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## Metody podtrzymywania efektów terapii elektrowstrząsowej w depresji w różnych częściach świata

Methods for maintaining the effects of electroconvulsive therapy in depression treatment in various parts of the world

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### Streszczenie

**Wprowadzenie:** Terapia elektrowstrząsowa (EW) jest jedną z najskuteczniejszych metod leczenia w psychiatrii. Celem pracy jest przedstawienie innowacyjnych metod zapobiegania nawrotom depresji po leczeniu EW z wykorzystaniem EW kontynuującej (*continuation electroconvulsive therapy*, c-ECT), EW podtrzymującej (*maintenance electroconvulsive therapy*, m-ECT) oraz farmakoterapii, a także porównanie podejść do ich stosowania w różnych częściach świata. **Materiał i metody:** Dokonano przeglądu dostępnej literatury poprzez przeszukanie baz PubMed i Google Scholar przy użyciu następujących słów kluczowych: „c-ECT”, „m-ECT”, „continuation electroconvulsive therapy”/„kontynuacja terapii elektrowstrząsowej”, „maintenance electroconvulsive therapy”/„podtrzymująca terapia elektrowstrząsowa”, „major depressive disorder”/„duże zaburzenia depresyjne”, „continuation pharmacotherapy”/„kontynuacja farmakoterapii”, włączając prace oryginalne, metaanalizy i prace przeglądowe w języku polskim i angielskim opublikowane w latach 1999–2023. W celu utrzymania wysokiej jakości przeglądu narracyjnego zastosowano skalę SANRA. **Wyniki:** W leczeniu podtrzymującym c-ECT i m-ECT osiąga się porównywalne efekty jak przy leczeniu farmakologicznym. Najskuteczniejszą metodą jest połączenie leczenia farmakologicznego i c-ECT. c-ECT i m-ECT mogą skrócić czas, koszt i liczbę hospitalizacji. Jednocześnie jednym z głównych trendów w praktyce EW w ostatnich 20 latach było przejście z leczenia szpitalnego na ambulatoryjne. **Wnioski:** c-ECT i m-ECT są niewystarczająco wykorzystywane i niedostatecznie zbadane pomimo pozytywnych doświadczeń klinicznych obejmujących ponad 70 lat. Choć stosuje się je na całym świecie, nie ma konkretnych wytycznych ani ujednoczonych metod prowadzenia tych terapii. Prowadzone obecnie badania powinny dostarczyć zaleceń dotyczących wyboru, częstotliwości i czasu trwania c-ECT i m-ECT.

**Słowa kluczowe:** duże zaburzenia depresyjne, terapia elektrowstrząsowa, farmakoterapia, terapia podtrzymująca

### Abstract

**Introduction:** Electroconvulsive therapy (ECT) is one of the most effective treatments in psychiatry. The aim of this study is to present innovative methods for preventing the recurrence of depression after ECT treatment using continuation ECT (c-ECT), maintenance ECT (m-ECT), and pharmacotherapy, as well as to compare different approaches to the use of these methods across different parts of the world. **Materials and methods:** A review of the available literature was performed by searching the PubMed and Google Scholar databases using the following keywords: “c-ECT”, “m-ECT”, “continuation electroconvulsive therapy”/“kontynuacja terapii elektrowstrząsowej”, “maintenance electroconvulsive therapy”/“podtrzymująca terapia elektrowstrząsowa”, “major depressive disorder”/“duże zaburzenia depresyjne”, “continuation pharmacotherapy”/“kontynuacja farmakoterapii” for original papers, meta-analyses, and review papers both in Polish and English, published from 1999 to 2023. The SANRA scale was used to maintain the quality of the narrative review. **Results:** In maintenance treatment, c-ECT and m-ECT achieve effects comparable to those of pharmacological treatment. The most effective method is a combination of pharmacological

therapy and c-ECT. c-ECT and m-ECT can reduce the time and cost, and the number of hospitalisations. At the same time, one of the major trends in ECT practice over the past 20 years has been the shift from inpatient to outpatient treatment. **Conclusions:** c-ECT and m-ECT are underutilised and understudied despite positive clinical experience spanning over 70 years. Although they are used all over the world, there are no specific guidelines or standardised methods for conducting this therapy. Studies that are currently underway should provide recommendations regarding the selection, frequency, and duration of c-ECT and m-ECT.

