Review Article

Frequency and Duration of Course of ECT Sessions: An Appraisal of Recent Evidence

Jagadisha Thirthalli, Shalini S. Naik, Girish Kunigiri[1]

ABSTRACT

Aims and Method: This paper aims to review the recent literature regarding factors influencing the frequency and number of sessions during a course of electroconvulsive therapy (ECT) for different psychiatric disorders. We systematically reviewed English-language papers of clinical trials of ECT published since the year 2000 in terms of frequency and number of sessions of ECT. **Results:** None of the 30 studies meeting our inclusion criteria were specifically designed to study frequency or number of sessions of ECT. A preliminary inference may be drawn regarding the number of sessions from the information available in these papers. For depression, patients receiving brief-pulse ECT needed fewer sessions than those receiving ultra-brief ECT when these were delivered at 8-times the threshold with unilateral electrode placement or at 2.5-times the threshold with bilateral placement. For schizophrenia, those receiving bifrontal ECT and ECT at 4-times the threshold-level stimulus needed fewer sessions than those receiving bitemporal ECT and 2-times the threshold-level stimulus, respectively. There were no clinical trials of the frequency of ECT sessions. **Clinical Implications:** As there is a dearth of studies specifically examining frequency and number of ECT sessions, broad recommendations from professional bodies should continue to guide practice.

Key words: Electroconvulsive therapy, frequency, schedule

Electroconvulsive therapy (ECT) continues to be an important treatment modality in psychiatry even after about eight decades of its first use. For well-defined indications, ECT is highly effective. An important concern regarding ECT is the cognitive adverse effects associated with it. A substantial body of research has concentrated on reducing the cognitive adverse effects while not compromising on its therapeutic usefulness. Researchers have explored variations in electrical aspects of the stimulus, electrode placement (EP), co-prescribed medications, anesthetic agents, etc., to achieve this. Frequency and number of sessions during a course of ECT are also important considerations in this context.

In this paper, we review the literature related to

Access this article online	
Website: www.ijpm.info	Quick Response Code
DOI: 10.4103/IJPSYM.IJPSYM_410_19	

How to cite this article: Thirthalli J, Naik SS, Kunigiri G. Frequency and duration of course of ECT sessions: An appraisal of recent evidence. Indian J Psychol Med 2020;42:207-18.

Department of Psychiatry, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, India, [1]Consultant Psychiatrist, Bradgate Mental Health Unit, Leicester, England, UK

Address for correspondence: Dr. Jagadisha Thirthalli
Department of Psychiatry, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru - 560 029, Karnataka, India.
E-mail: jagatth@yahoo.com

Submitted: 06-Oct-2019, **Revised:** 14-Dec-2019, **Accepted:** 03-Apr-2020, **Published:** 25-Apr-2020

frequency and number of sessions during a course of ECT. Three influential sources reviewed the knowledge about these aspects in the early 2000s.[1-3] We first provide the gist from these sources; then, we follow this up with a systematic review of the research published since the turn of this millennium.

The frequency of ECT sessions has varied across regions and settings. In the US and Israel, thrice-weekly ECT is a common practice,[4,5] while in the UK, twice-weekly sessions are commonplace.[6] Some authors[7] have argued for 4-5 sessions of ECT per week to enhance the speed of recovery. Based on the extended research in this field, the Taskforce Report of the American Psychiatric Association (APA) on ECT[1] recommends twice or thrice weekly ECT sessions, with a caution that more frequent sessions could result in higher cognitive deficits and a suggestion that frequency of sessions should be reduced if cognitive effects are of serious concern. The Royal College of Psychiatrists' (RCP) ECT Handbook[2] recommends the use of twice weekly ECTs for bilateral ECT; it suggests that the use of thrice-weekly bilateral ECT should be reserved only for life-threatening illnesses and for as long as the threat is high. It suggests that unilateral ECT be administered twice weekly. In his book on ECT, Abrams[3] recommended the use of twice weekly ECT with bilateral ECTs; he also observed that biweekly ECT might need fewer sessions to achieve comparable efficacy as thrice weekly ECT.

The number of sessions in a course of ECT is largely determined by individual patient's response. Generally, the ECT course is stopped as soon as remission from symptoms is achieved or if the initial improvement remains unchanged for two additional sessions.[1] Research examining the optimum number of ECTs for different indications is sparse. APA task force report suggests 6–12 sessions for depression, with a caveat that given patients may need more or less than these number of sessions. The number could be higher for patients in whom ECT protocol was changed and those with schizophrenia. Based on the observation by Segman *et al*.,[8] the RCP handbook suggested that bilateral ECTs for depression may be stopped if there is no improvement at all during the first six treatments; if there is some improvement, then a substantial minority of patients would respond and, hence, it may be worthwhile continuing ECTs for up to 12 sessions. Abrams'[3] recommendations regarding bilateral ECT for depression were largely similar to the ones by the RCP handbook.

We aimed to review the recent literature about the number and frequency of ECT sessions. We examined the literature for factors that may influence the number and frequency of ECT sessions for different psychiatric conditions and synthesized the findings. These factors include anesthetic agents used during ECT, electrical aspects of ECT, and ECT EPs.

METHOD

For this review, we followed the relevant sections of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We searched the PubMed database with the following search term: Electroconvulsive therapy [mesh]. We used "English," "clinical trials," "human," "articles with abstracts," and "publication dates between January 1st, 2000 and March 31st, 2019" as filters. A single author, SSN reviewed all the abstracts and selected papers that met the following inclusion criteria: the paper describes a clinical trial or posthoc analysis of data from clinical trials, and there is mention of the number of ECT sessions in the comparative groups or there is a comparison of different treatment schedules in terms of the number of ECT sessions. We excluded studies for reasons listed in Figure 1. SSN reviewed the full texts of all the selected studies and excluded further studies if they had both fixed number of ECT treatment sessions and fixed frequency of ECT treatments, no information was provided on both treatment schedules and total number of ECT treatment sessions, and if they were anecdotal case series/reports, articles on the same study cohort and reported the same observations,[9,10] or a study that was included in our previous review.[11] Figure 1 provides the details of this process. This systematic review protocol was not registered in any online database.

Each full-text paper was reviewed thoroughly, and the following details were extracted: aim of the study, sampling details, sample size, diagnosis, indication for ECT, comparison groups, details of anesthetic agents, details of electrical stimulus, EP, frequency of sessions, the total number of ECTs, and the reasons for terminating ECTs. In this paper, we focus on the findings on the frequency and number of ECT sessions. In some studies, there were major changes in ECT protocols (e.g. switching from unilateral to bilateral ECT). In such cases, we took into consideration only the details of the ECT sessions before the change.

