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Authors' Affiliation:
[1]Regional Specialist Hospital in Wrocław, Research and Development Center, Kamieńskiego 73a, 51-124 Wrocław, Poland

***Corresponding author:**
Kacper Kulik,
Regional Specialist Hospital in Wrocław, Research and Development Center, ul. H. M. Kamieńskiego 73a, 51-124 Wrocław; E-mail: k.kulik2000@gmail.com

ORCID List:
Kacper Kulik - 0009-0004-1492-0438
Martyna Saleh - 0009-0008-0089-5605
Jakub Tomczyszyn - 0009-0007-1097-0851
Patrycja Pogorzelska - 0009-0007-3619-8177
Paulina Żuk - 0009-0005-5288-9029

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Management of status epilepticus: Treatment strategies and barriers to implementation

Kacper Kulik[1]*, Martyna Saleh[1], Jakub Tomczyszyn[1], Patrycja Pogorzelska[1], Paulina Żuk[1]

ABSTRACT

Background: Status epilepticus is considered a life-threatening condition that requires immediate treatment. Although internationally structured pharmacological treatment algorithms exist, their implementation can be hampered by factors such as insufficient benzodiazepine supply and insufficient availability of continuous electroencephalography monitoring. *Objective*: This narrative review summarizes the current knowledge regarding the management of status epilepticus in adults, with a particular focus on the barriers to implementing the presented treatment guidelines. *Methods*: A literature search was conducted using PubMed and Google Scholar for English-language articles published between January 2000 and January 2026. This work was based on systematic and narrative reviews, clinical trials, and consensus guidelines for the management of status epilepticus in adults. *Results*: Benzodiazepines are the first-line treatment for status epilepticus. However, if the condition is prolonged, the next step is to use antiseizure medication (ASM) such as levetiracetam, valproic acid, or fosphenytoin. Refractory status epilepticus requires emergency procedures, including intensive care unit treatment and continuous monitoring of vital parameters. Continuous electroencephalography (cEEG) plays an important role in monitoring seizure activity. Significant barriers include delayed administration of benzodiazepines and insufficient dosing, which manifests as underdosing and limited use of continuous electroencephalography. *Conclusions*: Improving the management of status epilepticus requires both evidence-based pharmacological treatment and reliable systems for its adequate implementation. Further prospective studies could help determine whether specific organizational interventions improve functional outcomes and mortality.

Keywords: status epilepticus; antiseizure medications; benzodiazepines; clinical guidelines; continuous electroencephalography

1. INTRODUCTION

Status epilepticus (SE) occurs when seizure activity persists as a result of failure of the mechanisms responsible for seizure termination or activation of mechanisms leading to its abnormally prolonged duration (Trinka et al., 2015). The balance between excitatory and inhibitory neuronal processes is disrupted, allowing seizure activity to sustain itself (Betjemann and Lowenstein, 2015; Alshehri et al., 2025). This is one of the most serious emergencies in neurology.

Status epilepticus occurs in several clinical forms. Convulsive status epilepticus is characterized by prolonged or recurrent bilateral tonic-clonic seizures without a return to the state of consciousness from before the seizure. Non-convulsive status epilepticus (NCSE) consists of prolonged or fluctuating disturbances of mental status without clear convulsive activity. It usually requires confirmation on electroencephalography (EEG). Focal status epilepticus may manifest as recurrent or prolonged sensory, cognitive, motor, autonomic symptoms, or speech disturbances, and this may or may not be accompanied by disturbances of consciousness (Trinka et al., 2015).

To make the definitions more precise, contemporary guidelines introduced the operational time points T1 and T2, replacing the previous clinical definitions. In bilateral tonic-clonic status epilepticus, T1 was set at 5 minutes, indicating the time point after which the seizure will probably not stop spontaneously, and treatment should be started immediately. T2 was set at approximately 30 minutes and means the time after which ongoing seizure activity carries an increased risk of long-term consequences, such as neuronal injury, neuronal death, and remodeling of neuronal networks. The T1 and T2 values differ depending on the type of status epilepticus and have been best defined for bilateral tonic-clonic status epilepticus (Trinka et al., 2015).

