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Original article

# Self-assessed remission rates after electroconvulsive therapy of depressive disorders

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ABSTRACT

*Background:* Electroconvulsive therapy (ECT) effectively treats severe depression, but not all patients remit. The aim of the study was to identify clinical factors that associate with ECT-induced remission in a community setting.
*Methods:* Depressed patients who underwent ECT in 2011–2014 were identified from the Swedish National Quality Register for ECT. Remission was defined as self-rated Montgomery-Åsberg Depression Rating Scale scores of 0–10 after ECT. Other registers provided data on previous antidepressant use, comorbidities, and demographics.
*Results:* Of 1671 patients fulfilling the inclusion criteria, 42.8% achieved remission. Older age, education length over 9 years, psychotic symptoms, shorter duration of preceding antidepressant use, pulse width stimulus $\geq$ 0.50 ms, absence of substance use disorders, anxiety diagnosis, lamotrigine, and benzodiazepines, were associated with remission.
*Conclusions:* This study shows that psychotic subtype of depression and older age are clinically relevant predictors of a beneficial ECT effect. Additionally, ECT outcomes can be further improved by optimizing the treatment technique and concomitant medication.


## 1. Introduction

Electroconvulsive therapy (ECT) is effective for patients with depressive disorders, but not all patients benefit. While clinical trials show that the remission rate is often 50% or more after ECT [1,2], a large-scale population-based study in a community setting reported somewhat lower remission rates [3].

Accurate prediction of treatment outcomes in different subgroups of patients with depression are of great importance. Although there are some candidates, a reliable biomarker that predicts responsiveness to ECT has not been established [4,5]. Therefore, clinicians must rely on clinical history, signs, and symptoms when selecting candidates for ECT. A recent meta-analysis showed that shorter episode duration and absence of prior antidepressant medication associate with higher responsiveness to ECT [6]. The impact of several other factors such as age, presence of psychosis, and symptom severity remains unclear due to discrepancies between studies [6].

*Abbreviations:* CGI-S, Clinical Global Impression Severity Scale; CI, confidence interval; ECT, electroconvulsive therapy; ICD, International Classification of Diseases; MADRS-S, Montgomery-Åsberg Depression Rating Scale; OR, odds ratio; Q-ECT, The Swedish National Quality Register for ECT.

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Technical factors may also influence the effectiveness of ECT. The stimulus pulse width is of particular interest because ultra-brief (< 0.50 ms) stimulus associates with fewer memory disturbances than brief (0.50–1.50 ms) pulse stimulus [7,8]. On the other hand, a recent meta-analysis suggested that ultra-brief stimulus reduces the rate of remission compared with brief pulse stimulus [8]. The aim of this population-based study in a community setting was to identify the clinical and methodological factors that associate with the self-assessed remission rate after ECT.

## 2. Methods

### 2.1. Patient selection

All 57 hospitals offering ECT in Sweden have been reporting data to the Swedish National Quality Register for ECT (Q-ECT) since 2011 [9]. The study cohort consisted of consecutive patients who underwent ECT for depression in Sweden between March 2011 and December 2014. They were identified using the Swedish version of the International Classification for Diseases (ICD)-10 codes F32.1–F32.3 F33.1–F33.3, and F31.3–F31.5 in the Q-ECT [10]. While the Q-ECT is a voluntary register, 85–90% of the patients who receive ECT in Sweden agree to participate in the register [9]. When a patient had multiple ECT treatment series for depression during the study period, only the earliest treatment series was used. Patients were excluded if any of the following information was missing in the Q-ECT: the self-rated Montgomery-Åsberg Depression Rating Scale (MADRS-S) score after treatment, the diagnosis, the severity of symptoms as rated by the Clinical Global Impression Severity Scale (CGI-S) before ECT [11], the treatment setting, the number of ECT sessions in the treatment series, electrode placement, the pulse width, the frequency, the duration or the current. The diagnoses were categorized as unipolar or bipolar depression with or without psychotic features.

### 2.2. Retrieval of data from registers

Additional data were obtained from three other national registers that were linked by using the personal identity numbers of the patients identified in the Q-ECT. The Swedish National Patient Register, which is held by the National Board of Health and Welfare, includes data on inpatient episodes, dates of admission and discharge, and main and secondary diagnoses. ICD-10 codes are used to classify the health problems in the patient register. The register is mandatory for all patients in Sweden and the coverage is estimated to exceed 99%. For the present study, we used this register to determine whether a personality disorder (F60, F61) anxiety disorder (F41), obsessive-compulsive disorder (F42) or (non-nicotine) substance use disorder (F10–F16, F18, and F19) had been ever diagnosed [12].

