SM, Bailine SH, Kellner CH, 2004. Speed of Response and Remission in Major Depressive Disorder with Acute

Electroconvulsive Therapy (ECT): A Consortium for Research in ECT (CORE) Report. J. Clin. Psychiatry 65, 485–491. 10.4088/JCP.v65n0406 [PubMed: 15119910]

Kellner CH, Husain MM, Knapp RG, McCall WV, Petrides G, Rudorfer MV, Young RC, Sampson S, McClintock SM, Mueller M, Prudic J, Greenberg RM, Weiner RD, Bailine SH, Rosenquist PB, Raza A, Kaliora S, Latoussakis V, Tobias KG, Briggs MC, Liebman LS, Geduldig ET, Teklehaimanot AA, Lisanby SH, CORE/PRIDE Work Group, 2016. Right Unilateral Ultrabrief Pulse ECT in Geriatric Depression: Phase 1 of the PRIDE Study. Am. J. Psychiatry 173, 1101–1109. 10.1176/appi.ajp.2016.15081101 [PubMed: 27418379]

Kellner CH, Knapp R, Husain MM, Rasmussen K, Sampson S, Cullum M, McClintock SM, Tobias KG, Martino C, Mueller M, Bailine SH, Fink M, Petrides G, 2010. Bifrontal, bitemporal and right unilateral electrode placement in ECT: randomised trial. Br. J. Psychiatry J. Ment. Sci 196, 226–234. 10.1192/bjp.bp.109.066183

Kellner CH, Knapp RG, Petrides G, Rummans TA, Husain MM, Rasmussen K, Mueller M, Bernstein HJ, O'Connor K, Smith G, Biggs M, Bailine SH, Malur C, Yim E, McClintock S, Sampson S, Fink M, 2006a. Continuation Electroconvulsive Therapy vs Pharmacotherapy for Relapse Prevention in Major Depression: A Multisite Study from the Consortium for Research in Electroconvulsive Therapy (CORE). Arch. Gen. Psychiatry 63, 1337–1344. 10.1001/archpsyc.63.12.1337 [PubMed: 17146008]

Kellner CH, Knapp RG, Petrides G, Rummans TA, Husain MM, Rasmussen K, Mueller M, Bernstein HJ, O'Connor K, Smith G, Biggs M, Bailine SH, Malur C, Yim E, McClintock S, Sampson S, Fink M, 2006b. Continuation Electroconvulsive Therapy vs Pharmacotherapy for Relapse Prevention in Major Depression: A Multisite Study from the Consortium for Research in Electroconvulsive Therapy (CORE). Arch. Gen. Psychiatry 63. 10.1001/archpsyc.63.12.1337

Kho KH, Blansjaar BA, Vothknecht S, Cornelissen NMP, Koomen E, Zwinderman AH, Linszen DH, 2004. A Study into Predictors for the Speed of Response to Electroconvulsive Therapy: J. ECT 20, 154–159. 10.1097/00124509-200409000-00006 [PubMed: 15342999]

Luccarelli J, Henry ME, McCoy TH, 2020a. Demographics of Patients Receiving Electroconvulsive Therapy Based on State-Mandated Reporting Data. J. ECT 36, 229–233. 10.1097/YCT.0000000000000692 [PubMed: 32453188]

Luccarelli J, McCoy TH, Seiner SJ, Henry ME, 2020b. Charge required to induce a seizure during initial dose titration using right unilateral brief pulse electroconvulsive therapy. Brain Stimul. Basic Transl. Clin. Res. Neuromodulation 13, 1504–1506. 10.1016/j.brs.2020.08.009

Luccarelli J, McCoy TH, Seiner SJ, Henry ME, 2020c. Maintenance ECT is associated with sustained improvement in depression symptoms without adverse cognitive effects in a retrospective cohort of 100 patients each receiving 50 or more ECT treatments. J. Affect. Disord 271, 109–114. 10.1016/j.jad.2020.03.152 [PubMed: 32479305]

Luccarelli J, McCoy TH, Shannon AP, Forester BP, Seiner SJ, Henry ME, 2021a. Rate of continuing acute course treatment using right unilateral ultrabrief pulse electroconvulsive therapy at a large academic medical center. Eur. Arch. Psychiatry Clin. Neurosci 271, 191–197. 10.1007/s00406-020-01202-2 [PubMed: 33196856]