We assessed the methodological quality of the studies using the Jadad score[12] if they were clinical trials. It is a system of evaluating the quality of clinical trials on the basis of randomization, blinding, and method of addressing dropouts. The score ranges from zero to five, a higher score indicating better quality.

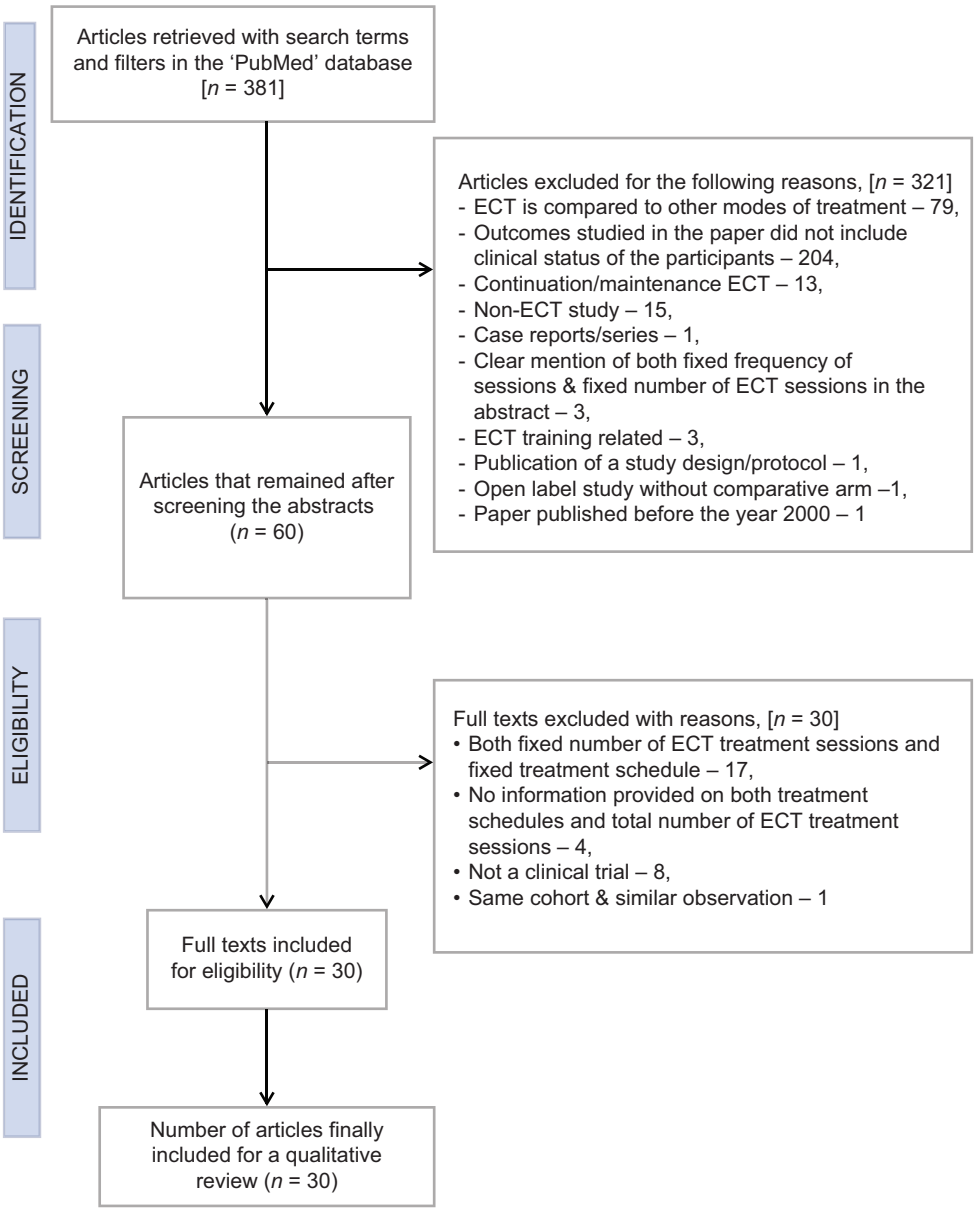

Figure 1: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for the selection of studies

RESULTS OF THE SYSTEMATIC REVIEW

Table 1 shows the details of the studies reviewed. We classified the studies as those examining the effects of anesthetic agents, EP, stimulus parameters such as pulse width and stimulus intensity, concurrent use of anticonvulsants, and clinical characteristics. We have synthesized the results for each of these influencing factors.

To understand the importance of the number of sessions, it is vital to know the reason for the termination of ECT. In 8 (26.7%) of the 30 studies, there was no mention of the policy to determine the number of sessions. In all but one[13] of the rest of the studies, the decision was left to the treating clinicians. Nine (30%) of the 30 studies provided the details of patients in whom ECT was terminated because of adverse effects;[13-21] in all these studies, these numbers were too small for meaningful statistical analysis. However, none of the studies provided information about the proportion of patients in whom ECT was terminated due to a lack of clinical improvement.

Seven studies[14-16,22-25] examined the influence of anesthetic agents. All but two studies included patients with depression. Canbek *et al*.[24] included patients with diagnoses of mania, psychosis, catatonia, or depression. Tripathi *et al*.[23] included patients with depression, schizophrenia, or mania. In none of these studies, there was a significant difference between the compared groups in terms of the number of ECTs received [Table 1].