The Swedish Pharmaceuticals Registry is mandatory and provides complete coverage of all prescribed drug dispenses since 2005 [13]. Drugs that are administered in hospitals are not included. For the present study, this register was used to determine if the patients had had antidepressant drugs dispensed prior to ECT. The Swedish health care system insures the lowest costs for the patient if prescriptions are collected every three months or more often.

The Swedish Longitudinal Integration Database for Health Insurance and Labour Market Studies is an integrated register of demographic data held by Statistics Sweden. The register is mandatory. For the present study, this register was used to determine the education level, income, and marital status of the patients [14].

### 2.3. Definition of remission

Remission status was determined on the basis of the patient-assessed MADRS-S score within 1 week of completing ECT [15]. This self-rated scale consists of nine items and each item is scored from 0 (no symptoms) to 6 (severe symptoms). The maximum possible score is 54 points. A patient was deemed to be in remission after ECT if the post-ECT MADRS-S score was 0–10. Patients with scores of ≥ 11 after ECT were considered not to be in remission [16].

### 2.4. ECT

ECT was administered by using the bidirectional constant current brief pulse Mecta (Mecta Corp, Lake Oswego, OR, USA) or Thymatron (Somatics Inc., Lake Bluff, IL, USA) devices. During the procedure, the patients were sedated with propofol or thiopenthal. Succinylcholine (0.5–1.0 mg/kg) served as a muscle relaxant and glycopyrrolate (0.2 mg) or atropine served as an anticholinergic agent when necessary. The electrodes were placed unilaterally, bitemporally or bifrontally.

### 2.5. Statistical methods

The association between remission and various clinical factors was evaluated using logistic regression analysis in both unadjusted and adjusted models. Continuous variables were categorized to identify potential non-linear relationships with the outcome. The following potential confounding variables were included in the adjusted models: sex, age group, marital status, income, education, unipolar/bipolar status, psychotic features, substance use disorder, personality disorder, obsessive compulsive disorder, prior anxiety disorder, prior antidepressant treatment, CGI-S score within 1 week before ECT, treatment setting, coercion, medications at the end of ECT, number of ECT sessions, electrode placement and stimulus parameters. Linear trends of odds ratios (ORs) of age and stimulus parameters were tested using likelihood ratio test. Stratified analyses were carried out, separating patients with unipolar and bipolar depression as well as patients with and without psychotic features, personality disorders, and substance use disorders. Interactions between factors that were statistically significant in the adjusted model were examined pairwise using logistic regression models. Odds ratios and corresponding 95% confidence intervals (CIs) were calculated. *P*-values of 0.05 or less were considered statistically significant. Excluded patients were compared to the patients who were included in the study in terms of sex, by using $Chi^2$ tests and age as well as CGI scores using Student's *t*-tests. Spearman's correlation was calculated for correlation between pulse width and number of sessions. The data were managed and analyzed by using the statistical packages SPSS 22 (IBM Corp, Armonk, NY, USA) and SAS 9.4 (SAS Institute, Cary, NC, USA). Fig. 1 was created using Microsoft Excel 2010 (Microsoft, Redmond, WA, USA).

### 2.6. Ethics

The Regional Ethical Vetting Board in Uppsala approved the study (2014/174). The patients were informed that their data would be included in the Q-ECT unless they declined to participate.

## 3. Results

### 3.1. Included and excluded patients

In total, 5976 patients with depression treated in 57 hospitals were included in Q-ECT during the study period. Of these,

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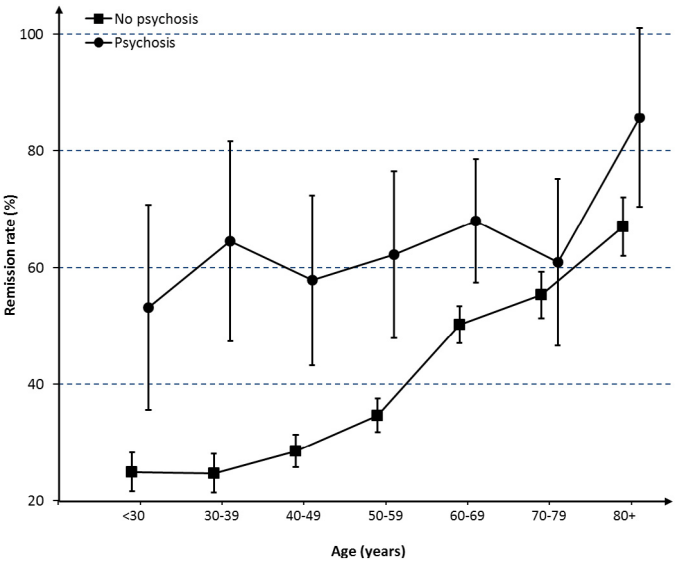


**Fig. 1.** Remission rate over age and psychosis status.

852 patients were treated in 12 hospitals that did not report complete data, and 1355 were treated before each hospital started reporting complete data. Of the remaining 3769 study subjects, 2098 were excluded because at least one factor of interest was missing (435 stimulus parameters, 277 CGI-S before ECT and 1878 MADRS-S after ECT). Thus, 1671 patients formed the patient cohort in this study.