Although clearly defined operational time points have been introduced in contemporary definitions, implementation of these recommendations into everyday clinical practice still constitutes a serious challenge. Available clinical data indicate that the recommended treatment is not consistently followed in hospital departments due to the use of too low drug doses, too late initiation of first-line treatment, or too late initiation of second-line treatment when initial treatment is ineffective (Sathe et al., 2021; Jindal et al., 2023).

These findings suggest incomplete implementation of guideline-based care. Despite the existence of international guidelines, such as the recommendations of the American Epilepsy Society (AES), which present detailed management algorithms, considerable differences still exist between individual guidelines concerning the subsequent stages of treatment, i.e., the choice of second-line antiseizure medications or management of non-convulsive status epilepticus (Vignatelli et al., 2024).

The aim of this review is therefore to analyze the gap between guideline-based recommendations and their actual implementation in clinical practice. The work summarizes the recommended treatment strategies. It identifies the most important irregularities that hinder their application in practice. In addition, strategies that may facilitate making decisions concerning treatment and improve adherence to management protocols in the therapy of status epilepticus in adults were discussed.

2. REVIEW METHODS

In this narrative review, the literature was searched using PubMed and Google Scholar, including English-language articles published between January 2000 and January 2026. To find the relevant papers, the following phrases were used in different combinations using the Boolean operators “AND” and “OR”: “status epilepticus”, “antiseizure medications”, “benzodiazepines”, “clinical practice guidelines”, “evidence-based management”, “emergency treatment”, “refractory status epilepticus”, and “non-convulsive status epilepticus”. A total of 139 records were found. Database searching showed 102 records. 37 were identified manually. Only 43 full-text articles were assessed, of which only 26 were selected for analysis, as shown in the PRISMA flow diagram (Figure 1).

English-language articles containing systematic and narrative reviews, clinical studies, and agreed guidelines for the management of status epilepticus in adults were qualified for this review. Papers were qualified if they contained management algorithms, pharmacological treatment guidelines, implementation barriers, and were based on evidence-based medicine. Items that focused excessively on the pediatric population, reported single cases, or were not in English were excluded. We also analyzed the reference lists of the relevant guidelines to identify additional publications important for the aims of this review.

3. RESULTS AND DISCUSSION

Step-by-step management in acute status epilepticus

Management of status epilepticus in adults requires decisive, coordinated, and time-appropriate therapeutic intervention (Glauser et al., 2016; Jindal et al., 2023). A delay in initiating treatment significantly decreases the chance of termination of seizure activity. Prolonged convulsive activity is associated with increased internalization of γ-aminobutyric acid type A (GABAA) receptors and increased surface expression of excitatory α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors at synapses. These mechanisms cause increased resistance to the medications used (Naylor et al., 2005; Alshehri et al., 2025).