Table 1: Details of clinical trials included in the systematic review

First author, year [Type of clinical trial]	Aim of the study	Diagnosis [Treatment resistance status]	Sample	Reason for termination of ECT	Whether groups were compared for reasons for termination	Results for number of ECT in the groups Mean (SD)	Conclusion of the study regarding clinical outcome (other than number of sessions)	Change in treatment strategy	Blinding (Jadad score)[12]
Studies comparing anesthetic agents									
Ingram, 2007[22] [CT]	To compare efficacy and cognitive effects of 2 anesthetic agents during ECT	Depression [NM]	Thiopentone=12; Propofol=18	LC	No	Thiopentone=8.8 (3.2); Propofol=9.5 (3.5) *P*-n.s	Both were comparable	Switched from BL to RUL in 1 case in each group due to cognitive adverse effects	Rater-blinded (2)
Bauer, 2009[14] [CT]	To compare effects of 2 anesthetic agents on seizure duration, Stimulus charge, clinical effect, and cognitive side effects.	Depression [NM]	Thiopentone=31; Propofol=31	LC	Yes	Thiopentone=13 (NM); Propofol=10.2 (NM) *P*-n.s	Propofol[109.8 (49.5) mC] needed significantly (P=0.026) higher stimulus electrical charge [79.5 (50.7) mC] than thiopentone and both were comparable for clinical efficacy and cognitive profile	2 subjects of thiopentone group switched to RUL electrode placement due to post ECT confusion	Only rater blind (4)
Tripathi, 2014[23] [CT]	To explore effects of pre-treatment low dose propofol on the acceptance of ECT	Multiple diagnoses [NM]	Propofol - 49; Unmodified ECT -50	NA	No	Propofol-6.1 (2.1); Unmodified - 5.5 (2) *P*-n.s	Using low dose propofol pre-treatment did not compromise ECT efficacy and had reduced anxiety surrounding the treatment	No	None blinded (1)
Canbek, 2015[24] [CT]	To compare the effects of 3 anesthetic agents on cardiovascular system, seizure, recovery, cognitive functions, and response to treatment	Multiple diagnoses [NM]	Propofol=20; Etomidate=16; Thiopentone=15	LC	No	Propofol=8.4 (1.6); Etomidate=8.6 (2.5); Thiopentone=8.1 (1.7) *P*-n.s	Similar clinical improvement and CVS findings were observed without deterioration in cognitive functions in all three groups	No	Patients and rater-blind (3)
Loo, 2012[25] [CT]	To test neuroprotective and enhanced clinical efficacy effects of sub-anesthetic dose of ketamine as an adjunct anesthetic agent	Depression [Mixed]	Ketamine=22; Placebo=24	LC	No	Ketamine=9.5 (4.7); Placebo=9.7 (3.3) *P*-n.s	Sub-anesthetic dose of ketamine, given as an adjunct anesthetic agent did not show any additional benefit for clinical efficacy as well as cognitive side effects	Similar proportion of subjects received shift from RUL to BL in case of insufficient clinical response	Patients and rater-blind (5)
Fernie, 2017[15] [CT]	To establish if ketamine speeds up response to ECT with less cognitive impairment	Depression [NM]	Ketamine=20; Propofol=20	LC	Yes	Ketamine=7.9 (3.2); Propofol=7.3 (2.2) *P*-n.s	No significant difference ratings of depression severity or cognitive function	No	Patients, rater and treating psychiatrist-blind (5)
Carspecken, 2018[16] [CT]	To compare efficacy of 2 anesthetic agents	Depression [TR]	Ketamine=27; Methohexital=23	LC	Yes	Ketamine=5.5 (2.7) Methohexital=5.8 (1.6) *P*-n.s	Both are equally efficacious	Switching over to BL electrode placement to attain or enhance clinical response. [Ketamine - 1 (4%) Methohexital - 7 (26%) X2-4.41; *P*=0.03]	Patients and rater-blind (5)

Contd...

Table 1: Contd...

First author, year [Type of clinical trial]	Aim of the study	Diagnosis [Treatment resistance status]	Sample	Reason for termination of ECT	Whether groups were compared for reasons for termination	Results for number of ECT in the groups Mean (SD)	Conclusion of the study regarding clinical outcome (other than number of sessions)	Change in treatment strategy	Blinding (Jadad score)[12]
Studies comparing electrode placement (EP)									
Bailine, 2000[26] [CT]	To compare clinical and cognitive effects of two bilateral EPs	Depression [NM]	BF=24; BT=24	NA	No	BF=5.9 (2.5); BT=5.4 (2.5) *P*-n.s	Both EPs were comparable in efficacy	No	Rater blind (2)
Stoppe, 2006[13] [CT]	To compare efficacy and tolerability of 2 EPs given at fixed high dose	Depression [Mixed]	BL=22; RUL=17	By blind rater (PI) based on clinical response scored on MADRS	Yes	RUL -10 (3.5); BL-10 (2.8) *P*-n.s	Efficacy and speed of response were comparable;	No	Patient and Rater blind (3) ECT course decision maker was blind to EP
Hiremani, 2008[27] [CT]	To compare the short-term efficacy and adverse effects of two kinds of bilateral EP	Acute Mania [Mixed]	BF=17; BT=19	LC	No	BF=7.6 (2.9); BT=7.5 (2.7) *P*-n.s	Comparable clinical efficacy but BF had shown faster response than BT [Breslow statistic (1) = 5.52 (1); *P*=0.019]	No	Patient, Rater and Consulting clinician - blind (5)
Sienaert, 2009[10] [CT]	To compare the efficacy of 2 EPs using an ultrabrief pulse width	Depression [NM]	RUL=32; BF=32	LC	No	RUL=10 (3.6); BF=12.4 (5.9) *P*-n.s	Estimated odds of 2.7 times faster response with RUL at 6 times threshold-level stimulus in compared to BF at 1.5 times threshold-level stimulus at each evaluation (*P*=0.04; 95% CI: 1.065-6.893)	In 4 patients electrode placement (BF: *n*=2; UL: *n*=2) was changed to bitemporal or left UL because of poor response/adverse effects	Rater-blind (3)
Kellner, 2010[17] [CT]	To compare the efficacy and cognitive effects of BF with BT and RUL ECT	Depression [Mixed]	RUL=77; BF=81; BT=72	NA	Yes	RUL=5.9 (2.3); BF=6.2 (2.6); BT=5.5 (2.3) *P*-n.s	Efficacy was comparable across the three EPs.	No	Patient, rater-blind (5)
Phutane, 2013[28] [CT]	To compare clinical and cognitive effects of 2 BL EPs	Schizophrenia [Mixed]	BF=62; BT=60	LC	No	BF=7.5 (2.1); BT=8.4 (2.5) *P*=0.04	BF is advantageous over BT for short-term symptomatic and cognitive outcomes	No	Patient, Rater and Consulting clinician - blind (5)
Bjølseth, 2015[29] [CT]	To compare efficacy and safety of 2 EPs in elderly depression	Depression [Mixed]	BL=36; RUL=37	LC	No	BF - 7.7 (2.8); RUL - 8.4 (2.3) *P*-n.s	Efficacy and speed of response were comparable	No	Rater and patient-blind (5)
Dybedal, 2016[30] [CT]	To compare cognitive effects of 2 EPs in elderly depression	Depression [NM]	BL=31; RUL=34	LC	No	BF - 9.3 (3.6); RUL - 9.3 (3.0) *P*-n.s	Efficacy and cognitive effects were comparable	No	Rater and patient-blind (5)

Contd...