There was no difference in sex proportion among the 2098 excluded patients and the 1671 included patients (61.0% and 61.1% women, respectively). However, the included patients were older than the excluded patients (mean ± standard deviation 52.6 ± 18.0 and 53.9 ± 17.6 years, respectively $P = 0.023$). The proportion of patients with Clinical Global Impression Improvement score 1 or 2 (much or very much improved) after ECT was higher among included ($n = 1511$) than excluded ($n = 1278$) patients (79.6% and 74.5%, respectively, $P = 0.001$). The mean CGI-S score before ECT was lower for included than excluded patients (5.06 ± 0.78, $n = 1526$ and 5.13 ± 0.88, $n = 1189$, respectively, $P = 0.033$). There was no difference in mean CGI-S score after ECT between included and excluded patients (2.88 ± 1.34, $n = 1526$ and 2.86 ± 1.35, $n = 1686$, respectively, $P = 0.078$).

### 3.2. Study population

The majority (79.8%) of the included 1671 patients were treated with ECT for a unipolar depressive episode. Psychotic features were present in 17.7% of the patients. Comorbid diagnosis of anxiety was present in 32.7% of the patients, obsessive-compulsive disorder in 3.8%, substance use disorder in 20.9% and personality disorder in 12.7% of the patients. The mean number of ECT sessions in the index series was 8.16. Unilateral electrode placement was used in 90.2% of the patients, and bitemporal and bifrontal in 6.3% and 3.5%, respectively. The majority of treatments were given with a pulse width of 0.50 ms (68.4%). An ultra-brief pulse width (< 0.50 ms) was used in 19% and a pulse width of (0.51–1.0 ms) in 12.6%. The average frequency, duration, and current were 61.9 Hz, 7.01 s, and 842.0 mA, respectively, and the mean charges were (mean ± standard deviation) 355 ± 145 mC, 409 ± 168 mC, and 278 ± 84 mC for patients with unilaterally, bitemporally, and bifrontally placed electrodes respectively.

### 3.3. Overall remission rate

The mean rate of remission (defined as MADRS-S score of 0–10) was 42.8%. The mean MADRS-S was 33.1 ± 9.0, $n = 1330$ before ECT and 14.4 ± 10.7, $n = 1671$ within 1 week after ECT.

### 3.4. Demographic factors that associated with remission

The analysis showed that compared with the 18–30 year old patients, older age patients (above 60 years of age) had a statistically significant association with higher remission rates (Table 1). When including age as a continuous variable, there was also a linear effect (OR: 1.03, 95% CI: 1.02–1.03). Sex did not associate significantly with remission. The increased remission rate in patients with 10–12 years of education was statistically significant when compared with the patients with less education in the multivariate model (Table 1). Marital status and income did not associate significantly with remission in the multivariate model (Table 1).

### 3.5. Diagnostic factors that associated with remission

The patients with and without psychotic features had remission rates of 63.7% and 38.4%, respectively, and psychotic features were also significantly associated with higher remission rates in the multivariate model (OR: 1.94, 95% CI: 1.41–2.68, $P < 0.001$). Patients without psychotic symptoms aged below 31 or between 31 and 40 had lower remission rates (24.9% and 24.7%, respectively) than the same aged psychotic patients (53.1% and 64.5%) and patient groups above 60 years with or without psychotic symptoms (54.8–68.3%) (Fig. 1). Patients with pre-treatment CGI-S scores of 6 (severely ill) or 7 (extremely ill) had remission rates of 51.3% and 54.5%, respectively. By contrast, patients with pre-treatment CGI-S scores of 5 (markedly ill), 4 (moderately ill), and 2–3 (borderline–mildly ill) had remission rates of 40.2%, 38.8%, and 32.3%, respectively. However, the trend for severe illness to associate with remission did not achieve statistical significance after adjustment in the multivariate model. Patients with unipolar and bipolar depression had remission rates of 44.9% and 34.7%, respectively. Polarity did not associate significantly with remission in the multivariate model after adjustment for antiepileptic medication. Patients with comorbid anxiety disorders had a lower remission rate (33.3%) than the patients without anxiety (47.5%). This association remained statistically significant after adjustment in the multivariate model (OR: 0.72, 95% CI: 0.56–0.92, $P = 0.009$). Patients with substance use disorders or specifically alcohol use disorder had lower remission rates (29.0% and 25.6%, respectively) than the patients who did not engage in substance abuse (46.8% and 41.8%, respectively). Substance use disorders associated with poorer remission rates in the multivariate model (OR: 0.74, 95% CI: 0.55–1.00, $P = 0.047$). Patients with comorbid personality disorder had a lower remission rate (25.8%) than patients without personality disorder (45.3%). Personality disorder diagnoses did not associate significantly with remission in the multivariate model (Table 1).