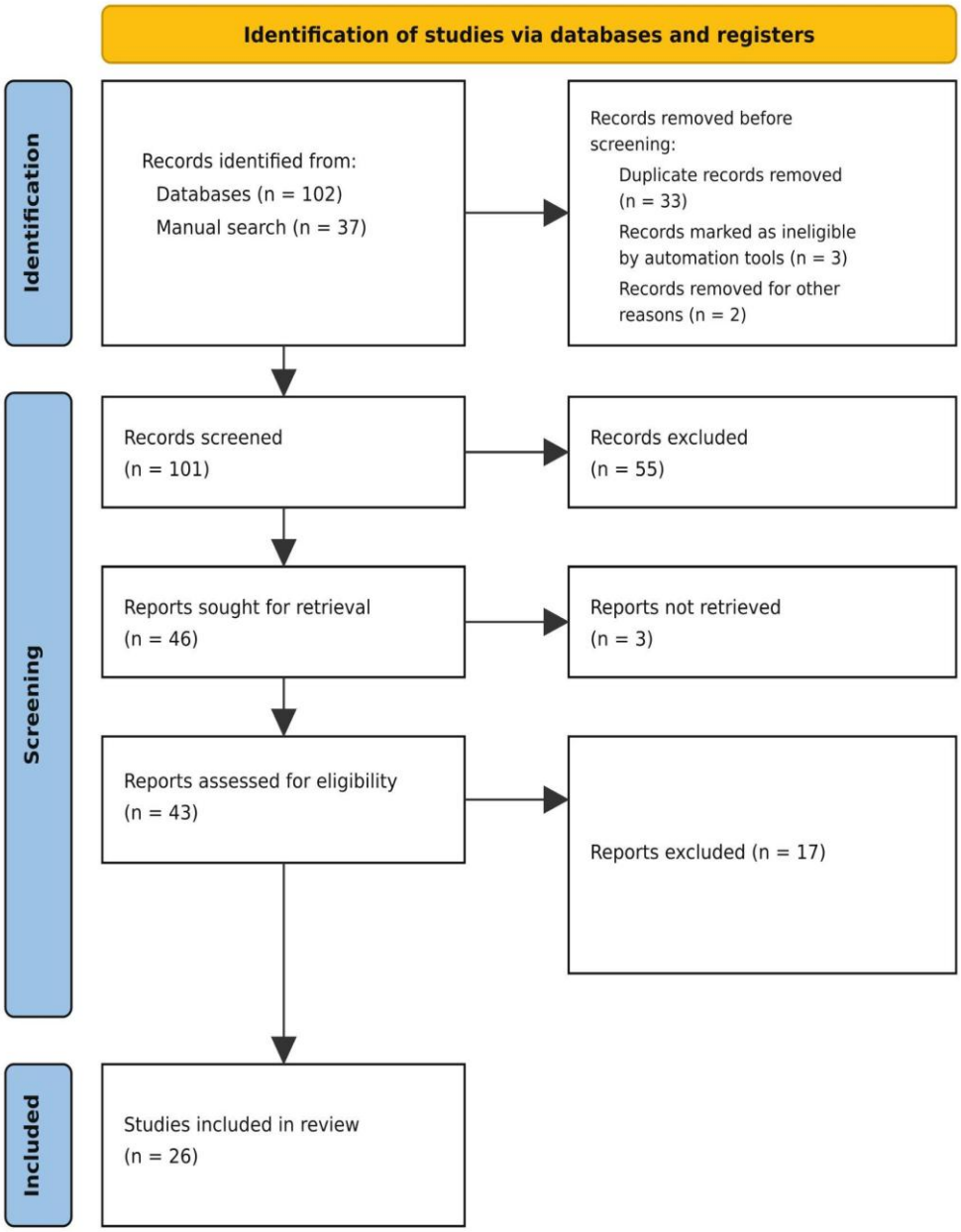

Figure 1. PRISMA flow diagram of the literature identification and selection process.

Phase 1: Early status epilepticus (0–20 Minutes)

This early phase lasts up to 20 minutes from the onset of status epilepticus and consists of an attempt to immediately stabilize the patient's condition and coordinate first-line therapy (Glauser et al., 2016). It's important to achieve stabilization, including airway patency, breathing, and circulation by the 5th minute. Establishing intravenous access is urgent, but attempts can't delay the implementation of antiseizure treatment. Clinicians should promptly measure blood glucose and select further blood tests and investigations according to the suspected metabolic, toxic, or infectious cause. Initial pharmacological treatment should be started if the seizure persists for 5 minutes. This phase lasts until approximately 20 minutes, after which the effectiveness of the medications used should be assessed, because after this time their effect should be visible, which determines the need for further interventions (Brophy et al., 2012; Glauser et al., 2016). The first-line medications recommended in the treatment of status epilepticus in adults are benzodiazepines, which have high effectiveness in terminating seizure activity (Glauser et al., 2016). These are substances that are positive allosteric modulators of the GABAA receptor complex, increasing inhibitory neurotransmission and thereby facilitating the interruption of epileptic seizures (Rogawski and Löscher, 2004).