Table 1: Contd...

First author, year [Type of clinical trial]	Aim of the study	Diagnosis [Treatment resistance status]	Sample	Reason for termination of ECT	Whether groups were compared for reasons for termination	Results for number of ECT in the groups Mean (SD)	Conclusion of the study regarding clinical outcome (other than number of sessions)	Change in treatment strategy	Blinding (Jadad score)[12]
Semkovska, 2016[18] [CT]	To assess the effectiveness and cognitive side effects of moderate-dose bitemporal ECT with high-dose unilateral ECT in real-world practice	Depression [Mixed]	BT=69; RUL=69	LC	Yes	BT - 8.3 (2.4); RUL - 7.8 (2.5) *P*-n.s	Efficacy was comparable	No	Rater and patient-blind (5)
Studies comparing pulse width									
Spaans, 2013[19] [CT]	To examine antidepressive efficacy of UBP Vs BP RUL ECT, both at 8X ST	Depression [Mixed]	BP=38; UBP=50	LC	Yes	BP=7.1 (2.6); UBP=9.2 (2.3) *P*=0.001	Efficacy and speed of response of RUL is superior with BP compared to UBP with equal cognitive side effects	Switched to BL EP[UBP - 4; BP - 3] or thrice weekly treatment schedule[UBP - 1; BP - 0]	Rater and patient-blind (5)
Loo, 2015[31] [CT]	To examine clinical and cognitive outcome of 8ST UBP Vs 5ST BP RUL ECT	Depression [Mixed]	UBP=47; BP=48	LC	No	UBP=8.6 (3.4); BP=8.4 (3.2) *P*-n.s	Efficacy and cognitive profile were comparable	No	Patient, Rater and Consulting clinician - blind (5)
Studies comparing combination of electrode placement and pulse width									
Sackeim, 2008[32] [CT]	To explore effects of pulse width and electrode placement on the efficacy and safety of ECT [UBP-RUL Vs UBP-BL Vs BP-RUL Vs BP-BL]	Depression [Mixed]	UBP-RUL=22; UBP-BL=23; BP-RUL=22; BP-BL=23	LC	No	UBP-RUL=8.7 (2.4); UBP-BL=8.9 (2.5); BP-RUL=8.5 (2.5); BP-BL=6.2 (2.4) *P*<0.0001	Anti-depressant response of ECT in the UB-BL group was significantly poorer than in the other three groups (all *P*'s<0.001)	Nonresponders (no response after 10 ECTs) received an open, crossover course of brief pulse (1.5 ms) BL ECT	Rater and patient-blind (5)
Studies comparing stimulus intensity									
Chanpattana, 2000[33] [CT]	To examine the effects of electrical stimulus intensity on the speed of response and efficacy of BL ECT	Schizophrenia [TR]	ST=21; 2X ST=21; 4X ST=20	LC	No	ST=18.6 (5); 2X ST=12.5 (3.8); 4X ST=9.2 (1.5) *P*<0.0001	Responders and Remitters were the same across all three groups but faster response in high dose BL groups [*P*<0.0001]	Similar proportions of patients received 3 weeks of stabilization treatment schedule after attaining BPRS <25	Patient, rater, and consulting psychiatrist-blind (4)
McCall, 2000[34] [CT]	To compare antidepressant and cognitive effects of two dosing strategies of RUL ECT	Depression [NM]	Titrated moderate dose (2.5X ST) = 36; Fixed high dose of 403mC=36	LC	No	Titrated moderate dose (2.5X ST) = 5.7 (1.6); Fixed high dose of 403mC=5.6 (1.6) *P*-n.s	Both group were comparable however clinical efficacy and cognitive impairment showed dose-response relationship mathematically with stimulus dose relative to seizure threshold (SDRST)	If insufficient response, changed over to BL ECT ; No difference between the two groups	Patient, rater, and consulting psychiatrist-blind (5)

Contd...

Table 1: Contd...

First author, year [Type of clinical trial]	Aim of the study	Diagnosis [Treatment resistance status]	Sample	Reason for termination of ECT	Whether groups were compared for reasons for termination	Results for number of ECT in the groups Mean (SD)	Conclusion of the study regarding clinical outcome (other than number of sessions)	Change in treatment strategy	Blinding (Jadad score)[12]
Mohan, 2009[35] [CT]	To compare speed of improvement and remission rate with different stimulus intensities	Mania [Mixed]	ST=26; 2.5XST=24	LC	No	ST=7.6 (2.0); 2.5X ST=7.6 (4.4) *P*-n.s	Both were comparable	No	Patient, rater, and consulting psychiatrist-blind (5)
Studies comparing combination of electrode placement and stimulus intensity									
Sackeim, 2000[20] [CT]	To compare efficacy of various electrical stimulus dose strengths of RUL with standard dose of BT	Depression [Mixed]	1.5X ST RUL=20; 2.5X ST RUL=20; 6XST RUL=20; 2.5XST BT ECT=19	LC	Yes	6X ST RUL=8.3 (2); 2.5X ST RUL=9.2 (1.8) 1.5X ST RUL=9.9 (4); 2.5X ST BT=8.3 (2.2) *P*-n.s	High dose RUL and BL are equally efficacious and superior to low and moderate dose RUL	Non-responder (up to 10 ECTs) switched to standard EP [Data in each group-NM]	Patient, rater, and consulting psychiatrist-blind (5)
Heikman, 2002[21] [CT]	To compare efficacy of high and moderate -dose RUL ECT, and low dose BF ECT	Depression [TR]	5X ST RUL=8; 2.5ST RUL=7; T BF=7	LC	Yes	5X ST RUL=7(NM); 2.5X ST RUL=8(NM); T BF=12(NM) *P*-n.s	All three groups were comparable on clinical and cognitive parameters.	No	Patient, rater, and consulting psychiatrist-blind (5)
Tew, 2002[36] [CT]	To compare efficacy of 2.5X ST RUL ECT non responders after they were randomized to either 5.5X ST RUL or 2.5X ST BL	Depression [NM]	BF=11; RUL=13	LC	No	BF - 11.8 (2.8); RUL - 12.5 (1.7) *P*-n.s	BL ECT exhibited significantly greater cognitive impairment than RUL ECT by mean MMSE score difference of 2.8 (*P*=0.02) with equal clinical efficacy	No	Patient, rater, and consulting psychiatrist-blind (3)
Studies on concurrent use of anticonvulsants									
Jahangard, 2012[37] [CT]	To compare clinical outcome of concurrent use of Sodium Valproate during ECT course	Bipolar-Mania [NM]	On Valproate=21; Off Valproate=21	LC	No	On Valproate=7.71 (1.58) Off Valproate=7.04 (1.35) *P*-n.s	Continuation of Valproate neither adversely affected nor enhanced the efficacy of ECT	No	Patient, rater, and consulting psychiatrist-blind (5)
Rakesh, 2017[38] [CT]	To compare the impact of dose strengths of anticonvulsants on ECT	BPAD [Non-TR]	Full dose=19; half-dose=11; stop anticonvulsant=18	LC	No	Full dose=7.6 (2.3); Half dose=7.5 (2.8); Stop=7.5 (3) *P*-n.s	All groups were comparable for electrical charge, dose, seizure duration, clinical efficacy and cognitive side effects	No	Patient, rater, and consulting psychiatrist (5)
Studies comparing clinical characteristics									
Remitters Vs non-remitters									
Rhebergen, 2015[39] [PHA]	To identify course trajectories and putative predictors of ECT	Depression [Mixed]	Remitters=60; Responders=36; Non-remitters=24	NA	No	Remitters=7.5 (2.5); Responders=17.0 (9.0); Non-remitters=20.7 (4.7) *P*<0.001	Age positively influenced response to treatment. Mean age was significantly higher in remitters than in responders) [*F* (df) =6.3 (1) *P*=0.01]	No	NA