### 3.6. Association between remission and prior antidepressant medication

Shorter duration of antidepressant treatment before ECT was associated with higher remission rates (Table 1).

### 3.7. Effect of treatment setting on remission rates

Patients in whom ECT was initiated when they were inpatients had higher remission rates (44.4%) than patients in whom ECT was initiated when they were outpatients (33.0%). Moreover,

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**Table 1**
Remission rates and results of regressions.

| | Non-remission (%) | Remission (%) | Unadjusted | | Adjusted[a] | |
|---|---|---|---|---|---|---|
| | | | OR (95% CI) | *P*-value | OR (95% CI) | *P*-value |
| Sex | | | | | | |
| Female | 588 (57.6) | 433 (42.4) | Reference | | Reference | |
| Male | 367 (56.5) | 283 (43.5) | 1.05 (0.86–1.28) | 0.649 | 0.97 (0.76–1.23) | 0.872 |
| Age, year | | | | | | |
| 18–30 | 142 (70.6) | 59 (29.4) | Reference | | Reference | |
| 31–40 | 139 (69.2) | 62 (30.8) | 1.07 (0.70–1.64) | 0.744 | 1.12 (0.68–1.84) | 0.655 |
| 41–50 | 207 (67.2) | 101 (32.8) | 1.17 (0.80–1.73) | 0.414 | 1.13 (0.70–1.82) | 0.579 |
| 51–60 | 195 (61.5) | 122 (38.5) | 1.51 (1.03–2.20) | 0.034 | 1.27 (0.78–2.05) | 0.276 |
| 61–70 | 151 (45.8) | 179 (54.2) | 2.85 (1.96–4.14) | <0.001 | 2.09 (1.27–3.43) | 0.002 |
| 71–80 | 89 (43.4) | 116 (56.6) | 3.14 (2.08–4.73) | <0.001 | 2.18 (1.25–3.80) | 0.003 |
| 81–95 | 32 (29.4) | 77 (70.6) | 5.79 (3.47–9.66) | <0.001 | 5.03 (2.54–9.96) | <0.001 |
| Marital status | | | | | | |
| Married/registered partner | 324 (52.9) | 288 (47.1) | Reference | | Reference | |
| Unmarried/no reg. partnership | 372 (64.1) | 208 (35.9) | 0.63 (0.50–0.79) | <0.001 | 0.98 (0.73–1.32) | 0.901 |
| Widowed | 53 (40.8) | 77 (59.2) | 1.63 (1.11–2.40) | 0.012 | 0.86 (0.54–1.38) | 0.513 |
| Divorced | 206 (59.0) | 143 (41.0) | 0.78 (0.60–1.02) | 0.068 | 0.87 (0.64–1.18) | 0.370 |
| Disposable income | | | | | | |
| Lowest quartile | 182 (57.2) | 136 (42.8) | Reference | | Reference | |
| Second quartile | 219 (55.4) | 176 (44.6) | 1.08 (0.80–1.45) | 0.632 | 0.97 (0.68–1.38) | 0.853 |
| Third quartile | 277 (59.6) | 188 (40.4) | 0.91 (0.68–1.21) | 0.514 | 0.79 (0.56–1.13) | 0.203 |
| Highest quartile | 277 (56.2) | 216 (43.8) | 1.04 (0.79–1.39) | 0.769 | 0.90 (0.62–1.29) | 0.555 |
| Education | | | | | | |
| Maximum 9 years or missing | 207 (58.5) | 147 (41.5) | Reference | | Reference | |
| 10 to 12 years | 412 (54.5) | 344 (45.5) | 1.18 (0.91–1.52) | 0.214 | 1.59 (1.18–2.15) | 0.003 |
| More then 12 years | 336 (59.9) | 225 (40.1) | 0.94 (0.72–1.24) | 0.671 | 1.27 (0.93–1.79) | 0.142 |
| Depression diagnosis | | | | | | |
| Unipolar depression | 735 (55.1) | 599 (44.9) | Reference | | Reference | |
| Bipolar depression | 220 (65.3) | 117 (34.7) | 0.65 (0.51–0.84) | 0.001 | 1.10 (0.78–1.53) | 0.603 |
| Psychotic features | | | | | | |
| No | 848 (61.6) | 528 (38.4) | Reference | | Reference | |