The initial choice of a specific benzodiazepine depends on the availability of intravenous access. If such access exists, intravenous lorazepam at a dose of 0.1 mg/kg body weight (maximum 4 mg) or intravenous diazepam at a dose of 0.15-0.2 mg/kg body weight (maximum 10 mg) is preferred (Glauser et al., 2016). Lorazepam is chosen more often because of its lower lipid solubility compared with diazepam, which results in a longer duration of antiseizure action in the central nervous system due to slower redistribution to peripheral tissues (Prasad et al., 2014). When intravenous access is unavailable, the preferred route is intramuscular administration of midazolam at a dose of 10 mg, and administration should not be delayed to obtain intravenous access (Glauser et al., 2016; Silbergleit et al., 2012). Favorable absorption through the intramuscular route is particularly useful in prehospital management, when the availability of the intravenous route may be considerably limited (Silbergleit et al., 2012).

A Trap in Practice: Underdosing

A significant problem in clinical practice is the administration of benzodiazepines at doses lower than recommended in guidelines. Reducing benzodiazepine doses is most likely due to excessive fear of respiratory failure or excessive sedation in the patient (Sathe et al., 2021; Vignatelli et al., 2024). This phenomenon may cause a reduction in the effectiveness of early termination of status epilepticus. In addition, errors in correct dosing may in this way lead to progression of status epilepticus into treatment-refractory status epilepticus (Sathe et al., 2021; Jindal et al., 2023). It should be remembered that status epilepticus itself threatens the occurrence of respiratory failure; therefore, concerns about adverse effects should not lead to systematic reduction of the dosing of first-line medications (Glauser et al., 2016; Sathe et al., 2021).

Next phase: Prolonged status epilepticus (20-40 minutes)

Prolonged status epilepticus is diagnosed when clinical symptoms or persistent changes in the electroencephalographic recording occur after administration of first-line medications. The management of choice in such a clinical context is to initiate second-line pharmacological therapy with antiseizure treatment. Importantly, one should not wait until the end of this phase to administer the medications. Administration should be started immediately within this first 20-minute frame. Among second-line medications, intravenous levetiracetam at a dose of 60 mg/kg body weight (maximum 4500 mg), intravenous valproic acid at a dose of 40 mg/kg body weight (maximum 3000 mg), and intravenous fosphenytoin at a dose of 20 mg phenytoin equivalents/kg body weight (maximum 1500 mg phenytoin equivalents) should be distinguished (Glauser et al., 2016).

The multicenter Established Status Epilepticus Treatment Trial (ESETT) showed that levetiracetam, fosphenytoin, and valproate caused seizure cessation and improvement of consciousness within 60 minutes in approximately half of the treated patients, without proving a clear advantage of any of the compared medications (Kapur et al., 2019). Valproic acid has broad use in combating seizure activity of different etiologies, but attention should be paid to contraindications to its use, such as liver disease or pregnancy. The few drug interactions of levetiracetam mean that it is often included in therapy (Trinka et al., 2014; Patsalos, 2000). Fosphenytoin requires particular caution in its use in patients with conduction abnormalities of the cardiac conduction system or hemodynamic instability (Brophy et al., 2012; Glauser et al., 2016).

Clinical observations

Irregularities in the timing of administration and an insufficient dose of benzodiazepines decrease the effectiveness of second-line therapy (Sathe et al., 2021; Jindal et al., 2023). In addition, prolonged status epilepticus and spontaneous excitability are due to GABAA receptor internalization and excessive NMDA receptor activity, which explains the reduced response to treatment that stimulates GABAergic receptors (Naylor et al., 2005; Alshehri et al., 2025).