Luccarelli J, McCoy THJ, Seiner SJ, Henry ME, 2021b. Total Charge Required to Induce a Seizure in a Retrospective Cohort of Patients Undergoing Dose Titration of Right Unilateral Ultrabrief Pulse Electroconvulsive Therapy. J. ECT 37, 40–45. 10.1097/YCT.0000000000000714 [PubMed: 32826707]

Luccarelli J, McCoy THJ, Shannon AP, Forester BP, Seiner SJ, Henry ME, 2021c. Duration of Treatment in Electroconvulsive Therapy Among Patients Beginning with Acute Course Right Unilateral Brief Pulse Stimuli. J. ECT 37, 238–242. 10.1097/YCT.0000000000000768 [PubMed: 33840804]

Medda P, Mauri M, Toni C, Mariani MG, Rizzato S, Miniati M, De Simone L, Perugi G, 2014. Predictors of Remission in 208 Drug-Resistant Depressive Patients Treated with Electroconvulsive Therapy. J. ECT 30, 292–297. 10.1097/YCT.0000000000000119 [PubMed: 24625706]

Nordenskjöld A, von Knorring L, Engström I, 2012. Predictors of the short-term responder rate of Electroconvulsive therapy in depressive disorders--a population-based study. BMC Psychiatry 12, 115. 10.1186/1471-244X-12-115 [PubMed: 22900754]

O'Connor MK, Knapp R, Husain M, Rummans TA, Petrides G, Smith G, Mueller M, Snyder K, Bernstein H, Rush AJ, Fink M, Kellner C, 2001. The influence of age on the response of major depression to electroconvulsive therapy: a C.O.R.E. Report. Am. J. Geriatr. Psychiatry Off. J. Am. Assoc. Geriatr. Psychiatry 9, 382–390.

Pinna M, Manchia M, Oppo R, Scano F, Pillai G, Loche AP, Salis P, Minnai GP, 2018. Clinical and biological predictors of response to electroconvulsive therapy (ECT): a review. Neurosci. Lett 669, 32–42. 10.1016/j.neulet.2016.10.047 [PubMed: 27793702]

Rush AJ, Carmody TJ, Ibrahim HM, Trivedi MH, Biggs MM, Shores-Wilson K, Crismon ML, Toprac MG, Kashner TM, 2006. Comparison of Self-Report and Clinician Ratings on Two Inventories of Depressive Symptomatology. Psychiatr. Serv 57, 829–837. 10.1176/ps.2006.57.6.829 [PubMed: 16754760]

Rush AJ, Trivedi MH, Ibrahim HM, Carmody TJ, Arnow B, Klein DN, Markowitz JC, Ninan PT, Kornstein S, Manber R, Thase ME, Kocsis JH, Keller MB, 2003. The 16-Item Quick Inventory of Depressive Symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. Biol. Psychiatry 54, 573–583. 10.1016/s0006-3223(02)01866-8 [PubMed: 12946886]

Semkovska M, Landau S, Dunne R, Kolshus E, Kavanagh A, Jelovac A, Noone M, Carton M, Lambe S, McHugh C, McLoughlin DM, 2016. Bitemporal Versus High-Dose Unilateral Twice-Weekly Electroconvulsive Therapy for Depression (EFFECT-Dep): A Pragmatic, Randomized, Non-Inferiority Trial. Am. J. Psychiatry 173, 408–417. 10.1176/appi.ajp.2015.15030372 [PubMed: 26892939]

Spaans H-P, Verwijk E, Stek ML, Kho KH, Bouckaert F, Kok RM, Sienaert P, 2016. Early Complete Remitters After Electroconvulsive Therapy: Profile and Prognosis. J. ECT 32, 82–87. 10.1097/YCT.0000000000000298 [PubMed: 26796500]

Szegedi A, Jansen WT, van Willigenburg APP, van der Meulen E, Stassen HH, Thase ME, 2009. Early improvement in the first 2 weeks as a predictor of treatment outcome in patients with major depressive disorder: a meta-analysis including 6562 patients. J. Clin. Psychiatry 70, 344–353. 10.4088/jcp.07m03780 [PubMed: 19254516]

Tor P-C, Bautovich A, Wang M-J, Martin D, Harvey SB, Loo C, 2015. A Systematic Review and Meta-Analysis of Brief Versus Ultrabrief Right Unilateral Electroconvulsive Therapy for Depression. J. Clin. Psychiatry 76, e1092–e1098. 10.4088/JCP.14r09145 [PubMed: 26213985]

van Diermen L, van den Ameele S, Kamperman AM, Sabbe BCG, Vermeulen T, Schrijvers D, Birkenhäger TK, 2018. Prediction of electroconvulsive therapy response and remission in major depression: meta-analysis. Br. J. Psychiatry 212, 71–80. 10.1192/bjp.2017.28 [PubMed: 29436330]