Contd...

Table 1: Contd...

First author, year [Type of clinical trial]	Aim of the study	Diagnosis [Treatment resistance status]	Sample	Reason for termination of ECT	Whether groups were compared for reasons for termination	Results for number of ECT in the groups Mean (SD)	Conclusion of the study regarding clinical outcome (other than number of sessions)	Change in treatment strategy	Blinding (Jadad score)[12]
Spaans, 2016[40] [PHA]	To investigate characteristics of remitters with ultra-brief pulse RUL ECT	Depression [Mixed]	Early complete remitters (ECR) = 12; Late complete remitters (LCR) = 9 Non-remitters (NR) =27	NA	No	ECR=5.2 (1.3); LCR=11.0 (1.2); NR=11.6 (1.2) $P<0.001$	Older patients [F (df) = 6.1 (1) $P<0.0001$] with psychotic depression [X2(df) = 5.5 (1); $P=0.01$] predicted rapid remission with ECT	Switched to BL EP or thrice weekly treatment schedule	NA
Diagnosis									
Sienaert, 2009[41] [PHA]	To compare response and speed of response of patients with UP and BP depression treated with ultra-brief pulse ECT	Depression [TR]	Unipolar=51; Bipolar=13	NA	No	Bipolar=6.9±3.05; Unipolar=9.5±3.84 $P=0.03$	Remission rates are same in both groups but faster response noted in BP group [t (48)=2.05, $P=0.05$]	In 4 patients, EP was changed to BT due to poor response or cognitive effects [Data in each group-NM]	NA

BF- Bifrontal ECT; BT – Bitemporal ECT; BP – Brief pulse; CT – Clinical trial; LC – Left to treating clinicians' decisions; NM – Not mentioned; NA- Not applicable; n.s – Not significant; PHA – *Post-hoc* analysis of clinical trials; RUL – Right unilateral ECT; ST –Seizure Threshold; TR – treatment-resistant; UBP –Ultra-brief pulse

Nine studies[10,13,17,18,26-30] investigated the effects of EP. Six of these compared right unilateral (RUL) EP with another EP. The rest three compared different bilateral EP with one another. Seven studies included patients with depression; Hiremani *et al*.[27] and Phutane *et al*.[28] examined patients with mania and schizophrenia, respectively. Phutane *et al*.[28] found that schizophrenia patients treated with bifrontal ECTs received one less session than those treated with bitemporal ECTs. Other studies found no difference in the number of ECTs between the compared groups.

Two studies[19,31] compared ECT with brief (BP) and ultra-brief (UBP) pulse widths in patients with depression. Patients in the BP ECT group received significantly less number of ECTs [Mean (SD) = 7.1 (2.6)] than those in the UBP group [9.2 (2.3)] by two ECT treatment sessions when both BP and UBP ECTs were administered using unilateral EP and stimulus at eight times the initial seizure threshold (ST).[19] However, BP-ECTs at five times ST and UBP-ECTs using unilateral EP at eight times ST were comparable.[31] One study[32] researched the effects of both EP and pulse width in patients with medication-resistant depression. Those in the UBP bilateral EP group had a significantly higher number of ECTs [Mean (SD) = 8.9 (2.5)] as well as a larger proportion of non-responders to ECT when compared to the three groups, UBP-RUL [8.7 (2.4)], BP bilateral [6.2 (2.4)], and BP-RUL [8.5 (2.5)].

Three studies[33-35] examined the effects of electrical stimulus intensity. Chanpattana *et al*.,[33] Mc Call *et al*.,[34] and Mohan *et al*.[35] included patients with schizophrenia, depression, and mania, respectively. Chanpattana *et al*. study showed that patients of treatment-resistant schizophrenia receiving high stimulus dosage bilateral-ECT [2ST = 12.5 (3.8); 4ST = 9.2 (1.5)] needed significantly less number of ECTs than those receiving low stimulus dose bilateral ECT [ST = 18.6 (5)]. The rest two did not find a significant difference in the number of ECTs.

Three studies[20,21,36] compared the clinical efficacy of various dose strengths of electrical stimulus using RUL EP with that of standard BL in patients with depression. None of them found a significant difference among compared groups with respect to the number of ECT treatments.

Two studies[37,38] explored the effects of concurrent use of anticonvulsants. Both were conducted in patients with bipolar affective disorder. Neither found any significant influence of continuing anticonvulsants in terms of the number of ECT sessions.

Two studies[39,40] explored the putative predictors of early response to ECT in depression. Expectedly, those

with early-course remission needed significantly less number of ECTs than late or non-responders. Older age,[39,40] use of BP stimulus waveforms,[31] and the presence of psychotic symptoms[40] were associated with early course remission.

Sienaert *et al*.[41] studied the speed of response to ECT in pharmacotherapy resistant depressive patients, comparing the polarity of their mood disorder. Patients with bipolar depression needed significantly less number of ECTs than those with unipolar depression by about three ECT sessions.