**Keywords:** major depressive disorder, electroconvulsive therapy, pharmacotherapy, maintenance therapy

## INTRODUCTION

Depression is one of the most prevalent mental illnesses in the world, affecting 280 million people of all ages globally. It is also the primary cause of disability and a major contributor to the global disease burden (Trivedi, 2020; World Health Organization, 2023). Even with the availability of effective pharmacologic and psychological treatments, the rates of depression diagnosis and treatment remain low. The prevalence of depression is estimated to be 3.8% of the population, with 5% of adults (4% of men and 6% of women) and 5.7% of individuals over 60 having the disorder (World Health Organization, 2023). Women are approximately 50% more likely than males to experience depression. Globally, more than 10% of pregnant women and women who have just given birth experience depressive disorder (Woody et al., 2017). An estimated 700,000 people lose their lives to suicide each year. The fourth most common cause of mortality for individuals aged 15 to 29 is suicide. Despite the fact that there are proven effective treatments for mental disorders, over 75% of people in countries with low or middle incomes do not receive treatment at all (Evans-Lacko et al., 2018). According to the ICD-11, a depressive episode is characterised by the co-occurrence of at least five of 10 symptoms, which must be present for the majority of the day, almost every day, for a minimum of two weeks. A depressed mood or a noticeably decreased interest or pleasure in activities must be one of these symptoms. Significant functional impairment must be directly caused by the mood disturbance and cannot be attributed to another health condition, the side effects of drugs or alcohol, or a recent bereavement that would offer a better explanation. The ten symptoms include a depressed mood, markedly diminished interest or pleasure in activities, reduced capability to concentrate and sustain attention or marked indecisiveness, beliefs of low self-worth or excessive or inappropriate guilt, hopelessness about the future, recurring suicidal thoughts or suicidal ideation or evidence of attempted suicide, severe disruptions in sleep or excessive sleep, notable changes in weight or appetite, psychomotor agitation or retardation, and fatigue or energy deficiencies (McGlinchey et al., 2006; Stein et al., 2020). When it comes to major depressive disorder (MDD), less than 30% of patients achieve remission during their first antidepressant trial (Gaynes et al., 2009). It raises the burden of functional impairment in the areas of physical health, social connections, and occupation (Kennedy and Ceniti, 2018; Milev et al., 2016).

In much of Europe and North America, major depressive disorder continues to be the most common indication for electroconvulsive therapy (ECT) (Kellner et al., 2020). ECT involves the use of electrical stimulation within the central nervous system, which causes a short, controlled epileptic seizure (Milev et al., 2016). ECT was originally introduced for the treatment of schizophrenia, but it has demonstrated benefits in a variety of psychiatric and neurological conditions (Trevino et al., 2010). Its effectiveness is tested throughout the duration of the procedure, with approximately 15 minutes passing from the moment the patient is anaesthetised until they wake up (Lupke et al., 2023; Teodorczuk et al., 2019; Weiss et al., 2019). When applied to the right patient at the right time, ECT can save lives by relieving symptoms (Kellner et al., 2020). Significant advances in the practice of ECT have improved the safety, tolerability, and effectiveness of the procedure. These include the use of anaesthetics and muscle relaxants (modified ECT), new approaches to electrode placement, electroencephalogram (EEG) monitoring, dosing based on determining the seizure threshold, and changing stimulus parameters in the use of short and very short pulse widths. In rare cases, tolerability problems with ECT, such as negative cognitive effects, anxiety over anaesthesia, headaches, or nausea, might require its interruption or discontinuation (Andrade et al., 2016; Charlton, 1999; Fink, 1999; Kellner et al., 2020; Nielsen et al., 2014). A basic ECT series includes 8–15 treatments performed 2–3 times a week (Antosik-Wójcińska et al., 2021). However, patients should get ECT treatments until they either achieve remission or a plateau of improvement; there is no set number of treatments required for an acute course (Kellner et al., 2020). Certain severely ill patients may receive treatment every day until improvement is observed (Fink et al., 2016). Clinical trial response and remission rates are consistently high, frequently exceeding 60% for remission and 70% for response (Kellner et al., 2016, 2010, 2006). Catatonic characteristics and the psychotic subtype of depression are indicators of a particularly good response. Melancholic features and higher baseline depressive symptom intensity are probably linked to a better ECT response, as are older age, psychotic symptoms, and shorter episode duration (Kellner et al., 2020). Most patients with depression who are referred for ECT have a severe and incapacitating disease that has not improved with either medication or psychotherapy. The decision to recommend ECT is often dictated by the urgency of the clinical situation, which is frequently characterised by acute suicidal