Yao Z, McCall WV, Essali N, Wohl E, Parker C, Rosenquist PB, Youssef NA, 2019. Precision ECT for major depressive disorder: A review of clinical factors, laboratory, and physiologic biomarkers as predictors of response and remission. Pers. Med. Psychiatry 17–18, 23–31. 10.1016/j.pmip.2019.07.001

Significant Outcomes:

- Among individuals treated with ECT, 32.7% responded by treatment #5 (early response), and 23.4% responded after treatment #5 (late response)
- Among non-responders by treatment #5, a switch to brief pulse from ultrabrief pulse ECT had increased odds of response after treatment #5 (aOR = 1.55, 95% CI: 1.16 – 2.07)

Limitations:

- Although the sample size is large, all data is derived from a single study center from retrospective chart review
- Effects of concomitant medication changes cannot be assessed
- Patients excluded if unable to complete self-reported outcome measures, which may exclude the most ill patients

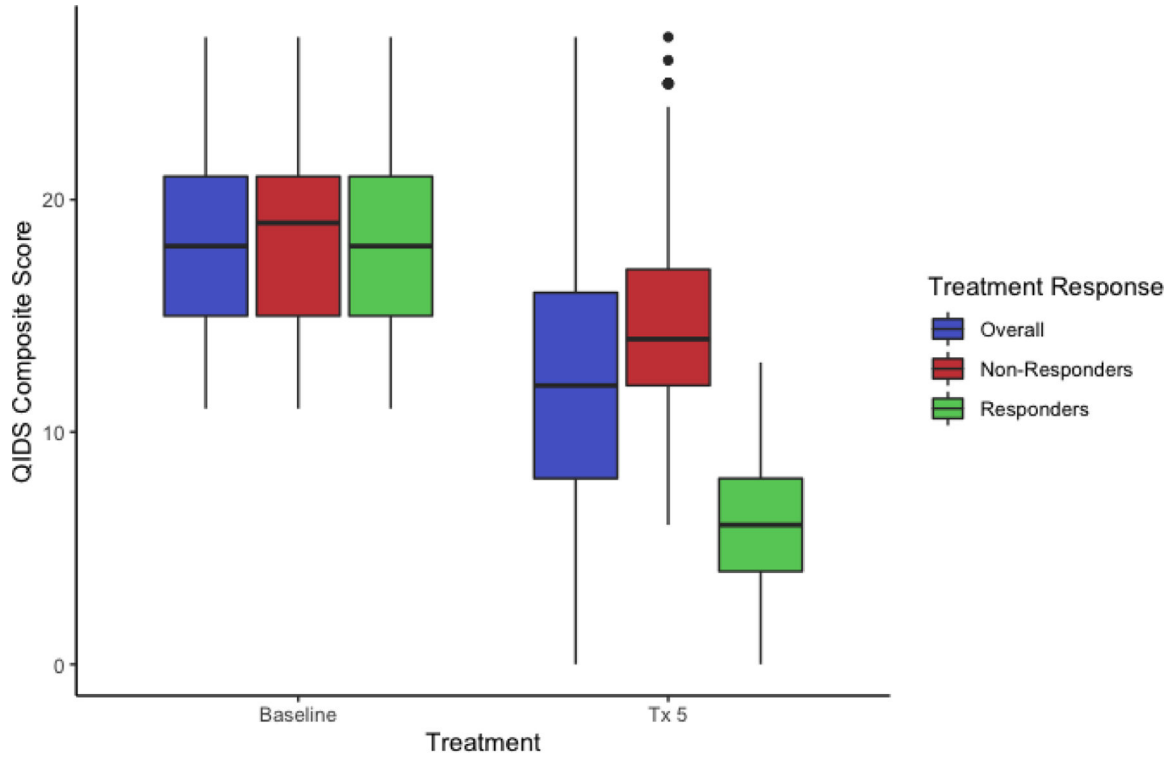

Figure 1:
Composite QIDS score stratified by response at Treatment #5

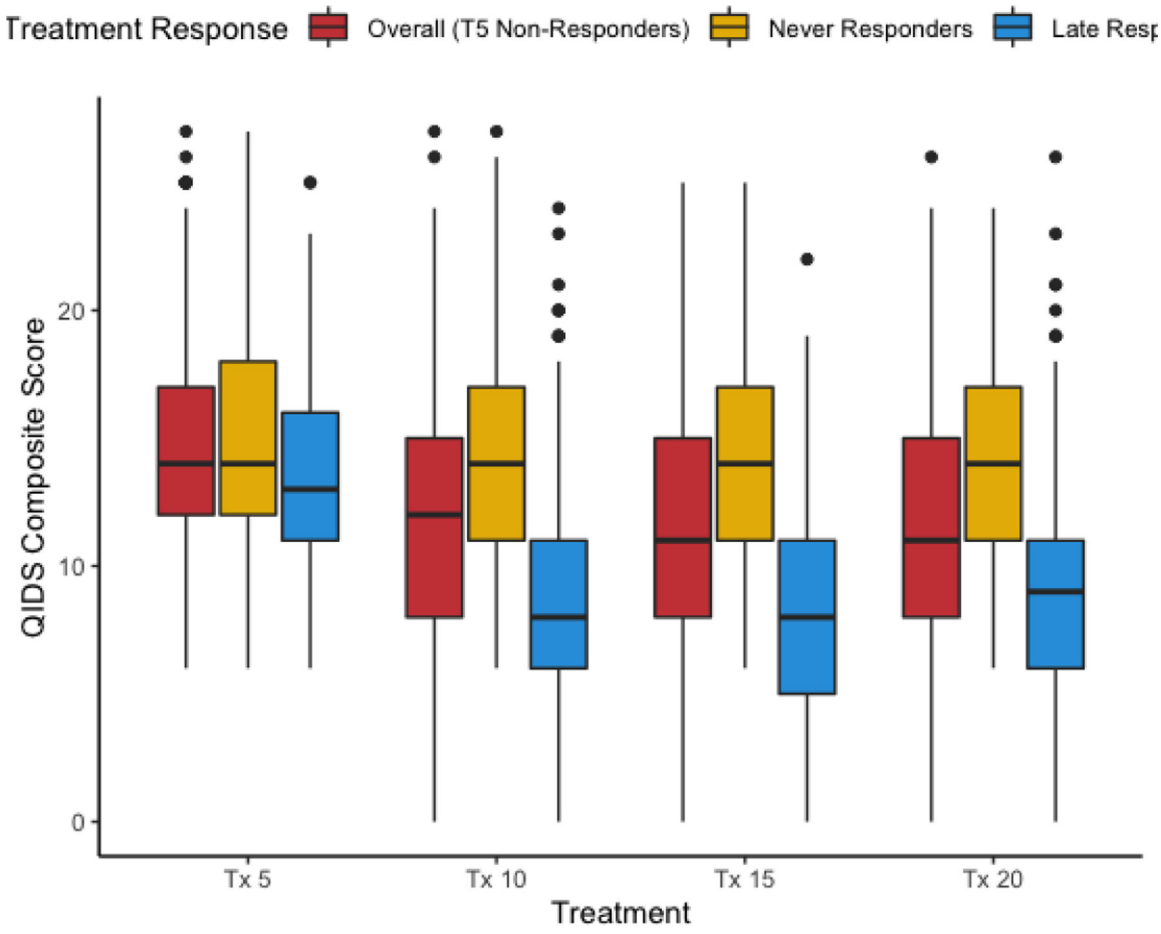

Figure 2:

Composite QIDS score stratified by response after Treatment #5

Note: Data is limited to patients not meeting criteria for response at treatment #5. The overall group includes all patients not responding at treatment #5, irrespective of response after treatment 5. Late Response is defined at any timepoint after Treatment #5

Table 1:

Baseline demographic data stratified by overall response to ECT treatment

	Never-Responders	***Responders***	***Overall***
	(N, %)	**(N, %)**	**(N, %)**
N	747	952	1699
Age (mean (SD)), years	43.36 (15.68)	46.11 (16.20)	44.9 (16.03)
Sex (Female)	448 (59.97)	565 (59.35)	1013 (59.62)
Race			
White	683 (91.43)	876 (92.02)	1559 (91.76)
American Indian / Alaskan Native	4 (0.54)	12 (1.26)	16 (0.94)
Asian	20 (2.68)	30 (3.15)	50 (2.94)
Black	13 (1.74)	17 (1.79)	30 (1.77)
Native Hawaiian / Pacific Islander	0 (0.00)	0 (0.00)	0 (0.00)
Other / Unknown	4 (0.54)	12 (1.26)	16 (0.94)
Ethnicity			
Latino/Latina	12 (1.61)	21 (2.21)	33 (1.94)
Missing	370 (49.53)	498 (52.31)	868 (51.09)
Employment in past 30 days			
Full-time	114 (15.26)	115 (12.08)	229 (13.48)
Part-time	52 (6.96)	56 (5.88)	108 (6.36)
None	449 (60.11)	578 (60.71)	1027 (60.45)
Student (yes)	109 (14.59)	112 (11.76)	221 (13.01)
On disability (yes)	228 (30.52)	252 (26.47)	480 (28.25)
Education			
8th Grade or Less	2 (0.27)	3 (0.32)	5 (0.29)
Some high school	28 (3.75)	22 (2.31)	50 (2.94)
High school graduate/GED	87 (11.65)	92 (9.66)	179 (10.54)
Some college	218 (29.18)	267 (28.05)	485 (28.55)
4-year college graduate	179 (23.96)	256 (26.89)	435 (25.60)
Post-college education	226 (30.25)	304 (31.93)	530 (31.19)
Subjective Physical Health			
Very poor	12 (1.61)	13 (1.37)	25 (1.47)
Poor	114 (15.26)	120 (12.61)	234 (13.77)
Good	419 (56.09)	538 (56.51)	957 (56.33)
Very Good	157 (21.02)	219 (23.00)	376 (22.13)
Excellent	38 (5.09)	56 (5.88)	94 (5.53)
Ever been homeless (yes)	59 (7.90)	60 (6.30)	119 (7.00)
Initial Treatment Location			
Inpatient	457 (61.18)	671 (70.48)	1128 (66.39)
Outpatient	280 (37.48)	274 (28.78)	554 (32.61)

	Never-Responders	***Responders***	***Overall***
	(N, %)	**(N, %)**	**(N, %)**
Clinical Diagnosis			
Major depressive disorder	593 (79.38)	745 (78.26)	1338 (78.75)
Bipolar affective disorder	154 (20.62)	207 (21.74)	361 (21.25)
ECT electrode placement (baseline)			
Unilateral	726 (97.19)	926 (97.27)	1652 (97.23)
Bitemporal/Bifrontal	21 (2.81)	26 (2.73)	47 (2.77)
ECT pulse width (baseline)			
Brief pulse (0.5–2 ms)	37 (4.95)	63 (6.62)	100 (5.89)
Ultrabrief pulse (<0.5 ms)	710 (95.05)	889 (93.38)	1599 (94.11)
Baseline QIDS Score (Mean (SD))	18.2 (3.83)	18.3 (3.72)	18.3 (3.77)

Table 2:

Logistic regression to predict response at treatment #5

	OR	*95% Confidence Interval*	
Age	1.01	1.00	1.01
Sex: Male	0.98	0.79	1.21
Diagnosis			
BPAD	1.03	0.79	1.32
MDD	*Ref.*	-	-
Treatment Location (baseline)			
Outpatient treatment	0.49	0.39	0.62
Inpatient treatment	*Ref.*	-	-
Baseline QIDS Score (baseline)	0.97	0.95	1.00
Pulse Width			
Ultrabrief	0.73	0.43	1.23
Brief	*Ref.*	-	-
Electrode Placement (baseline)			
Unilateral	1.46	0.69	3.18
Bilateral (bitemporal or bifrontal)	*Ref.*	-	-

Note: MDD = major depressive disorder, BPAD = bipolar affective disorder; Ref. indicates reference level for categorical variables.

Table 3:

Logistic regression of factors associated with response after treatment #5

	OR	***95% Confidence Interval***	
Age	1.01	1.00	1.02
Sex: Male	1.04	0.80	1.34
Diagnosis			
BPAD	1.04	0.76	1.41
MDD	*Ref.*	-	-
Treatment Location			
Outpatient treatment (treatment #5)	1.00	0.77	1.29
Inpatient treatment (treatment #5)	*Ref.*	-	-
Percent Change in QIDS (baseline to treatment #5)	0.97	0.97	0.98
Laterality			
Bitemporal/bifrontal ECT during treatment series	0.60	0.42	0.85
Unilateral ECT	*Ref.*	-	-
Pulse Width			
Ultrabrief pulse changed to brief pulse	1.55	1.16	2.07
Only brief pulse	1.73	0.89	3.32
Only ultrabrief pulse	*Ref.*	-	-

Note: MDD = major depressive disorder, BPAD = bipolar affective disorder; Data is limited to patients not meeting criteria for response at treatment #5. Late response is defined as response at any timepoint after treatment #5. Ref. indicates reference level for categorical variables.