Final stage: Refractory status epilepticus

Refractory status epilepticus is a condition in which seizure activity continues despite giving recommended medications. Refractory status epilepticus is associated with an unfavorable prognosis because of high mortality. Therefore, it is treated as an acute life-threatening condition requiring the use of extraordinary forms of therapy (Hocker et al., 2013). In these patients, endotracheal intubation with mechanical ventilation and anesthesia administered by continuous intravenous infusion are indicated. Clinical response and electroencephalography determine the dose of anesthetic medications. Thiopental, midazolam, propofol, and pentobarbital are used for these indications. The choice of medication depends on the patient's hemodynamic status, comorbid condition, and the experience of the medical team (Ferlisi and Shorvon, 2012). A useful tool for adequate anesthetic titration is the use

of continuous electroencephalographic monitoring. The therapeutic aim should be the cessation of status epilepticus; however, the optimal depth of suppression of seizures recorded in the electroencephalographic trace has not been unequivocally established (Brophy et al., 2012).

It should be noted that Super-Refractory status epilepticus is defined as status epilepticus that persists despite treatment according to the management algorithm described so far above for 24 hours after the initiation of extraordinary forms of therapy in the intensive care unit (Shorvon and Ferlisi, 2011). Super-Refractory status epilepticus is a cause of prolonged stay in the intensive care unit, systemic complications, and an unfavorable neurological prognosis (Ferlisi and Shorvon, 2012; Shorvon and Ferlisi, 2011). Each time, management in the case of super-refractory status epilepticus requires verification of its etiology and consideration of additional therapeutic strategies such as a ketogenic diet, immunotherapy, inhaled anesthetics, therapeutic hypothermia, stereotactic epilepsy surgery, neuromodulation, or electroconvulsive therapy (Shorvon and Ferlisi, 2011). The evidence confirming the effectiveness of these approaches comes mainly from observational studies, case series and expert opinions, so no generally accepted treatment sequence in this area has been established to date (Ferlisi and Shorvon, 2012; Shorvon and Ferlisi, 2011).

Discrepancies between guidelines and clinical practice

International guidelines provide structured treatment algorithms, but their implementation in clinical practice remains inconsistent. Retrospective analyses and clinical studies indicate numerous practical and organizational barriers that result in an inappropriate dose of antiseizure medications, delay in the introduction of treatment, and difficulty in timely escalation of therapy (Sathe et al., 2021; Brigo et al., 2022; Lamberta et al., 2025; Villamar et al., 2018; Sairanen et al., 2019).

Lack of practical management instructions and detailed organizational solutions

The applicable international guidelines prepared by experts determine the choice of treatment and the time frame for its implementation. The organizational aspects necessary for rapid application of treatment in a patient are most often established at the level of individual medical facilities (Vignatelli et al., 2024; Lamberta et al., 2025). Despite clearly defined guidelines – the type of medications and when treatment should be escalated – the practical aspects of their implementation, such as ready-made dosing schemes, the method of medication preparation, medication infusion and the division of duties in the medical team, may differ significantly between facilities (Lamberta et al., 2025). Such variability may lead to differences in the sequence of therapeutic actions undertaken, the method of preparing medications and the timeliness of treatment escalation, particularly in situations requiring immediate intervention.

Challenges related to status epilepticus developing in a patient during a hospital stay

Most algorithms focus mainly on the acute treatment of convulsive status epilepticus, presenting the recommended rapid diagnostics and sequential escalation of treatment in emergency medicine settings (Glauser et al., 2016; Brophy et al., 2012). Much less attention has been devoted to status epilepticus that develops in patients already staying in hospital.

In the case of status epilepticus developing during hospitalization, the speed of diagnosis and implementation of treatment may differ depending on the place where the seizure occurs, the availability of previously developed management schemes, staff experience, and cooperation between departments. Individual medical centers translate guideline recommendations into clinical practice in different ways. This is evidenced by the differences in the treatment protocols used in epilepsy treatment centers. Moreover, it was shown that implementation of a status epilepticus alert pathway is associated with a shorter time to administration of a second-line antiseizure medication (Villamar et al., 2018). Treatment delays may begin before hospital arrival, highlighting the need for early seizure recognition and prompt prehospital treatment (Sairanen et al., 2019).