In two-thirds of the studies, the mean number of ECTs was between 6 and 10. In 4 (14.3%) studies, it was less than six and in 7 (25%) studies, it was more than 10. Patients (treatment-resistant schizophrenia) in the study by Chanpattana *et al*.[33] had received a substantially higher number of ECTs than the patients in other studies, but this number includes sessions of both acute course as well as the "stabilization" phase. Those with early and late remission in the study by Spaans *et al*.[40] received less than six and more than 10 ECT sessions, respectively, on an average. In Rhebergen *et al*.[39] study, patients with non-remission received up to 20 ECTs.

Of the 30 studies, 27 were clinical trials, and three studies were posthoc analyses of clinical trials. The quality of most studies was good. Eighteen (66.7%) studies had Jadad score[12] of 5. Two (7.4%), 4 (14.8%), 2 (7.4%), and 1 (3.7%) had Jadad score of 4, 3, 2, and 1, respectively.

We did not find any original research study examining the effect of the frequency of ECT sessions, published during the review period. Gangadhar and Thirthalli published a narrative review of studies of the frequency of ECT sessions in 2010.[42] They observed that for acute management of depression with bilateral ECT, the antidepressant effect was comparable between twice-weekly and thrice-weekly schedules. While a tendency of those receiving thrice-weekly ECT experiencing faster improvement was noted, it was associated with more cognitive deficits as well. Overall, the twice-weekly schedule had the best balance between efficacy and cognitive outcomes. Samples of most studies did not reflect patients who would receive ECT in clinical practice—for instance, in several studies, patients were either off antidepressant medications for a few weeks or were treatment-naïve at the time of the trials. Regarding acute management of schizophrenia and mania as well as continuation/maintenance ECT for any indication, the authors noted a serious dearth of quality studies to guide practice.

DISCUSSION

In this systematic review, we did not find any original research study examining the issue of frequency of ECT sessions. We found 30 studies that examined the number of ECT sessions. However, in none of them, the primary aim was to examine the number of ECTs—it was one of the secondary objectives in all these studies.

Studies researched a wide array of questions: the influence of anesthetic agents, EP, stimulus parameters such as pulse width and stimulus intensity, concurrent use of anticonvulsants, and clinical characteristics. A few studies reported significant results: Patients with schizophrenia receiving ECT with bifrontal EP had about one ECT session less than those who received ECT with bitemporal EP.[28] Patients with depression receiving brief-pulse ECT needed about two sessions less than those receiving ultra-brief ECT when both were administered with unilateral EP using stimulus at eight times the seizure-threshold.[19] When patients were treated for depression with bilateral ECT, those receiving brief pulse ECT needed about two sessions less than those treated with ultra-brief pulse ECT.[32] Treatment-resistant schizophrenia patients receiving bilateral ECT at four times their seizure-threshold needed seven and nine ECT sessions less than those receiving two times and barely above their threshold levels, respectively.[33] In depression, rapidly remitting patients received 10 and 13 ECTs less than slowly remitting and non-remitting patients, respectively.[39,40] Patients with bipolar depression received three ECT sessions less than those with unipolar depression.[41] In all these studies, as expected, the results for the number of ECTs reflected the findings on the efficacy of ECT measured using alternative methods. Most studies did not find a significant difference between the compared groups in terms of the number of ECT sessions. Interestingly, in three studies,[10,27,34] though there was a significant difference between comparison arms in terms of clinical outcomes, it did not reflect in the number of ECT sessions.

In all but one of the studies, the policy of when the ECT course is terminated was either not mentioned or was left to the clinicians. Clinicians may decide to terminate ECT sessions based on several factors: achievement of therapeutic target (i.e., some threshold of improvement), plateauing of response after an initial improvement, development of significant adverse effects (particularly cognitive ones), or as per the patients' choice. Unfortunately, the proportion of patients in whom the ECT course was terminated for different reasons is not mentioned in these papers. Hence, the interpretation of both the positive and the negative findings becomes hard. In most studies, the

mean number of ECT sessions was between 6 and 10; in the absence of data on reasons for stopping ECT between responders and non-responders, it is difficult to interpret this finding as well.

It is apparent that when rapid improvement is clinically warranted, thrice-weekly ECT may be preferred. Given that both twice-weekly and thrice-weekly ECTs are equally efficacious, what are the cost implications when clinical situations do not warrant rapid improvement? Costs depend on the number of ECT sessions and duration of inpatient stay. In the UK, for instance, six treatment sessions of ECT cost about £ 2475;[43] inpatient costs are estimated as about £ 171 per day. Unfortunately, the current literature does not provide useful insights into this important aspect. Of the four studies that compared twice- vs. thrice-weekly ECTs in depression, three used bilateral ECT, which is recommended to be used only when there is clinical urgency. The only study that used unilateral ECT[44] did not specify the dose of the electrical stimulus, and hence, it is uncertain if it reflects contemporary ECT practice. Among the ones which studied bilateral ECT, one study[45] had fixed the number of ECTs, and hence it is not possible to assess the cost advantage; two other studies[5,46] found that patients receiving thrice-weekly ECT received more sessions than those receiving twice-weekly ECT. However, the criteria used for termination of ECT in these studies do not reflect clinical practice, and hence, the translational value of this observation is doubtful.

ECT is frequently used in situations where rapid improvement is required, e.g. acutely suicidal/catatonic/aggressive patients. In fact, APA taskforce observes, "primary use of ECT should be considered when a rapid or a higher probability of response is needed, such as when patients are severely medically ill or at risk to harm themselves or others." ECT is also frequently used when medical conditions (including pregnancy) either preclude the use of a full dose of antidepressants or warrant urgent relief of symptoms. There are two important reasons as to why literature from clinical trials may not be useful while making clinical decisions: (a) Most ECT literature comes from research conducted on patients who do not belong to the above categories. (b) When clinicians use ECT for such indications, then the number of ECTs and the decision to terminate a course may depend on a number of factors including achieving a specific clinical target (for example, reduction of suicidal risk, resolution of catatonic symptoms, patient starting to eat, etc.) and not necessarily because the patient had achieved response, remission, or plateauing of response.

Barring a few studies,[24,34,37,40] the SD for the number of sessions is more than 2. It is reasonable to assume that the difference in the mean number of ECT sessions between the compared groups should be at least one for the finding to be clinically meaningful. For studies to show a clinically meaningful difference of one session between the compared groups with a conservative estimate of SD of 2 (i.e., a standardized mean difference of 0.5), the sample size in each of the compared groups should be about 60 in each group with 80% power and with type-1 error rate of 0.05.[47] It may be noted that most studies included much smaller samples and hence were underpowered with regard to the number of ECT sessions.