preoccupation and drive. Patients are often administered many sequential trials of antidepressant drugs while they remain significantly depressed for extended periods of time. This is the current practice in many countries. However, it may have detrimental financial effects in addition to causing prolonged suffering and a risk of suicide death. Only two failed antidepressant prescription trials would make it cost-effective to consider ECT, according to a recent health economics study conducted in the United States (Ross et al., 2018). ECT is regarded as a first-line treatment for severe depressive episodes that are life-threatening and when a quick response is necessary, according to the majority of ECT guidelines and recommendations for the treatment of depressive disorder. ECT is primarily indicated in cases with psychotic characteristics, catatonia, high suicide risk, and/or rejection of food or fluids (Bauer et al., 2013; Malhi et al., 2015; Milev et al., 2016; Schlaepfer et al., 2010). Furthermore, most guidelines consider a previous positive response to ECT (Malhi et al., 2015; Milev et al., 2016) and patient preference as indications for using ECT as a first-line treatment (Jaffe, 2002; Malhi et al., 2015; Milev et al., 2016). ECT is regarded as a second-line treatment for patients suffering from severe major depressive episodes that do not respond to psychotherapeutic or pharmacological interventions (Kellner et al., 2020).

After the series of treatment is completed, maintenance therapy is usually prescribed to prevent recurrence of depression. It may be of different nature, usually it is a continuation of pharmacological treatment (Geddes et al., 2003; Kellner et al., 2020). The majority of patients who remit after an acute course of ECT should be offered continuation ECT (c-ECT) and maintenance ECT (m-ECT), usually with an antidepressant medication or a combination of psychotropic drugs (Geddes et al., 2003; Petrides et al., 2011). The term “c-ECT” refers to the continuation of ECT immediately after completing the basic series of ECT treatments, usually with breaks lasting from one week to one month. The duration of c-ECT therapy is usually six months. The term “m-ECT” defines procedures performed after six months of c-ECT treatment. The intervals between treatments are usually four to 10 weeks. The duration of m-ECT treatments typically spans several months (Brown et al., 2014; Elias et al., 2014; Rabheru, 2012). Many patients also require a combination of several of the above-mentioned methods (Jaffe, 2002; Petrides et al., 2011; Rabheru, 2012; Trevino et al., 2010). According to the recommendations of the American Psychiatric Association, c-ECT and m-ECT should be considered as treatment options for patients who meet the following criteria:

- course of the disease with relapses with good clinical response to ECT treatments in the basic series;
- poor tolerance of pharmacological treatment after the basic series of ECT treatments or low effectiveness of pharmacotherapy in preventing disease relapses (Jaffe, 2002);
- good cooperation with the patient and their acceptance of long-term maintenance ECT treatment (Palińska et al., 2008b).

The aim of this study was to present innovative methods of preventing recurrence of depression after ECT treatment using c-ECT, m-ECT, and pharmacotherapy, as well as to compare different approaches to the use of these methods in various parts of the world.

## MATERIALS AND METHODS

A review of the available literature was performed by searching the PubMed and Google Scholar databases using the following keywords: “c-ECT”, “m-ECT”, “continuation electroconvulsive therapy”/”kontynuacja terapii elektrowstrząsowej”, “maintenance electroconvulsive therapy”/”podtrzymująca terapia elektrowstrząsowa”, “major depressive disorder”/”duże zaburzenia depresyjne”, “continuation pharmacotherapy”/”kontynuacja farmakoterapii”. Original papers, meta-analyses, and review papers both in Polish and English, published between 1999 and 2023, were included. The SANRA scale and the ANDJ narrative review checklist (Baethge et al., 2019) were used to maintain the quality of the narrative review.

