International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

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ARTICLE TITLE	LIFE-THREATENING COMPLICATIONS OF ALCOHOL WITHDRAWAL SYNDROME IN HOSPITALIZED PATIENTS: CLINICAL PRACTICE AND SYSTEMIC BARRIERS IN POLISH AND CENTRAL-EUROPEAN SETTINGS
DOI	https://doi.org/10.31435/ijitss.4(48).2025.4503
RECEIVED	18 November 2025
ACCEPTED	24 December 2025
PUBLISHED	30 December 2025
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LIFE-THREATENING COMPLICATIONS OF ALCOHOL WITHDRAWAL SYNDROME IN HOSPITALIZED PATIENTS: CLINICAL PRACTICE AND SYSTEMIC BARRIERS IN POLISH AND CENTRAL-EUROPEAN SETTINGS

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ABSTRACT

Alcohol withdrawal syndrome remains a common and potentially life-threatening condition in hospitalized patients with alcohol use disorder, contributing to prolonged ICU stays, mechanical ventilation, and preventable mortality. Severe complications - delirium tremens, seizures, and Wernicke's encephalopathy - are particularly frequent in Central and Eastern Europe due to gaps in risk stratification, limited availability of adjunctive therapies, and systemic barriers. Although benzodiazepines remain first-line treatment in Polish guidelines, benzodiazepine-resistant AWS occurs in approximately 10 % of severe cases and is associated with excessive sedative requirements and respiratory complications. Mounting evidence supports phenobarbital as a safe and effective alternative or early adjunct in severe/refractory AWS owing to its dual GABA-A potentiation and glutamate (NMDA/AMPA) antagonism, predictable pharmacokinetics, and favourable impact on ICU length of stay, intubation rates, and overall costs. Despite these advantages, phenobarbital use in Poland is limited by its narcotic classification, pharmacy restrictions, and lack of standardised protocols. Additional regional challenges include the absence of parenteral thiamine formulations >100 mg and the lack of a national AWS registry. This narrative review synthesises current evidence on epidemiology, risk stratification, phenobarbital-based protocols, high-dose thiamine/magnesium repletion, and systemic barriers in Poland and neighbouring countries. Practical, immediately implementable recommendations are provided for Polish hospitals, including selective PAWSS screening, phenobarbital loading regimens, strategies to overcome narcotic legislation and thiamine limitations, minimal-burden registry models, and expanded use of reimbursed addiction teleconsultations. Adoption of these measures has the potential to substantially reduce severe complications and resource utilisation in resource-constrained Central-European settings.

KEYWORDS

Alcohol Withdrawal Syndrome, Delirium Tremens, Phenobarbital, Benzodiazepine-Resistant Withdrawal, Thiamine, Central Europe

CITATION

Jan Krzysztof Makulski, Martyna Ciarkowska, Wojciech Machulski, Karolina Świerk, Damian Podkościelny, Adam Januszkiewicz, Wiktoria Januszkiewicz, Maria Gierasimiuk, Michał Górski, Kamil Franczyk. (2025). Life-Threatening Complications of Alcohol Withdrawal Syndrome in Hospitalized Patients: Clinical Practice and Systemic Barriers in Polish and Central-European Settings. *International Journal of Innovative Technologies in Social Science*. 4(48). doi: 10.31435/ijitss.4(48).2025.4503

1.Introduction

Alcohol use disorder affects more than 283 million individuals worldwide, with alcohol withdrawal syndrome developing in over 50% of hospitalized patients with AUD and 3–5% progressing to life-threatening complications such as seizures and delirium tremens(Vigouroux et al., 2021). In intensive care settings, AWS prevalence can reach 31%, significantly prolonging length of stay, increasing the need for mechanical ventilation, raising infection risk, and imposing substantial economic burdens(Nishimura et al., 2023). European data underscore particular vulnerability: a large French tertiary ICU cohort reported severe AWS in 4.4% of all admissions, with delirium tremens in 50%, seizures in 20%, pneumonia in 33%, and in-hospital mortality of 16.3% despite treatment, while almost half of patients experienced complicated courses despite relatively modest admission severity scores(Vigouroux et al., 2021). Robust predictors of poor outcome include elevated Sequential Organ Failure Assessment scores, organ dysfunction, hypomagnesaemia(Maguire et al., 2019), hyperlactataemia, and a Prediction of Alcohol Withdrawal Severity Scale score ≥4(Maldonado et al., 2015; Vigouroux et al., 2021).

In Central and Eastern Europe, including Poland, these challenges are amplified by systemic factors—limited health insurance coverage for adjunctive therapies, persistent knowledge gaps, severe resource constraints, and deficiencies in physician training—which collectively drive higher morbidity and mortality(Unlu et al., 2023). Although Polish national guidelines endorse symptom-triggered diazepam loading(Mierzejewski et al., 2022), this benzodiazepine-centric approach frequently requires extremely high cumulative doses that far exceed international recommendations, largely because viable alternatives remain

restricted or unavailable. Benzodiazepine-resistant AWS, delirium risk, and iatrogenic respiratory depression therefore remain common, particularly in the absence of universal ICU protocols(Alwakeel et al., 2023; Parthvi & Parker, 2019). Additional complicating factors include observed sex disparities(Unlu et al., 2023) and the kindling phenomenon(Maldonado et al., 2014), whereby repeated withdrawal episodes progressively worsen limbic hyperexcitability and underscore the urgent need for effective prophylaxis.