| Yes | 107 (36.3) | 188 (63.7) | 2.82 (2.17–3.66) | <0.001 | 1.94 (1.41–2.68) | <0.001 |
| Substance use disorders | | | | | | |
| No | 707 (53.5) | 615 (46.5) | Reference | | Reference | |
| Yes | 248 (71.1) | 101 (28.9) | 0.47 (0.36–0.60) | <0.001 | 0.74 (0.55–1.00) | 0.047 |
| Personality disorder | | | | | | |
| No | 797 (54.7) | 661 (45.3) | Reference | | Reference | |
| Yes | 158 (74.2) | 55 (25.8) | 0.42 (0.30–0.58) | <0.001 | 0.75 (0.51–1.10) | 0.137 |
| Obsessive compulsive disorder | | | | | | |
| No | 911 (56.7) | 697 (43.3) | Reference | | Reference | |
| Yes | 44 (69.8) | 19 (30.2) | 0.56 (0.33–0.98) | 0.040 | 1.01 (0.55–1.86) | 0.953 |
| Anxiety disorder | | | | | | |
| No | 591 (52.5) | 534 (47.5) | Reference | | Reference | |
| Yes | 364 (66.7) | 182 (33.3) | 0.55 (0.45–0.68) | <0.001 | 0.72 (0.56–0.92) | 0.009 |
| Antidepressant before ECT | | | | | | |
| Never | 28 (31.5) | 61 (68.5) | 4.03 (2.51–6.48) | <0.001 | 2.11 (1.23–3.61) | 0.010 |
| Not 0–3 months before ECT | 221 (57.6) | 163 (42.4) | 1.37 (1.06–1.76) | 0.016 | 1.36 (1.02–1.83) | 0.007 |
| 0–3 months, not 3–6 | 149 (46.1) | 174 (53.9) | 2.16 (1.66–2.83) | <0.001 | 1.54 (1.14–2.09) | 0.039 |
| 0–3 months & 3–6, not 6–9 | 94 (58.0) | 68 (42.0) | 1.34 (0.95–1.90) | 0.099 | 1.12 (0.76–1.67) | 0.569 |
| 0–3 months & 3–6 & 6–9 | 463 (64.9) | 250 (35.1) | Reference | | Reference | |
| CGI-S before | | | | | | |
| Borderline/mildly ill | 21 (67.7) | 10 (32.3) | 0.45 (0.21–0.98) | 0.045 | 0.56 (0.24–1.30) | 0.174 |
| Moderately ill | 205 (61.2) | 130 (38.8) | 0.60 (0.45–0.81) | 0.001 | 0.82 (0.58–1.17) | 0.277 |
| Markedly ill | 509 (59.8) | 342 (40.2) | 0.64 (0.50–0.81) | <0.001 | 0.83 (0.63–1.10) | 0.186 |
| Severely ill | 205 (48.7) | 216 (51.3) | Reference | | Reference | |
| Extremely ill | 15 (45.5) | 18 (54.5) | 1.14 (0.56–2.32) | 0.720 | 1.01 (0.44–2.31) | 0.991 |
| Initial treatment setting | | | | | | |
| Inpatient | 803 (55.6) | 641 (44.4) | Reference | | Reference | |
| Outpatient | 152 (67.0) | 75 (33.0) | 0.62 (0.46–0.83) | 0.001 | 0.85 (0.61–1.20) | 0.364 |
| Coercion | | | | | | |
| Voluntary treatment | 880 (58.8) | 616 (41.2) | Reference | | Reference | |
| Involuntary hospitalization | 75 (42.9) | 100 (57.1) | 1.85 (1.37–2.50) | <0.001 | 1.39 (0.94–2.07) | 0.102 |
| Antidepressant medication | | | | | | |
| Yes | 836 (57.5) | 619 (42.5) | 0.91 (0.68–1.21) | 0.512 | 0.75 (0.53–1.07) | 0.111 |
| No | 119 (55.1) | 97 (44.9) | Reference | | Reference | |
| Lithium | | | | | | |
| Yes | 175 (65.1) | 94 (34.9) | 0.67 (0.51–0.88) | 0.004 | 0.74 (0.53–1.04) | 0.081 |
| No | 780 (55.6) | 622 (44.4) | Reference | | Reference | |
| Lamotrigine | | | | | | |
| Yes | 131 (78.4) | 36 (21.6) | 0.33 (0.23–0.49) | <0.001 | 0.48 (0.31–0.75) | 0.001 |
| No | 824 (54.8) | 680 (45.2) | Reference | | Reference | |
| Valproate | | | | | | |
| Yes | 32 (71.1) | 13 (28.9) | 0.53 (0.28–1.02) | 0.059 | 0.58 (0.28–1.21) | 0.146 |
| No | 923 (56.8) | 703 (43.2) | Reference | | Reference | |