## RESULTS

After ECT, antidepressant treatment is recommended, as relapse rates are nearly double without it (Jelovac et al., 2013). In a randomised controlled trial conducted by Sackeim et al. (2001) the nortriptyline-lithium combination significantly reduced relapse rates compared to placebo or nortriptyline alone. Nevertheless, the recurrence rate with nortriptyline and lithium was still significant (39.1%). Authors suggest that these two non-exclusive strategies should be evaluated. Both treatments are supported by the evidence that relapse occurs especially in the period immediately following ECT. During the acute treatment phase, antidepressants and mood stabilisers take several weeks to exert their therapeutic benefits. Abruptly discontinuing effective somatic treatment can increase the risk of recurrence, which is common at the conclusion of an ECT course. One approach is to taper ECT over a few weeks, as is usual with pharmacological treatments, to provide alleviation of symptoms throughout the most vulnerable period. Second, the antidepressant drugs used in maintenance therapy may be started during the ECT procedure, followed by the addition of lithium afterward. Controlled research using ECT with antidepressants focused on improving response rather than reducing post-ECT recurrence rates. Nonetheless, trials in which patients began taking an antidepressant at the beginning of their ECT treatment revealed a low post-ECT recurrence rate. Consequently, these two complementary strategies present an opportunity to further enhance the benefits observed with the nortriptyline-lithium therapy and resolve the issue of the high rate of early relapse with continuation pharmacotherapy after ECT (Sackeim et al., 2001). A study conducted by the Canadian Network for Mood and Anxiety Treatments (CANMAT) (Milev

et al., 2016) showed that c-ECT and m-ECT were comparably effective and safe as pharmacotherapy in preventing disease relapses. Six months after the completion of ECT and c-ECT, the recurrence rate was 37.2%, and in the case of pharmacotherapy – 37.7%. When it comes to preventing relapse using medications, the combination of nortriptyline and lithium has also been shown to be more effective than using the same medications alone.

Continuation/maintenance (c/m) ECT is one of the therapeutic options available for relapse prevention following acute ECT remission, with maintenance ECT suggested for a minority of patients. Contemporary ECT treatment includes tapering the acute course and continuing/maintaining ECT in an increased number of patients than in the past. Tapering the acute ECT course from two or three treatments per week to weekly for a few weeks has been suggested to decrease the risk of recurrence, potentially by treating through the period of vulnerability to relapse into the current episode (Brown et al., 2014; Kellner et al., 2020). Sustained continuation (beyond the taper phase) and maintenance ECT are usually reserved for patients who have experienced repeated severe episodes and have failed to respond effectively to medications. While there are no commonly acknowledged standard schedules, the dosage and duration of continued ECT are normally adapted to the individual patient's needs, depending on a history of prior episodes, their number and severity, as well as the estimated urgency of preventing future episodes (Kellner et al., 2020). In general outline, electrode placement and stimulus dosing in c/m-ECT are the same as in the acute course, nevertheless Bailine et al. (2019) recently made arguments for the use of more powerful forms of ECT (bilateral electrode placements and higher stimulus doses), considering a decreased risk of cognitive effects with infrequent treatments. Maintenance ECT can be sustained indefinitely. The period between treatments is suggested to be increased to a duration considered to be protective, typically not exceeding 2–3 months. The majority of patients will be given a course of treatment that will last between three and eight weeks. Some patients might still need longer periods of up to weekly m-ECT in order to remain well. The risk-benefit assessment for m-ECT in every individual receiving treatment should be reassessed on a regular basis, about every 6–12 months. Gill and Kellner's (2019) latest publication provides an outline of recommendations for c/m-ECT.

The use of maintenance therapy varies across different countries around the world. There is also a limited amount of data in the available literature on this subject. In the US, after a course of ECT, some patients receive c-ECT and m-ECT at weekly, biweekly or monthly intervals. One of the important trends in ECT practice over the past 20 years has been the shift from inpatient to outpatient treatment. For example, at Duke University Hospital, the rate of outpatient ECT increased from 32.3% in 1993 to 75.6% in 2009 and further to 83.5% in 2011 (Case et al., 2013). The frequency of c-ECT and m-ECT should be determined according