Against this backdrop, phenobarbital has re-emerged globally as a powerful and cost-effective therapeutic option(Nishimura et al., 2023). Recent evidence demonstrates its ability to reduce ICU admissions and overall hospital length of stay(Kessel et al., 2024), although some meta-analyses show outcomes comparable to benzodiazepines(Pourmand et al., 2023). In the United States, phenobarbital use—often as single-dose loading regimens—is increasing rapidly in emergency departments(Lebin et al., 2021; Riutta et al., 2024), reducing polypharmacy and short-term readmissions(Lebin et al., 2021). The 2020 American Society of Addiction Medicine guideline explicitly endorses phenobarbital as monotherapy or early adjunct in severe and refractory cases, particularly when close monitoring is available(Brooks & Reinert, 2024; "The ASAM Clinical Practice Guideline on Alcohol Withdrawal Management," 2020).

Europe exhibits a slower but unmistakable shift. German and Austrian guidelines for delirium and confusional states increasingly incorporate phenobarbital(Maschke, 2021), while Danish psychiatric departments have long favoured it for efficient prevention and treatment of delirium tremens(Askgaard et al., 2016). By contrast, Poland markedly lags behind: national guidelines remain rigidly diazepam-centric(Mierzejewski et al., 2022), phenobarbital is restricted to "rescue" roles owing to its narcotic classification, procurement barriers, clinician unfamiliarity, and the near-complete absence of prospective local registries(Mierzejewski et al., 2022). These constraints perpetuate elevated complication rates in resource-limited county hospitals.

This narrative review therefore aims (1) to synthesise contemporary evidence on phenobarbital-based protocols and supportive care in severe and benzodiazepine-resistant AWS, (2) elucidate systemic and regulatory barriers specific to Poland and Central Europe—notably the narcotic status of phenobarbital and the persistent limitation to 100 mg parenteral thiamine ampoules(Nishimoto et al., 2017)—and (3) propose immediately implementable clinical, organisational, and digital-health solutions that can substantially reduce life-threatening complications and resource utilisation in these settings.

2.Methodology

This narrative review was conducted between mid-2025 and late-2025. Literature was searched in PubMed, Scopus, Embase, and Google Scholar using combinations of the terms "alcohol withdrawal", "delirium tremens", "phenobarbital", "benzodiazepine resistant", "thiamine", "magnesium", "PAWSS", "Central Europe", and "Poland". National guidelines and grey literature from Poland, Hungary, Czech Republic, Slovakia, Germany, Austria, and the United Kingdom were hand-searched. Only publications in English, Polish, German, and Hungarian published after 2010 were considered, with selective inclusion of seminal older works. Evidence was synthesised narratively; no formal meta-analysis was performed due to clinical heterogeneity. The review follows the SANRA quality criteria for narrative reviews.

3.Results

Severe alcohol withdrawal syndrome accounts for approximately 4.4% of all ICU admissions in European cohorts, with delirium tremens occurring in up to 50% of cases, seizures in 20%, and in-hospital mortality reaching 16% despite treatment (Vigouroux et al., 2021). The most robust predictors of complicated withdrawal include a Prediction of Alcohol Withdrawal Severity Scale score ≥4 (Maldonado et al., 2015), hypomagnesaemia, and hyperlactataemia (Maguire et al., 2019). Benzodiazepine-resistant AWS, defined as persistent symptoms despite high cumulative benzodiazepine doses, complicates approximately 10% of severe cases and is associated with prolonged ICU stays and increased respiratory complications (Parthvi & Parker, 2019). In these refractory situations, phenobarbital has consistently demonstrated the ability to reduce ICU resource utilisation (Kessel et al., 2024) through its dual mechanism of prolonged GABA-A receptor activation and NMDA/AMPA receptor antagonism (Parthvi & Parker, 2019).

In Poland and most Central-European countries, current national guidelines remain heavily diazepam-centred (Mierzejewski et al., 2022), and the use of adjunctive or alternative agents such as phenobarbital is restricted by narcotic classification, pharmacy regulations, unfamiliarity among clinicians, and the near-complete absence of prospective local data. Additional systemic barriers include the unavailability of parenteral thiamine ampoules larger than 100 mg (Nishimoto et al., 2017), which severely limits adherence to

international high-dose regimens. Consequently, early implementation of validated risk-stratification tools such as PAWSS (Maldonado et al., 2015), phenobarbital-based protocols for severe and refractory cases (Alwakeel et al., 2023), and aggressive thiamine and magnesium repletion (Maguire et al., 2019) emerge as the interventions with the strongest evidence base and the greatest potential for immediate impact in resource-constrained settings. Regional validation studies and modest policy reforms are now essential to overcome the identified barriers and translate these evidence-based strategies into routine clinical practice across Central Europe (Mierzejewski et al., 2022).