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**Table 1** (*Continued*)

| | Non-remission (%) | Remission (%) | Unadjusted | | Adjusted[a] | |
|---|---|---|---|---|---|---|
| | | | OR (95% CI) | *P*-value | OR (95% CI) | *P*-value |
| Benzodiazepines | | | | | | |
| Yes | 455 (62.6) | 272 (37.4) | 0.65 (0.53–0.79) | <0.001 | 0.73 (0.58–0.91) | 0.006 |
| No | 500 (53.0) | 444 (47.0) | Reference | | Reference | |
| Other antiepileptic medication | | | | | | |
| Yes | 86 (69.9) | 37 (30.1) | 0.55 (0.37–0.82) | 0.003 | 0.81 (0.52–1.26) | 0.340 |
| No | 869 (56.1) | 679 (43.9) | Reference | | Reference | |
| Antipsychotic medication | | | | | | |
| Yes | 429 (61.6) | 267 (38.4) | 0.73 (0.60–0.89) | 0.002 | 0.82 (0.65–1.04) | 0.108 |
| No | 526 (53.9) | 449 (46.1) | Reference | | Reference | |
| Number of ECT sessions | | | | | | |
| 1–5 | 124 (56.6) | 95 (43.4) | 0.78 (0.57–1.05) | 0.098 | 0.81 (0.58–1.14) | 0.229 |
| 6–8 | 408 (50.3) | 403 (49.7) | Reference | | Reference | |
| 9–12 | 325 (63.9) | 184 (36.1) | 0.57 (0.46–0.72) | <0.001 | 0.61 (0.47–0.78) | <0.001 |
| 13–53 | 98 (74.2) | 34 (25.8) | 0.35 (0.23–0.53) | <0.001 | 0.48 (0.30–0.76) | 0.002 |
| Electrode placement | | | | | | |
| Unilateral | 882 (58.5) | 625 (41.5) | Reference | | Reference | |
| Bitemporal | 45 (42.5) | 61 (57.5) | 1.91 (1.28–2.85) | 0.001 | 1.13 (0.71–1.80) | 0.618 |
| Bifrontal | 28 (48.3) | 30 (51.7) | 1.51 (0.89–2.56) | 0.123 | 1.02 (0.56–1.87) | 0.952 |
| Pulse width, ms | | | | | | |
| 0.25–0.47 | 225 (71.0) | 92 (29.0) | Reference | | Reference | |
| 0.50 | 636 (55.6) | 507 (44.4) | 1.95 (1.49–2.55) | <0.001 | 1.85 (1.32–2.59) | <0.001 |
| 0.51–1.00 | 94 (44.5) | 117 (55.5) | 3.04 (2.12–4.38) | <0.001 | 2.58 (1.64–4.06) | <0.001 |
| Frequency, Hz | | | | | | |
| 10–50 | 411 (61.6) | 256 (38.4) | Reference | | Reference | |
| 55–70 | 312 (57.2) | 233 (42.8) | 1.20 (0.95–1.51) | 0.123 | 0.98 (0.73–1.31) | 0.899 |
| 75–120 | 232 (50.5) | 227 (49.5) | 1.57 (1.24–2.00) | <0.001 | 1.19 (0.84–1.68) | 0.330 |
| Duration, s | | | | | | |
| 0.8–6.8 | 309 (54.4) | 259 (45.6) | Reference | | Reference | |
| 6.9–7.9 | 268 (58.9) | 187 (41.1) | 0.83 (0.65–1.07) | 0.149 | 0.95 (0.68–1.33) | 0.782 |
| 8.0 | 378 (58.3) | 270 (41.7) | 0.85 (0.68–1.07) | 0.168 | 1.11 (0.83–1.49) | 0.493 |
| Electric current, mA | | | | | | |
| 528–800 | 524 (56.5) | 404 (43.5) | Reference | | Reference | |
| 850–890 | 136 (63.8) | 77 (36.2) | 0.73 (0.54–1.00) | 0.050 | 0.87 (0.56–1.34) | 0.513 |
| 900–930 | 295 (55.7) | 235 (44.3) | 1.03 (0.83–1.28) | 0.766 | 1.12 (0.82–1.54) | 0.469 |
| Electric charge, mC | | | | | | |
| 75–288 | 383 (66.1) | 196 (33.9) | Reference | | | |
| 291–399 | 316 (56.3) | 245 (43.7) | 1.52 (1.19–1.93) | 0.001 | | |
| 400–1152 | 256 (48.2) | 275 (51.8) | 2.10 (1.65–2.67) | <0.001 | | |

CGI-S: Clinical Global Impression Severity Scale; ECT: electroconvulsive therapy; OR: odds ratio; CI: confidence interval.
[a] Adjusted for all variables in the table except for electric charge.

involuntary admitted patients had higher remission rates (57.1%) than voluntary admitted patients (41.2%). However, these associations with remission were not significant in the multivariate model (Table 1).