As described in the introduction section, professional bodies[1,2] and authors of textbooks on ECT[3] have made certain recommendations regarding the frequency of ECT sessions in the early 2000s. This review of the past two decades of research adds little to these recommendations. Regarding the recommendations about the number of ECTs, this review suggests that those receiving ultra-brief pulse ECT for depression and those receiving threshold-level stimulus with bilateral ECT for schizophrenia would require a greater number of ECT sessions, albeit with the caveats discussed above.

CONCLUSIONS

Frequency and number of sessions are important clinical aspects of ECT practice. In this paper, we attempted an appraisal of research pertaining to these aspects. There is a serious dearth of contemporary literature specifically examining these questions. The information available from studies with different aims provides important insights, which need to be pursued in future research. Until then, the broad recommendations suggested by professional bodies[1,2,48] should continue to guide ECT practitioners.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. American Psychiatric Association, Weiner RD, editors. The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training, and Privileging: A Task Force Report of the American Psychiatric Association. 2nd ed. Washington, D.C: American Psychiatric Association; 2001. p. 355.
2. Royal College of Psychiatrists (GB), Scott AIF. The ECT handbook. London: Gaskell; 2005.
3. Abrams R. Electroconvulsive Therapy. 4th ed. Oxford ; New York: Oxford University Press; 2002. p. 328.

4. Sackeim HA. ECT: Twice or Thrice a Week? Convuls Ther 1989;5:362-4.
5. Lerer B, Shapira B, Calev A, Tubi N, Drexler H, Kindler S, *et al*. Antidepressant and cognitive effects of twice- versus three-times-weekly ECT. Am J Psychiatry 1995;152:564-70.
6. Pippard J, Ellam L. Electroconvulsion treatment in Great Britain 1980. Lancet 1981;21160-1.
7. Strömgren LS. Therapeutic results in brief-interval unilateral ECT. Acta Psychiatr Scand 1975;52:246-55.
8. Segman RH, Gorfine M, Lerer B, Shapira B. Onset and time course of antidepressant action: Psychopharmacological implications of a controlled trial of electroconvulsive therapy. Psychopharmacology 1995;119:440-8.
9. Sienaert PA, Vansteelandt K, Demyttenaere K, Peuskens J. Predictors of patient satisfaction after ultrabrief bifrontal and unilateral electroconvulsive therapies for major depression. J ECT 2010;26:55-9.
10. Sienaert P, Vansteelandt K, Demyttenaere K, Peuskens J. Randomized comparison of ultra-brief bifrontal and unilateral electroconvulsive therapy for major depression: Clinical efficacy. J Affect Disord 2009;116:106-12.
11. Shapira B, Tubi N, Lerer B. Balancing speed of response to ECT in major depression and adverse cognitive effects: Role of treatment schedule. J ECT 2000;16:97-109.
12. Halpern SH, Douglas MJ, editors. Appendix: Jadad scale for reporting randomized controlled trials. In: Evidence-based Obstetric Anesthesia [Internet]. Oxford, UK: Blackwell Publishing Ltd; 2005. p. 237-8. Available from: http://doi.wiley.com/10.1002/9780470988343.app1. [Last cited on 2019 May 07].
13. Stoppe A, Louz?? M, Rosa M, Gil G, Rigonatti S. Fixed high-dose electroconvulsive therapy in the elderly with depression: A double-blind, randomized comparison of efficacy and tolerability between unilateral and bilateral electrode placement. J ECT 2006;22:92-9.
14. Bauer J, Hageman I, Dam H, Báez A, Bolwig T, Roed J, *et al*. Comparison of propofol and thiopental as anesthetic agents for electroconvulsive therapy: A randomized, blinded comparison of seizure duration, stimulus charge, clinical effect, and cognitive side effects. J ECT 2009;25:85-90.
15. Fernie G, Currie J, Perrin JS, Stewart CA, Anderson V, Bennett DM, *et al*. Ketamine as the anaesthetic for electroconvulsive therapy: The KANECT randomised controlled trial. Br J Psychiatry 2017;210:422-8.
16. Carspecken CW, Borisovskaya A, Lan S-T, Heller K, Buchholz J, Ruskin D, *et al*. Ketamine anesthesia does not improve depression scores in electroconvulsive therapy: A randomized clinical trial. J Neurosurg Anesthesiol 2018;34:305-13.
17. Kellner CH, Knapp R, Husain MM, Rasmussen K, Sampson S, Cullum M, *et al*. Bifrontal, bitemporal and right unilateral electrode placement in ECT: Randomised trial. Br J Psychiatry 2010;196:226-34.
18. Semkovska M, Landau S, Dunne R, Kolshus E, Kavanagh A, Jelovac A, *et al*. Bitemporal versus high-dose unilateral twice-weekly electroconvulsive therapy for depression (EFFECT-Dep): A pragmatic, randomized, non-inferiority trial. Am J Psychiatry 2016;173:408-17.
19. Spaans H-P, Verwijk E, Comijs HC, Kok RM, Sienaert P, Bouckaert F, *et al*. Efficacy and cognitive side effects after brief pulse and ultrabrief pulse right unilateral electroconvulsive therapy for major depression: A randomized, double-blind, controlled study. J Clin Psychiatry 2013;74:e1029-36.
20. Sackeim HA, Prudic J, Devanand DP, Nobler MS, Lisanby SH, Peyser S, *et al*. A prospective, randomized, double-blind comparison of bilateral and right unilateral electroconvulsive therapy at different stimulus intensities. Arch Gen Psychiatry 2000;57:425-34.
21. Heikman P, Tuunainen A. Right unilateral and bifrontal electroconvulsive therapy in the treatment of depression: A preliminary study. J ECT 2002;18:26-30.
22. Ingram A, Schweitzer I, Ng CH, Saling MM, Savage G. A comparison of propofol and thiopentone use in electroconvulsive therapy: Cognitive and efficacy effects. J ECT 2007;23:158-62.
23. Tripathi A, Winek NC, Goel K, D'Agati D, Gallegos J, Jayaram G, *et al*. Electroconvulsive therapy pre-treatment with low dose propofol: Comparison with unmodified treatment. J Psychiatr Res 2014;53:173-9.
24. Canbek O, Ipekcoglu D, Menges OO, Atagun MI, Karamustafaloglu N, Cetinkaya OZ, *et al*. Comparison of propofol, etomidate, and thiopental in anesthesia for electroconvulsive therapy: A randomized, double-blind clinical trial. J ECT 2015;31:91-7.
25. Loo CK, Katalinic N, Garfield JBB, Sainsbury K, Hadzi-Pavlovic D, Mac-Pherson R. Neuropsychological and mood effects of ketamine in electroconvulsive therapy: A randomised controlled trial. J Affect Disord 2012;142:233-40.
26. Bailine SH, Rifkin A, Kayne E, Selzer JA, Vital-Herne J, Blieka M, *et al*. Comparison of bifrontal and bitemporal ECT for major depression. Am J Psychiatry 2000;157:121-3.
27. Hiremani RM, Thirthalli J, Tharayil BS, Gangadhar BN. Double-blind randomized controlled study comparing short-term efficacy of bifrontal and bitemporal electroconvulsive therapy in acute mania. Bipolar Disord 2008;10:701-7.
28. Phutane VH, Thirthalli J, Muralidharan K, Naveen Kumar C, Keshav Kumar J, Gangadhar BN. Double-blind randomized controlled study showing symptomatic and cognitive superiority of bifrontal over bitemporal electrode placement during electroconvulsive therapy for schizophrenia. Brain Stimul 2013;6:210-7.
29. Bjølseth TM, Engedal K, Benth JŠ, Dybedal GS, Gaarden TL, Tanum L. Clinical efficacy of formula-based bifrontal versus right unilateral electroconvulsive therapy (ECT) in the treatment of major depression among elderly patients: A pragmatic, randomized, assessor-blinded, controlled trial. J Affect Disord 2015;175:8-17.
30. Dybedal GS, Bjølseth TM, Benth JŠ, Tanum L. Cognitive effects of bifrontal versus right unilateral electroconvulsive therapy in the treatment of major depression in elderly patients: A randomized, controlled trial. J ECT 2016;32:151-8.
31. Loo CK, Katalinic N, Smith DJ, Ingram A, Dowling N, Martin D, *et al*. A randomized controlled trial of brief and ultrabrief pulse right unilateral electroconvulsive therapy. Int J Neuropsychopharmacol [Internet] 2015;18. Available from: https://academic.oup.com/ijnp/article-lookup/doi/10.1093/ijnp/pyu045.
32. Sackeim HA, Prudic J, Nobler MS, Fitzsimons L, Lisanby SH, Payne N, *et al*. Effects of pulse width and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. Brain Stimul 2008;1:71-83.
33. Chanpattana W, Chakrabhand MLS, Buppanharun W, Sackeim HA. Effects of stimulus intensity on the efficacy of bilateral ECT in schizophrenia: A preliminary study. Biol Psychiatry 2000;48:222-8.
34. McCall WV, Reboussin DM, Weiner RD, Sackeim HA. Titrated moderately suprathreshold vs fixed high-dose right unilateral electroconvulsive therapy: Acute antidepressant and cognitive effects. Arch Gen Psychiatry 2000;57:438-44.
35. Mohan TS, Tharyan P, Alexander J, Raveendran NS. Effects of