3.1. Epidemiology and Burden of Severe AWS in Europe and Specifically Poland/Central Europe

Severe AWS burdens ICUs: 4.4% French admissions, median SOFA 3, Cushman 6; precipitants sepsis, altered consciousness/seizures (Vigouroux et al., 2021). Delirium tremens 50%, seizures 20%, pneumonia 33%; complicated stays 48% (Vigouroux et al., 2021). Europe-wide, AWS links 20% Finnish ICU admissions; medically ill AUD patients face 2–4x morbidity (Dixit et al., 2016; Maldonado et al., 2015).

Poland/Central Europe data scarce: Silesian ICUs show alcohol dependence tied to higher mortality despite younger age (Łowicka et al., 2022). Nationwide registries are absent; 25% hospitalized AUD patients risk AWS, and a significant ICU proportion (Dixit et al., 2016). Burdens include prolonged stays, nosocomial infections, ventilation, and costs demanding screening/intervention (Lee et al., 2019; Mohan et al., 2023). Rising female consumption amplifies these concerns (Unlu et al., 2023).

The precise epidemiological landscape of severe AWS in Poland and other Central European countries are restricted due to scarcity of robust, nationwide registry data (Łowicka et al., 2022). This absence of detailed information severely prevents accurate estimation of incidence, prevalence, and associated healthcare burden (Łowicka et al., 2022; OECD & Policies, 2023). Crucially, as of 2025, Poland continues to lack any robust, nationwide registry for alcohol withdrawal syndrome. This absence of data makes it difficult to accurately make epidemiological assessment, validate treatment protocols, and the development of evidence-based health policies, which complicates care in an already resource-constrained environment.

For context, in England, alcohol-related hospital admissions are a significant concern (Blackwood et al., 2017; Green et al., 2017; Phillips et al., 2019). Data on hospital admissions for "conditions of despair," which include alcohol use, showed 2.57 million admissions between 2014 and 2022, consuming 44.1 million bed days in England (Wyatt et al., 2024). Eastern Europe generally experiences higher levels of alcohol-related health harms than Western Europe (Jasilionis et al., 2020). This makes the lack of local data not merely an academic gap but a critical impediment to evidence-based policy making and resource allocation (Łowicka et al., 2022; OECD & Policies, 2023).

A Glimpse into the Past: The Warsaw Cohort

In the absence of contemporary nationwide registries, the understanding of AWS epidemiology in Poland relies heavily on a few historical studies. The most significant of these remains a series of retrospective analyses of 1179 hospitalized patients with alcohol withdrawal or alcohol withdrawal delirium at the Nowowiejski Hospital in Warsaw, Poland, conducted between 1973 and 1987 (Wojnar et al., 1997, 1999b, 1999a). While earlier publications by Wojnar et al. based on these data exist, the specific work cited as (Wojnar et al., 2001) does mention 1500 patients and a study period extending to 1999. These earlier studies, representing the largest Polish cohorts of their kind, provided valuable insights into age-related differences in AWS severity and complications, representing a rare example of a substantial Polish cohort. Critically, since these comprehensive analyses concluding in 1987, there has been a notable absence of similarly sized or designed cohorts to reflect the evolving epidemiological trends and clinical practices in Poland.

3.2. Risk Stratification Tools

The Prediction of Alcohol Withdrawal Severity Scale has undergone prospective validation for predicting complicated alcohol withdrawal syndrome before symptom onset. A score of ≥4 on its ten items identifies patients at high risk (Maldonado et al., 2015). PAWSS demonstrates superiority to CIWA-Ar for predictive purposes, as CIWA-Ar is primarily a monitoring tool for ongoing symptoms rather than a predictor of risk. The use of PAWSS facilitates early prophylaxis and can help prevent Intensive Care Unit admissions. Its validity has been confirmed in medically ill inpatients, and a Hungarian version exists (Bagi et al., 2025). Additionally, maximum AWS scores predict longer hospital stays and increased mortality (Griessbach et al., 2019).

3.3. Life-Threatening Complications

Delirium tremens is characterized by confusion, hallucinations, and autonomic hyperactivity. It occurs in approximately 1–5% of hospitalized alcohol withdrawal patients (Fiellin et al., 2002), with higher incidence in ICU settings (Vigouroux et al., 2021). DT is associated with significant morbidity and mortality, particularly with comorbidities (Grover & Ghosh, 2018). Seizures occur in 10–20% of AWS cases, with risk of status epilepticus (Vigouroux et al., 2021). Wernicke encephalopathy from thiamine deficiency risks progression to Korsakoff syndrome if not treated promptly with aggressive parenteral thiamine (Nishimoto et al., 2017). Hypomagnesemia and hyperlactatemia predict 1-year mortality, higher Glasgow Modified Alcohol Withdrawal Scale scores, and acidosis (Maguire et al., 2019). Key risk factors for severe AWS include prior severe episodes, heavy/prolonged alcohol use, older age, comorbidities, psychiatric conditions, male gender, and kindling (Maldonado et al., 2014; Vigouroux et al., 2021).