### 3.8. Association between remission and concurrent psychopharmacotherapy

Patients with concurrent lamotrigine treatment had significantly lower remission rates than patients without (Table 1). This effect remained in a multivariate model after stratification for unipolar/bipolar status (unipolar: OR: 0.56, 95% CI: 0.30–1.04, $P = 0.066$; bipolar: OR: 0.37, 95% CI: 0.17–0.78, $P = 0.009$).

The remission rate was not statistically significantly different between patients with and without valproate treatment. Similarly, after stratification for bipolar or unipolar status there was no statistically significant effect of valproate. Concurrent benzodiazepine treatment associated significantly with lower remission rates in the multivariate model (OR: 0.73, 95% CI: 0.58–0.91, $P = 0.006$). Antidepressants, lithium and other antiepileptic and antipsychotic medications did not associate significantly with remission in the multivariate model (Table 1).

### 3.9. ECT-related factors that associated with remission

Patients treated with brief pulse width stimuli, namely, 0.50 and 0.51–1.00 ms, had higher remission rates (44.4% and 55.5%, respectively) than the patients treated with ultra-brief (0.25–0.47 ms) pulse width stimulus (29.0%). In a multivariate regression model, in which pulse width was included as a continuous measure, pulse width was positively associated with remission (OR: 7.40, 95% CI: 2.77–19.74, $P < 0.001$). Increasing pulse width was weakly associated with a lower mean number of treatment sessions < 0.25–0.47 ms, 0.50 ms and 0.51–1.00 ms, 8.59, 8.02, and 8.24 respectively (Spearman's correlation coefficient −0.052, $P = 0.034$). Similarly, patients treated with higher charges required fewer ECT sessions on average. For charges of 75–288 mC, 291–399 mC, and 400–1152 mC, the mean numbers of sessions were 8.37, 8.13 and 7.96, respectively (Spearman's correlation coefficient −0.085, $P = 0.001$).

The other electrical stimulus parameters (frequency, duration, and current) did not associate with remission rate in the multivariate model. The remission rates were lower among patients with 9 or more ECT sessions than in patients with 6–8 sessions. Patients with unilateral, bitemporal, and bifrontal electrode placement had remission rates of 41.5%, 57.5%, and 51.7%, respectively. These differences were not statistically significant in the adjusted model (Table 1).

### 3.10. Interaction effects

There were statistically significant negative interaction effects between psychosis and substance use disorder (OR: 0.44, 95% CI: 0.19–1.00), psychotic features and anxiety disorder (OR: 0.49, 95% CI: 0.26–0.95), substance use disorder and no antidepressant use 0–3 months before inpatient treatment (OR: 0.49, 95%

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CI: 0.25–0.96), and ages over 60 years and an education lasting longer than 12 years as well as ages over 80 years and an education lasting longer than 9 years. The interaction effects between substance use disorder and pulse width of 0.51–1.00 ms and age group 61–70 and pulse width of 0.5 were positive (OR: 4.19, 95% CI: 1.48–11.93 and OR: 3.09, 95% CI: 1.13–8.47, respectively).

## 4. Discussion

The overall remission rate of 42.8% is consistent with the reported remission rate of ECT in another community setting (30.3–46.7%) [4]. Our large-scale study of depressed patients showed that psychotic features and an older age were predictive of higher remission rates after ECT. Patients with psychotic depression had higher remission rates than patients without psychotic features in all age groups (Fig. 1). That older and psychotically depressed patients have higher remission rates than younger and non-psychotic patients, respectively, has been reported in some [17,18] but not all previous studies [6]. We suggest that ECT should be considered for patients with psychotic or severe geriatric depression.

This study lends further support to the previously documented observation that patients who undergo prolonged pharmacological antidepressant treatment before ECT are less likely to benefit from ECT than patients who were not exposed to antidepressants or who were only treated for short periods of time [6].