Dilemmas related to non-convulsive status epilepticus

Management of non-convulsive status epilepticus (NCSE) remains one of the greatest diagnostic and organizational challenges in neurocritical care. Diagnosing NCSE based solely on primary symptoms is very difficult, as NCSE presents with unexplained mental states following a seizure. Confirmation of this condition requires electroencephalography (Zafar and Aljaafari, 2023).. In such situations, the physician must consider the potential consequences of unnecessary therapy in patients in whom epilepsy is not the cause of the disturbance of consciousness against the risk of delaying the treatment of persistent seizure activity. In situations where continuous electroencephalographic monitoring (continuous EEG, cEEG) is not possible, periodic EEG examinations are

recommended. It should, however, be remembered that their limited duration reduces the sensitivity of detecting seizures of an intermittent nature or variable electroencephalographic activity (Jette and Hirsch, 2005; Zafar and Aljaafari, 2023).

Transfer of algorithms based on scientific evidence to the practical treatment of status epilepticus

Standardized treatment schemes in emergencies

Effective translation of treatment protocols into everyday clinical practice still constitutes one of the most difficult challenges. The main obstacles hindering the implementation of management schemes in real clinical conditions are presented in Table 1. Clinical studies show that adherence to recommendations concerning first- and second-line treatment may be limited by the use of excessively low medication doses, delayed escalation of therapy, and differences between centers in the organization of treatment pathways (Sathe et al., 2021; Lamberta et al., 2025; Villamar et al., 2018). One of the most significant variable factors is the administration of excessively low doses of benzodiazepines in first-line treatment. This phenomenon may result from concerns regarding the occurrence of respiratory depression, hypotension, or excessive sedation (Sathe et al., 2021). It should not be forgotten that respiratory failure may be a consequence of both the applied treatment and persistent convulsive activity. For this reason, the fear of respiratory depression should not lead to the use of underdosed benzodiazepines. Instead, it should motivate physicians to ensure continuous patient monitoring and be ready to maintain a patent airway and provide respiratory support, in accordance with current recommendations (Glauser et al., 2016; Sathe et al., 2021).

Medical facilities should translate international pharmacological steps. Their use improves treatment implementation and limits the risk of errors in situations requiring immediate intervention. Examples of solutions include easily accessible medication kits intended for the management of status epilepticus, standardized electronic physician orders and body-weight-based dosing tables, which facilitate the preparation of medications and reduce the risk of errors in dose calculation. The above-mentioned solutions may be additionally supported by checklists for nursing staff containing detailed instructions concerning medication preparation, dilution, method of administration and maximum infusion rates of second-line antiseizure medications. Although these solutions appear justified from a clinical point of view, their impact on shortening the time to the introduction of treatment, improving adherence to protocols and patient treatment outcomes requires further studies.

Limitations of continuous EEG monitoring in refractory status epilepticus

Management of patients with treatment-refractory status epilepticus and non-convulsive status epilepticus (NCSE) is often hindered because of diagnostic uncertainty. Continuous electroencephalographic monitoring (continuous EEG, cEEG) enables the detection of persistent or recurrent seizure activity in the EEG recording and monitoring of treatment effectiveness in patients receiving a continuous infusion of anesthetic medications (Brophy et al., 2012; Jette and Hirsch, 2005). However, the availability of cEEG equipment and specialists experienced in interpreting EEG recordings differs between intensive care units (Koffman et al., 2020). When continuous EEG monitoring is not possible, therapeutic decisions are often based on clinical assessment of the patient and periodically performed EEG examinations. This increases uncertainty concerning the persistence of seizure activity visible only in the electroencephalographic recording and the assessment of response to the applied treatment. As a consequence, the physician must consider the risk of excessive sedation associated with increasing treatment intensity against the risk of persistent unrecognized epileptic seizures, which may lead to further damage to the central nervous system.

The use of Salzburg Consensus criteria may facilitate the interpretation of periodic EEG recordings in patients with suspected non-convulsive status epilepticus (NCSE) (Zafar and Aljaafari, 2023). In addition, the development of regional tele-EEG networks constitutes a promising prospect that increases access to specialist interpretation of electroencephalographic recordings in centers with limited local experience (Murphey and Anderson, 2022). Tele-encephalography and periodic EEG recordings will not fully replace cEEG monitoring. When continuous specialist supervision is not possible, they can provide valuable diagnostic support and facilitate therapeutic decision-making.