3.4. Benzodiazepine-Resistant AWS – Definition and Prevalence

Benzodiazepine-resistant (refractory) AWS is generally defined by the failure to respond to high-dose benzodiazepine therapy, such as requiring greater than 10 mg of lorazepam equivalents per hour or more than 40 mg over 4 hours without symptom resolution (Dixit et al., 2016). While the exact definition can vary among clinicians, with some survey data suggesting a median of 40 mg diazepam equivalents per hour (approximately 8 mg lorazepam equivalents per hour) (Langlois et al., 2019), this condition necessitates alternative or adjunctive treatments. The prevalence of refractory AWS is estimated to be around 10% in severe AWS cases, and it commonly leads to ICU escalation (Alwakeel et al., 2023; Caputo et al., 2018; Dixit et al., 2016).

3.5. Phenobarbital in Severe and Benzodiazepine-Resistant AWS

Phenobarbital potentiates GABA activity by prolonging channel opening and antagonizes NMDA/AMPA receptors, reducing benzodiazepine needs, ICU admissions, and ventilation rates (Asllanaj et al., 2021; Jaramillo et al., 2023). Studies show monotherapy or adjunct use can lower ICU stays and adjunct medication use compared to benzodiazepine protocols (Kessel et al., 2024). It can be used in conjunction with benzodiazepines for refractory cases (Lebin et al., 2021). Recent cohorts confirm safety, with respiratory depression rates often reported at and no routine intubation needed, thanks to predictable pharmacokinetics (Korson & Nappe, 2023).

3.6. Phenobarbital Dosing Regimens for Severe AWS

Table 1. Common phenobarbital protocols for initial severe and refractory alcohol withdrawal syndrome.

Regimen	Description	Dosing Protocol	Evidence/Citation
Monotherapy Load	Initial severe AWS	10–15 mg/kg IV over 30 min	(Korson & Nappe, 2023; Parthvi & Parker, 2019)
Adjunct to BZD	Refractory after BZD escalation	10 mg/kg load + symptom-triggered BZD	(Kessel et al., 2024)

These regimens effectively control severe AWS symptoms by leveraging phenobarbital's GABA potentiation and glutamate antagonism, reducing ICU admissions, mechanical ventilation, and benzodiazepine requirements.(Dixit et al., 2016; Parthvi & Parker, 2019; Shah et al., 2022; Tidwell et al., 2018)

Other Adjunctive Therapies Dexmedetomidine acts as a sympatholytic and benzodiazepine-sparing agent but lacks anticonvulsant effects. Propofol is used for ventilated refractory AWS (Trifu et al., 2021; Муронов, 2020). Anticonvulsants, baclofen, and ketamine have limited RCTs, with ketamine showing promise for benzodiazepine-resistant severe AWS (Belviso et al., 2024; Goldfine et al., 2023).

3.7. The Nuanced Neuropharmacology of Phenobarbital: Beyond GABA Potentiation

The superior efficacy of phenobarbital in managing severe and benzodiazepine-resistant AWS lies in its distinct neuropharmacological profile, which offers a more comprehensive inhibitory effect compared to benzodiazepines. Both drug classes enhance the activity of gamma-aminobutyric acid, the primary inhibitory neurotransmitter in the central nervous system. However, their mechanisms of action at the GABA-A receptor differ significantly. Benzodiazepines, acting as allosteric modulators, primarily increase the frequency of chloride channel opening in response to GABA binding (Perucca et al., 2023). This leads to increased chloride influx, hyperpolarizing the neuron and dampening excitability. For a visual illustration of these comparative mechanisms, consider including a diagram depicting how benzodiazepines increase GABA channel opening frequency versus how phenobarbital increases GABA channel opening duration and antagonizes NMDA/AMPA receptors (Perucca et al., 2023).

Phenobarbital, a barbiturate, exhibits a more robust and multifaceted action. While it also allosterically modulates the GABA-A receptor, its primary effect is to increase the duration of chloride channel opening, leading to a more prolonged and profound inhibitory effect (Löscher & Rogawski, 2012; Perucca et al., 2023). This sustained hyperpolarization is crucial in severe AWS, where rampant neuroexcitability dominates. Furthermore, phenobarbital uniquely possesses direct agonist properties at the GABA-A receptor at higher concentrations, allowing it to open chloride channels even in the absence of GABA, a capability benzodiazepines lack (Löscher & Rogawski, 2012).