We observed that the patients with psychiatric comorbidities tended to have lower remission rates than the patients without these comorbidities. This association was statistically significant in the multivariate model for anxiety disorders and substance use disorders. Personality disorders also tended to associate with lower remission rates, although this trend was not statistically significant in the multivariate model, possibly because of insufficient power. At odds with a small German study [19], comorbid alcohol abuse did not associate positively with remission in our study. The significant interaction effect between pulse width and substance use disorders could possibly be explained by the anticonvulsive effects of higher doses of anesthetics that are sometimes needed among patients with substance use disorders.

The remission rate was lower among patients who received 9 or more sessions than among those who received 6–8 sessions. This might suggest that after 8 sessions the incremental effect of more sessions tends to decrease. However, 30.4% of the remitters required more than 8 treatments and 4.7% required more than 12 treatments. It is necessary to examine patients regularly during index-ECT for remaining symptoms and memory effects in order to tailor the stimulus and treatment length optimally to the individual patient.

We found that an ultra-brief stimulus pulse reduced the effectiveness of ECT. This has been observed in previous studies [8]. While this loss of effectiveness should be balanced against the fact that ultra-brief stimulus also reduces ECT-induced memory disturbances [7,8], temporary memory disturbances are usually well-tolerated and thus the efficacy should be the priority in most cases. Additional studies that identify the optimal balance between memory disturbances and clinical effect in different patient groups are warranted. In particular, it would be of interest to determine the cost-benefit outcomes of starting with a brief pulse width and then decreasing the pulse width if marked memory disturbances occur. An alternative therapeutic strategy that could be explored is starting with an ultra-brief pulse width and then increasing it to a brief pulse width if remission does not occur.

The aim of the stimulus is to elicit an adequate epileptic seizure. We found that concurrent antiepileptic medication with lamotrigine and benzodiazepines was associated with reduced benefit from ECT, possibly by reducing the quality of the seizure. By contrast, some earlier studies did not find a strong impact on seizure quality by antiepileptic drugs and suggest that the anticonvulsant effect of the anesthetic is more important [20,21]. Moreover, benzodiazepines are sometimes needed to relieve symptoms of severe anxiety. In some cases, the patient might not even consider ECT if abstain from benzodiazepines is required. Another potential difficulty is that after reinitiating lamotrigine, the dose needs to be raised slowly. Experimental studies are needed to address if lowering the dose of antiepileptic drugs during ECT improves outcomes. Until these studies have been performed, we suggest that antiepileptic medication should be used carefully. If possible, benzodiazepines should be gradually tapered and finally stopped during the ECT-course.

An earlier randomized study suggested that concomitant antidepressant treatment with ECT had an additive effect [22]. Our study did not confirm this finding. More clinical trials that investigate the optimal concomitant pharmacotherapy with ECT are needed.

The outcome was dichotomized (remission/not remission). An alternative would be to analyze the change in MADRS-S. It could be statistically more powerful, but is also problematic since it would assume that an improvement of a certain amount of points is the same no matter what score the individual had before treatment. Moreover, the use of remission as an outcome in this study clarifies that the severely ill patients with psychotic symptoms, not only have greater improvements than patients with less severe symptoms, but also have higher remission rates after treatment.

### 4.1. Study limitations

In observational studies, indication bias can influence the association between treatment and outcome. This also applies to associations between concomitant medication and technical factors and ECT. Moreover, the agreement between physicians-ratings and self-ratings are generally acceptable, but somewhat lower among patients with cluster C personality traits. These patients tend to self-rate their symptoms more severely than the physician [23].

Some clinicians do not use any depression rating scale in the clinical routine or use an alternative rating scale to MADRS-S. Therefore, a large proportion of the patients treated with ECT in Sweden could not be included in this study. However, among the investigated parameters, the differences between included and excluded patients were modest.

The duration of the current depressive episode was impossible to control for in this study, other than by altering the duration of antidepressant treatment. Diagnoses were not always confirmed by structured interviews, so there may be some uncertainties regarding the unipolar or bipolar statuses of the patients. Moreover, comorbid disorders may sometimes go undiagnosed in clinical practice.

## 5. Conclusions

For depression in a community settings, ECT was effective in patients with psychotic symptoms and geriatric patients, but was less effective in younger patients, patients with comorbid psychiatric conditions, and in patients who had had prolonged treatment with antidepressant medication. More careful use of lamotrigine and benzodiazepines during ECT and using brief pulse stimuli may improve outcomes.

Many young patients suffering from depression undergo months of pharmacotherapy without experiencing sufficient relief. It is urgent to identify biomarkers to determine who among these patients could benefit from ECT. Until these biomarkers have been

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identified, ECT should be used cautiously in these patients and doctors should ensure that patients are adequately informed about the benefits and risks of the different treatments.

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## Disclosure of interest

The authors declare that they have no competing interest.

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