to the needs of a given patient; there are no studies defining the standards. Most often, treatments are performed weekly for four weeks, then once every two weeks for two months, and finally once a month. In case of recurrence, more sessions should be performed (Milev et al., 2016). An interesting study was undertaken in Sweden (Nordenskjöld et al., 2013), to evaluate if a combination of c-ECT and pharmacological treatment or solely pharmacotherapy would be more successful in preventing a recurrence of severe depression. Significantly fewer disease relapses occurred in patients who received both c-ECT and pharmacotherapy. After just two months of the study, a significant difference was visible. Only 18% of patients treated with medications and c-ECT experienced a recurrence of symptoms. In individuals treated with pharmacotherapy, this percentage was 29%. After half a year, 54% of subjects experienced a relapse after pharmacological treatment alone. In Australia, c-ECT is used for 6–9 months in 92% of facilities. 84.2% of people receiving this therapy are patients previously treated for severe depression. m-ECT prevents disease recurrence in 86% of hospitals. In 83% of cases, it is used to prevent relapses of severe depression (Chanpattana, 2007). However, in New Zealand, m-ECT accounts for 19.7% of all electroconvulsive treatments. A nine-year retrospective study showed a reduction in hospitalisation rates in 52% of patients thanks to the use of m-ECT (Stegmann et al., 2023). Psychiatrists from Western European countries also place great emphasis on maintenance therapy, especially in the treatment of severe depression (Petrides et al., 2011). Specialists from Belgium and the Netherlands have concluded that m-ECT has similar effectiveness to maintenance pharmacotherapy in geriatric patients with severe depression. Shortcomings in research on ECT in geriatric depression have also been noticed, including cognitive impairment, comorbidities, and clinical parameters in such patients (van Schaik et al., 2012). In 2011, in Great Britain, 26% of clinics declared that they treated patients with m-ECT and/or c-ECT. The average age of the patients was 60 years, with more women than men treated. m-ECT was administered for a longer period and less frequently than c-ECT (Gupta et al., 2011). Surprisingly, c-ECT in Germany is rarely used as a continuation therapy after achieving remission. With few exceptions, pharmacotherapy is mainly used for this purpose. There are no national guidelines regarding the use of c-ECT and m-ECT as forms of maintenance therapy (Petrides et al., 2011). French researchers have pointed out that residual clinical symptoms and numerous comorbidities are indications for c-ECT and m-ECT. However, there are no national guidelines regarding the indications and duration of maintenance therapy either (Bulteau et al., 2020). In Spain, researchers examined the impact of the implementation of c-ECT and m-ECT not only on the clinical improvement of patients, but also on the economic aspect of the public health care sector. After the introduction of therapy at the University Hospital, direct costs per day were reduced to 50.6% of previous bills, while costs related

to emergency department visits were reduced to 11.5% of previous charges. In terms of patients' perceived improvement in their health, 87.5% of patients rated the care and treatment they received as very satisfactory and 12.5% as satisfactory (Rodriguez-Jimenez et al., 2015).

After conducting a series of electroconvulsive treatments, clinical practice in Poland typically distinguishes between two approaches. The first one is based on the continuation of pharmacological treatment. Sometimes the doses of drugs are initially reduced to prevent the so-called therapeutic gap to ensure that pharmacotherapy maintains the achieved effect and prevents recurrence of the disease (Antosik-Wójcińska and Świącicki, 2014; Antosik-Wójcińska and Poleszczyk, 2015; Antosik-Wójcińska et al., 2021; Palińska et al., 2008a). The second approach is to gradually end ECT therapy with decreasing frequency, extending the intervals between treatments. Indications for the use of electroconvulsive therapy as a continuation of treatment include ineffectiveness or contraindication to the use of pharmacotherapy, good outcomes of ECT in the past, and the patient's preference for this method (Antosik-Wójcińska and Świącicki, 2014; Antosik-Wójcińska et al., 2021). Maintenance treatments in Poland are initially performed once a week for 2–4 weeks, then once every two weeks for a period of 1–2 months, and then once every 3–4 weeks (Antosik-Wójcińska and Świącicki, 2014, 2016; Antosik-Wójcińska and Poleszczyk, 2015; Palińska et al., 2008a; Zyss, 2010; Zyss et al., 2008). In accordance with the practice adopted at the Department of Psychiatry of the Medical University of Lodz, the frequency of treatments is further reduced to once every 8–10 weeks. This clinic is one of the main units performing supportive electroconvulsive treatments in Poland (Antosik-Wójcińska and Poleszczyk, 2015; Antosik-Wójcińska et al., 2021; Palińska et al., 2008a). According to 2020 research, nine centres offer it (56%). This procedure is the same as in the case of the basic ECT series, with patients hospitalised for the duration of the therapy, including obtaining consent and conducting all patient consultations (Antosik-Wójcińska et al., 2021; Palińska et al., 2008a).