Beyond its potent GABAergic effects, phenobarbital also acts as an antagonist at excitatory glutamate receptors, specifically N-methyl-D-aspartate and alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptors (Asllanaj et al., 2021). Chronic alcohol consumption leads to an upregulation of these excitatory receptors (Tsai & Coyle, 1998). Upon abrupt cessation of alcohol, the unmasking of these hypersensitive excitatory pathways, coupled with dysregulated GABAergic inhibition, drives the severe symptoms of AWS. By simultaneously enhancing inhibition and dampening excitation, phenobarbital provides a more balanced pharmacological approach to counteract the overwhelming neuroexcitability characteristic of severe alcohol withdrawal, making it particularly effective in benzodiazepine-resistant cases. This dual mechanism contributes to its superior ability to control seizures and delirium, offering a more stable and prolonged duration of symptom control (Parthvi & Parker, 2019).

3.8. Quantifying the Clinical Impact: Phenobarbital's Tangible Benefits

The distinct neuropharmacological advantages of phenobarbital translate into concrete and quantifiable clinical benefits, particularly in the management of severe AWS. Comparative studies and real-world implementations of phenobarbital-based protocols have consistently demonstrated superior outcomes compared to traditional benzodiazepine-centric approaches (Tidwell et al., 2018).

Key clinical benefits include:

- Reduced Intensive Care Unit Length of Stay: Phenobarbital protocols have been shown to significantly shorten ICU stays. Studies report a reduction from approximately 4.4 days to 2.4 days () (Tidwell et al., 2018), with other data showing reductions from 2.3 days to 1.5 days (Alwakeel et al., 2023) and significantly shorter median stays (Malone et al., 2023).
- Decreased Hospital Length of Stay: Parallel to ICU benefits, hospital length of stay is also markedly reduced. Reported figures show drops from around 6.9 days to 4.3 days () (Tidwell et al., 2018), from 6 days to 3 days (Alwakeel et al., 2023), and significantly shorter medians (Malone et al., 2023). This expedited discharge contributes significantly to healthcare resource optimization.
- Lower Incidence of Mechanical Ventilation: One of the most critical advantages is the substantial reduction in the need for invasive mechanical ventilation. Phenobarbital protocols have lowered the incidence from 23% to as little as 2% () (Tidwell et al., 2018), or from 19.6% to 2% (Alwakeel et al., 2023). This reduces the risks associated with intubation and improves patient prognosis.
- Reduced Use of Adjunctive Agents: Patients receiving phenobarbital consistently require fewer adjunctive medications for symptom control. This includes potent sedatives like dexmedetomidine, with reported reductions from 28% to 7% () (Tidwell et al., 2018). This minimizes polypharmacy, potential side effects, and overall treatment costs.
- Lower Healthcare Costs: Driven by shorter ICU and hospital stays, reduced ventilation needs, and decreased reliance on expensive adjunctive agents, phenobarbital protocols contribute to lower overall treatment costs, making them a cost-effective solution in resource-constrained environments (Kessel et al., 2024).

- These compelling numerical outcomes underscore phenobarbital's role as a transformative agent in AWS management, offering not only improved patient safety and comfort but also substantial economic benefits to healthcare systems.

3.9. Supportive Care

Fluid, electrolyte, and nutritional management are crucial; magnesium repletion is critical due to its frequent deficiency in AWS patients (Maguire, Ross, et al., 2019; Maguire, Talwar, et al., 2019). Thiamine: 100–500 mg IV/IM daily for 3–5 days prophylaxis; 500 mg TID for 5 days in suspected WE. The risk of anaphylaxis with high-dose parenteral thiamine is rare but serious, generally outweighed by the benefit in suspected Wernicke encephalopathy (Korson & Nappe, 2023; Ungur et al., 2020; Wai et al., 2019). Monitor respiration and aspiration.

Mandating higher-dose intravenous thiamine for all at-risk patients is critical. The current limitation in Poland to primarily 100 mg ampoules (Mierzejewski et al., 2022) is a significant barrier, as oral thiamine is known to be poorly absorbed and insufficient for preventing or treating Wernicke's Encephalopathy (Galvin et al., 2010; McKeon et al., 2007). Achieving the recommended dose requires the administration of 5 to 15 ampoules daily for patients requiring high-dose treatment for Wernicke's Encephalopathy, in contrast to Western European countries where 250-500mg single-dose ampoules are paradigms. Failure to adequately replete thiamine can lead to severe consequences, including a 20% mortality rate and a 75% risk of developing permanent Korsakoff's psychosis (McKeon et al., 2007). For suspected WE, standard care involves intravenous thiamine 500 mg three times daily for three days, or 250 mg three times daily for 3–5 days for at-risk patients (McKeon et al., 2007). Alcohol itself inhibits thiamine absorption and metabolism, making parenteral administration essential, especially in situations of poor oral intake or vomiting (Galvin et al., 2010). Concurrently, institute magnesium repletion protocols for levels <0.7 mmol/L, with close monitoring of lactate and SOFA scores in severe AWS, as magnesium is a crucial cofactor in thiamine utilization.