stimulus intensity on the efficacy and safety of twice-weekly, bilateral electroconvulsive therapy (ECT) combined with antipsychotics in acute mania: A randomised controlled trial. Bipolar Disord 2009;11:126-34.
36. Tew JD, Mulsant BH, Haskett RF, Dolata D, Hixson L, Mann JJ. A randomized comparison of high-charge right unilateral electroconvulsive therapy and bilateral electroconvulsive therapy in older depressed patients who failed to respond to 5 to 8 moderate-charge right unilateral treatments. J Clin Psychiatry 2002;63:1102-5.
37. Jahangard L, Haghighi M, Bigdelou G, Bajoghli H, Brand S. Comparing efficacy of ECT with and without concurrent sodium valproate therapy in manic patients. J ECT 2012;28:118-23.
38. Rakesh G, Thirthalli J, Kumar CN, Muralidharan K, Phutane VH, Gangadhar BN. Concomitant anticonvulsants with bitemporal electroconvulsive therapy: A randomized controlled trial with clinical and neurobiological application. J ECT 2017;33:16-21.
39. Rhebergen D, Huisman A, Bouckaert F, Kho K, Kok R, Sienaert P, *et al*. Older age is associated with rapid remission of depression after electroconvulsive therapy: A latent class growth analysis. Am J Geriatr Psychiatry 2015;23:274-82.
40. Spaans H-P, Verwijk E, Stek ML, Kho KH, Bouckaert F, Kok RM, *et al*. Early complete remitters after electroconvulsive therapy: Profile and prognosis. J ECT 2016;32:82-7.
41. Sienaert P, Vansteelandt K, Demyttenaere K, Peuskens J. Ultra-brief pulse ECT in bipolar and unipolar depressive disorder: Differences in speed of response. Bipolar Disord 2009;11:418-24.
42. Gangadhar BN, Thirthalli J. Frequency of electroconvulsive therapy sessions in a course. J ECT 2010;26:181-5.
43. 4 Evidence and interpretation | Guidance on the use of electroconvulsive therapy | Guidance | NICE [Internet]. Available from: https://www.nice.org.uk/guidance/ta59/chapter/4-Evidence-and-interpretation#cost-effectiveness. [Last cited on 2019 May 26].
44. McAllister DA, Perri MG, Jordan RC, Rauscher FP, Sattin A. Effects of ECT given two vs. three times weekly. Psychiatry Res 1987;21:63-9.
45. Shapira B, Tubi N, Drexler H, Lidsky D, Calev A, Lerer B. Cost and benefit in the choice of ECT schedule: Twice versus three times weekly ECT. Br J Psychiatry 1998;172:44-8.
46. Gangadhar BN, Janakiramaiah N, Subbakrishna DK, Praveen J, Reddy AK. Twice versus thrice weekly ECT in melancholia: A double-blind prospective comparison. J Affect Disord 1993;27:273-8.
47. Norman G, Monteiro S, Salama S. Sample size calculations: Should the emperor's clothes be off the peg or made to measure? BMJ 2012;345:e5278.
48. 2 Clinical need and practice | Guidance on the use of electroconvulsive therapy | Guidance | NICE [Internet]. Available from: https://www.nice.org.uk/guidance/ta59/chapter/2-Clinical-need-and-practice. [Last cited on 2019 May 26].