Interdisciplinary Protocols and Transitions of Care

The treatment of status epilepticus often requires gradual escalation of management between the emergency department, the neurology department, and the intensive care unit – from the initial administration of benzodiazepines, through the use of second-line antiseizure medications, to anesthetic treatment in cases of refractory status epilepticus (Glauser et al., 2016; Brophy et al., 2012). Although

pharmacological treatment schemes are becoming increasingly standardized, their effective introduction depends on administering medications within appropriate time frames, a clearly defined division of duties, and efficient cooperation between medical teams.

A study focusing on improving the quality of care found that implementing an alert procedure for status epilepticus reduced the time to administration of a second-line antiseizure medication (Villamar et al., 2018). For this reason, interdisciplinary management protocols involving emergency medicine physicians, neurologists, intensive care specialists, nursing staff, and hospital pharmacists may improve communication, precisely determine the scope of responsibility of individual team members, and also limit variability in the manner of conducting treatment between different centers and clinical teams (Lamberta et al., 2025; Villamar et al., 2018).

Table 1. Major implementation gaps in adult status epilepticus management and potential strategies for improvement

Implementation gap	Clinical consequence	Evidence	Potential strategy
Delayed or inadequate benzodiazepine administration	Reduced probability of early seizure termination and progression toward refractory SE	Benzodiazepine underdosing observed in clinical practice (Sathe et al., 2021)	Weight-based dosing protocols, predefined emergency medication pathways
Lack of standardized institutional workflows	Variability in treatment sequence and escalation decisions	Variation in SE protocols among epilepsy centers (Lamberta et al., 2025)	Multidisciplinary SE pathways and standardized order sets
Limited availability of continuous EEG	Diagnostic uncertainty in NCSE and difficulties with anesthetic titration	Heterogeneous cEEG availability across ICUs (Koffman et al., 2020)	Tele-EEG networks, expanded EEG access, rapid-response EEG systems
Delayed escalation after benzodiazepine failure	Prolonged seizure activity and delayed transition to second-line therapy	Shorter time to second-line ASM administration after implementation of an SE alert (Villamar et al., 2018)	Status epilepticus alert pathways

4. CONCLUSION

The above article states that effective treatment of status epilepticus depends on, among other things, appropriate drug selection, timely implementation of treatment, and rapid escalation. Despite increasingly standardized therapeutic regimens, discrepancies remain between guideline recommendations and their actual implementation in clinical practice. Implemented guidelines should be supported by practical organizational solutions for treatment pathways, alert systems, tools that facilitate medication dosing based on body weight, better access to EEG monitoring, and interpretation of its recordings. When the above organizational barriers are overcome, it is expected that the time to treatment implementation will be shortened and adherence to the principles of evidence-based management will increase. However, further clinical studies are necessary to assess whether implementation of specific organizational solutions also translates into improved outcomes and reduced mortality among patients with status epilepticus.

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Authors' Contributions

Conceptualization: Kacper Kulik, Martyna Saleh
Methodology: Patrycja Pogorzelska
Software: Jakub Tomczyszyn
Check: Paulina Żuk
Formal analysis: Kacper Kulik, Patrycja Pogorzelska
Resources: Martyna Saleh, Jakub Tomczyszyn
Investigation: Kacper Kulik, Paulina Żuk

Data curation: Patrycja Pogorzelska
Writing-rough preparation: Martyna Saleh, Jakub Tomczyszyn, Paulina Żuk
Writing-review and editing: Kacper Kulik, Jakub Tomczyszyn, Patrycja Pogorzelska
Visualization: Paulina Żuk
Supervision: Kacper Kulik
Project administration: Kacper Kulik
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Data and materials availability
All data associated with this study will be available based on the reasonable request to corresponding author.

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