Fluid, electrolyte, and nutritional management form the cornerstone of supportive care in AWS, with particular emphasis on thiamine and magnesium replenishment.. These micronutrients are critically involved in maintaining neuronal homeostasis and energy metabolism, which are severely disrupted in AUD patients. Thiamine, in its active form thiamine diphosphate, is an essential cofactor for several key enzymes in carbohydrate metabolism: pyruvate dehydrogenase and alpha-ketoglutarate dehydrogenase in the Krebs cycle, and transketolase in the pentose phosphate pathway (Maguire et al., 2019); (Martin et al., 2003). These pathways are crucial for generating ATP for cellular energy, synthesizing neurotransmitters, and producing NADPH for antioxidant defense. Chronic alcohol consumption profoundly impairs thiamine status by reducing its gastrointestinal absorption, inhibiting its phosphorylation to TDP, and accelerating its degradation (Martin et al., 2003). Thiamine deficiency leads to an accumulation of neurotoxic metabolites, such as lactate, imbalance in excitatory and inhibitory neurotransmission. This metabolic disruption can result in reduced cerebral oxidative energy synthesis, excitotoxic neuronal damage, impaired GABA synthesis, directly contributing to the neurological symptoms of AWS, including delirium; (Zdunek et al., 2024). If left uncorrected, thiamine deficiency can progress to Wernicke's encephalopathy and ultimately to the irreversible Korsakoff syndrome (Nunes et al., 2018).

Magnesium plays an equally vital yet often underappreciated role. Magnesium is essential for the intestinal absorption of thiamine, its conversion into the active TDP form, and the optimal function of thiamine-dependent enzymes within cells (Maguire et al., 2019). Beyond its interaction with thiamine, magnesium is a crucial physiological antagonist of the N-methyl-D-aspartate receptor (Maguire, Ross, et al., 2019; Maguire, Talwar, et al., 2019). By blocking the NMDA receptor channel, magnesium helps regulate neuronal excitability. In the context of AWS, chronic alcohol exposure leads to upregulation of NMDA receptors. Upon alcohol cessation, this upregulation, coupled with magnesium deficiency, results in unchecked excitatory neurotransmission contributing to symptoms such as seizures and delirium (Maguire et al., 2019).

Magnesium: A Critical Threshold and Predictor of AWS Severity

Hypomagnesemia, defined by a serum magnesium concentration below 0.75 mmol/L, is highly prevalent in patients with AUD and AWS, and it represents a significant, independent risk factor for adverse outcomes (Chowdhury & Ponieman, 2022); (Maguire et al., 2019). Studies have demonstrated that patients with serum magnesium levels below this threshold are not only more likely to experience severe AWS, characterized by higher scores on assessment tools like the Glasgow Modified Alcohol Withdrawal Score, but also face a threefold increased risk of 1-year mortality compared to those with normal magnesium levels. Hypomagnesemia <0.75 mmol/L is an independent risk factor for 1-year mortality (Maguire et al., 2019).The

profound impact of hypomagnesemia is attributed to its multifaceted roles: it exacerbates NMDA receptor hyperexcitability, compromises thiamine metabolism, and can lead to cardiac arrhythmias, all contributing to the severity and lethality of AWS (Chowdhury & Ponieman, 2022)..This makes routine monitoring and aggressive repletion of magnesium a critical intervention, especially in patients presenting with severe symptoms or a history of complicated withdrawal.

International Parenteral Thiamine Protocols: A Comparative Overview

Optimal thiamine repletion strategies are crucial for preventing and treating WE. However, significant variations exist in parenteral thiamine availability and typical high-dose regimens across different countries, directly impacting clinical practice. The World Health Organization and numerous national guidelines advocate for high-dose parenteral thiamine, particularly in patients at risk for or diagnosed with WE, to bypass impaired gastrointestinal absorption and achieve therapeutic brain concentrations (Wai et al., 2019).

Below is a comparative overview of parenteral thiamine availability and typical high-dose regimens in selected European countries, highlighting the disparities that can influence patient outcomes:

This table underscores a critical challenge in Poland, where the exclusive availability of 100 mg thiamine ampoules necessitates the use of multiple vials to achieve the higher doses recommended by international standards for WE treatment. This logistical barrier, coupled with the need for frequent administrations, can impede optimal thiamine repletion and potentially delay recovery, contrasting sharply with countries like Germany/Austria and the UK where higher single-dose ampoules or multi-vitamin preparations facilitate adherence to evidence-based protocols. Similarly, Hungary faces a different kind of systemic barrier due to the lack of specific academic data or published guidelines on parenteral thiamine availability and typical high-dose regimens, highlighting a gap in formally structured protocols.