In Asia, c-ECT is used in 17 countries after the acute course of the disease, for 6 to 9 months, in 115 hospitals (44.7%). Most centres performing c-ECT are in Japan (40 centres), followed by India (29 facilities). In other countries, c-ECT is performed in a much smaller number of centres: in Thailand in 11 hospitals, in Iran in eight facilities, in Israel in seven hospitals, and in South Korea only in four, in Hong Kong, Iraq and Nepal only in two, and in China, Vietnam, Singapore, Sri Lanka, Bangladesh, Pakistan and Turkey only in one hospital. The average effectiveness in preventing the recurrence of depression is 46%. M-ECT is performed in 14 countries, but only in 63 centres; 36.4% of the time in patients with severe depression (Chanpattana, 2007). The data from Japan alone matched the research for the whole of Asia. M-ECT was performed in 18 hospitals, most often in an attempt to stop the recurrence of severe depression (Chanpattana et al., 2005).

In Russia, maintenance treatment with c-ECT and m-ECT is used by 26% of facilities, but the procedure is not indicated in the official Russian guidelines. Outpatient ECT is available in 2% of Russian centres (Nelson, 2005). Regarding Africa and Latin America, reports on this subject are caustic. In the last case report, from 2021, the use of m-ECT was reported in a 64-year-old patient in South Africa (Magula et al., 2021).

## CONCLUSIONS

The urgent nature of the clinical situation, which is commonly characterised by severe suicidal preoccupation and drive, usually determines whether ECT is recommended in depression. Patients are frequently given multiple sequential trials of antidepressant medicines when they are severely depressed for extended periods of time. This is a standard practice in numerous countries. This approach may have a negative financial impact, as well as prolonging suffering and increasing the risk of suicide. According to a recent health economics analysis conducted in the United States, considering ECT might be cost-effective with just two failed antidepressant prescription trials (Ross et al., 2018). This is the reason why maintaining the effects of ECT in depression appears to be so important.

Maintenance treatment with c-ECT and m-ECT achieves effects comparable to those of pharmacological treatment. However, the most effective method is a combination of pharmacological treatment and c-ECT. When it comes to pharmacological continuation treatment, the combination of nortriptyline and lithium has been shown to be more effective than using the same medications alone (Sackeim et al., 2001). Patients who are resistant to therapy are less likely to achieve complete remission and more likely to relapse (Fekadu et al., 2009). A recent meta-analysis indicated that acute remission rates with ECT were lower in treatment-resistant individuals (48%) than in those who had not developed medication resistance (65%) (Heijnen et al., 2010). There is currently no agreement on the appropriate post-ECT relapse prevention treatment. Authors suggest that the majority of patients who remit after an acute course of ECT should be offered c-ECT and m-ECT (Geddes et al., 2003; Petrides et al., 2011). Nevertheless, there are no set recommendations for choosing an agent or determining the duration of treatment. Over the past three decades, most experimental work has focused on refining ECT treatment parameters (e.g. electrode placement, stimulus dose, and pulse width) to provide the greatest possible balance of clinical and cognitive outcomes (Jelovac et al., 2013). This could explain why so little information is available regarding maintenance ECT therapy.

At the same time, c-ECT and m-ECT can reduce the time, cost and number of hospitalisations (Stegmann et al., 2023). They have a beneficial impact not only in terms of the clinical improvement of patients, but also the economic aspect of the public health care sector (Rodriguez-Jimenez et al.,



2015). One of the major trends in ECT practice over the past 20 years has been the shift from inpatient to outpatient treatment (Case et al., 2013). Unfortunately, there is no detailed data on the use of m-ECT and c-ECT across different countries around the world. However, both modalities are underutilised and understudied despite positive clinical experience spanning over 70 years. Despite being used all over the world, there are no specific guidelines or standardised methods for conducting this therapy. This highlights the importance of ongoing research in this area, which should provide recommendations regarding the selection, frequency and duration of c-ECT and m-ECT (Gupta et al., 2011; Leiknes et al., 2012).

### Conflict of interest

*The authors report no conflict of interest. The authors do not report any financial or personal connections with other persons or organisations which might negatively affect the content of this publication and/or claim authorship rights to this publication.*

### Author contribution

*Collection, recording and/or compilation of data; analysis and interpretation of data; writing of manuscript: KO, ZW, AB. Original concept of study; critical review of manuscript; final approval of manuscript: KO, ZW, AB, MP.*

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