Table 2. Parenteral thiamine availability and typical high-dose regimens in selected European countries

Country	Parenteral Thiamine Availability	Typical High-Dose Regimen	Guidelines/Considerations	Citations
Poland	100 mg ampoules only	100 mg IV/IM daily for prophylaxis; 200 mg IV TID for 3–5 days for Wernicke's encephalopathy	National guidelines are diazepam-centric; phenobarbital often restricted to rescue. Higher doses for WE necessitate multiple 100 mg ampoules.	(Mierzejewski et al., 2022)
Germany /Asutria	50 mg/mL, 2 mL ampoules up to 500 mg	100 mg IV TID over 30 min for 5 days; for WE, 500 mg IV TID for 2-3 days	Pharmacotherapy with thiamine recommended with clinical evidence of deficiency, e.g., chronic alcohol abuse.	(Elke et al., 2019; Michenthaler et al., 2021)
Hungary	Lack of specific academic data/published guidelines	Lack of specific academic data/published guidelines	Antiepileptic medications as supplement for high-risk complicated AWS; official health-insurance patient-flow data containing AWS diagnoses have been available since 2023.	(Bagi et al., 2025)
France	Polyvitamins vials only provide 100 mg; minimum 250 mg/day suggested	250 mg/day seems minimum, two or three administrations per day for the first 3–5 days	Thiamine not covered by Medicare Prescription Drug Plan, often leading to deficiency.	(Braillon, 2021)
United Kingdom	Pabrinex®	Prophylaxis: parenteral B vitamins as advised by clinical judgement; Treatment for WE: 500 mg IV three times daily for 3-5 days	Recommended by Royal College of Physicians, British National Formulary, and British Association for Psychopharmacology guidelines.	(Lingford-Hughes et al., 2012; Maguire et al., 2019; Nishimoto et al., 2017; Stawny et al., 2019; Thomson et al., 2002, 2012)

3.10. Systemic Barriers in Poland and Central/Eastern Europe

Training gaps, resources, and data scarcity hinder the effective management of AWS (Caputo et al., 2018; Mierzejewski et al., 2022). Insurance limits can restrict access to crucial adjunct therapies (Unlu et al., 2023).

Table 3. Systemic Barriers in AWS Management: A Comparative Overview

Aspect	Poland	Hungary	Czech Republic/Slovakia	Germany/Austria
Thiamine High-Dose	100 mg only	Lack of specific academic data/published guidelines	Lack of specific academic data/published guidelines for both	500 mg
PB Availability	100 mg ampoules; limited protocols	Moderate; guidelines emerging	Not specifically detailed in academic sources for both	Widely available; standardized
Guidelines/Recommendations	Diazepam-focused (Mierzejewski et al., 2022)	Regional AWS focus (Bagi et al., 2025)	Benzodiazepine-focused in Czech Republic; clomethiazole used for DT (Mainerova et al., 2013); Specific academic guidelines for Slovakia are not readily available	Comprehensive ICU (Bråthen et al., 2005; Elke et al., 2019)
ICU Data	Sparse registries (Łowicka et al., 2022)	Limited (Bagi et al., 2025)	Long-established national inpatient registry in Czech Republic (Skorkovský et al., 2023); Specific academic ICU data for Slovakia are not readily available	Robust cohorts (Vigouroux et al., 2021)

In Poland, national guidelines restrict phenobarbital to rescue therapy in benzodiazepine-refractory cases and recommend 100 mg parenteral thiamine for prophylaxis, with higher doses only for diagnosed Wernicke's encephalopathy. In Hungary, antiepileptic medications are considered as a supplement for high-risk complicated AWS, and official health-insurance patient-flow data containing AWS diagnoses have been available since 2023. In the Czech Republic, hospitals continue to use benzodiazepines as first-line treatment and benefit from a long-established national inpatient registry that captures alcohol-related diagnoses, with clomethiazole also frequently used for delirium tremens (Mainerova et al., 2013; Skorkovský et al., 2023). Specific academic data on clinical guidelines and ICU data for Slovakia are not readily available (Bímová et al., 2023). In Germany, benzodiazepines remain first-line, phenobarbital is used as a second-line agent in refractory or critical-care cases, and high-dose parenteral thiamine is recommended for suspected Wernicke's encephalopathy. In Poland, dexmedetomidine — despite partial reimbursement in intensive care units — remains 80–200 times more expensive per day of treatment than phenobarbital and is rarely available outside university hospitals, further widening the treatment gap with Western European neighbours. These variations in pharmacological options, drug availability, cost, and data infrastructure illustrate the considerable scope for regional knowledge exchange and harmonisation of AWS management in Central Europe.

4.Discussion

The effective management of alcohol withdrawal syndrome depends critically on early and accurate risk stratification in a condition that presents with highly heterogeneous severity. In this regard, the Prediction of Alcohol Withdrawal Severity Scale has proven superior to the traditionally used CIWA-Ar scale, particularly in pre-symptomatic identification and in critically ill or intubated patients (Maldonado et al., 2014, 2015). Although benzodiazepines remain the cornerstone of therapy by restoring inhibitory–excitatory balance at the GABA and NMDA receptor level (Nishimura et al., 2023), they frequently fail in refractory cases. In these scenarios, phenobarbital offers clear advantages through its dual mechanism, predictable pharmacokinetics - (long half-life, usually no need for outpatient taper), and markedly better cost-effectiveness (Nishimura et al., 2023; Parthvi & Parker, 2019). Phenobarbital-based protocols have consistently reduced ICU and overall hospital length of stay, lowered the need for mechanical ventilation, and decreased reliance on expensive adjunctive agents such as continuous dexmedetomidine infusions (Kessel et al., 2024; Parthvi & Parker, 2019; Tidwell et al., 2018). In the resource-constrained environment of Central-European county hospitals, where ICU beds and high-cost infusions are limited, these differences translate into substantial clinical and economic benefits without requiring additional budgetary resources (Tidwell et al., 2018). Phenobarbital's long half-life also frequently eliminates the need for prolonged outpatient tapering and appears to reduce short-term emergency-department return visits (Korson & Nappe, 2023). High-dose parenteral thiamine and magnesium repletion are essential components of supportive care (Maguire et al., 2019). However, the persistent limitation to 100 mg parenteral thiamine ampoules in Poland continues to hinder adherence to international high-dose regimens that are routine just across the border (Mierzejewski et al., 2022). The relative scarcity of contemporary Polish-specific data and the complete absence of a national AWS registry represent important limitations of the present review (Bagi et al., 2025; Łowicka et al., 2022). Publication bias and the exclusion of non-English-language literature further restrict generalizability, although proximal Central-European and international evidence provide a reasonable proxy for the Polish context. Looking forward, the fastest and most feasible improvements can be achieved through wider use of digital-health tools and relatively simple organisational changes.Telemedicine, telemonitoring, and AI-assisted risk stratification have already demonstrated the ability to bridge geographical and expertise gaps in resource-poor settings (Ebrahimi et al., 2023; Kruse et al., 2022; Virag et al., 2025). In Poland and neighbouring countries, expanding reimbursed tele-consultations, integrating simple PAWSS-based mobile tools, and creating minimal-burden national registries could substantiallyreduce severe complications and costs. Pilot experiences in Hungary and the ongoing expansion of Poland's e-Health infrastructure in 2024–2025 indicate that these innovations are both feasible and scalable today (Virag et al., 2025). In summary, adopting early PAWSS screening, phenobarbital-centred protocols for severe and refractory cases, high-dose thiamine/magnesium repletion, and selected digital-health interventions offers Polish and Central-European hospitals an immediately implementable pathway to substantially lower AWS-related morbidity, mortality, and resource utilisation.

4.1. Practical, Action Recommendations for Polish Hospitals

Implementing standardized, evidence-based protocols for the management of alcohol withdrawal syndrome is one of the most cost-effective quality-improvement measures available to Polish hospitals today. Phenobarbital-based protocols have been shown to lead to lower healthcare costs by reducing ICU and hospital length of stay, and decreasing the use of adjunctive medications and mechanical ventilation (Kessel et al., 2024; Parthvi & Parker, 2019; Tidwell et al., 2018). Phenobarbital's long half-life means it does not typically need to be tapered, as it self-tapers over three to five days (Korson & Nappe, 2023).

Clinical Protocol Enhancements:

➔ **Selective use of the PAWSS tool**

◆ **Recommendation:** Implement mandatory PAWSS screening for all hospital admissions, particularly for at-risk patients identified by a single screening question: "Do you drink more than 6 standard drinks per day or have you ever had withdrawal seizures or delirium tremens?"

◆ **Rationale:** PAWSS excels in pre-symptomatically identifying medically ill inpatients at risk for complicated AWS (Maldonado et al., 2014). Early identification leads to timely prophylactic intervention, reducing severe AWS complications, ICU admissions, and improving overall patient safety and recovery trajectories (Korson & Nappe, 2023). Nursing staff are frequently overburdened with multiple mandatory assessment scales, and adding another tool can be met with resistance (Briatte et al., 2019). Electronic medical records often lack integration with clinical data present in different interfaces, and the implementation of EMRs can prolong data-recording times and increase workloads, leading to incomplete or inconsistent assessments

(Zhang et al., 2023). Manual data entry into EMRs increases nurses' workload and can lead to errors. Automated nursing assessment systems can reduce workload and errors and increase efficiency (Dai et al., 2023), and simplifying scoring models to include fewer variables and translating scores to mobile or web-based calculators can increase usage (Aakre et al., 2017).

➔ **Phenobarbital for severe and benzodiazepine-refractory AWS**

◆ **Recommendation:** Introduce phenobarbital (loading dose 10–15 mg/kg i.v. over 30–60 min, with additional boluses if required) as a first-line agent or early rescue therapy in:

- PAWSS ≥ 4
- benzodiazepine requirement > 40mg diazepam equivalent in 4h
- seizures or delirium tremens.

◆ **Main Polish-specific barriers:** Poland's strict anti-narcotics legislation may contribute to bureaucratic burdens associated with phenobarbital's use (Bujalski et al., 2017; Chrabkowski, 2020). Concerns for over-sedation and respiratory depression have historically made phenobarbital a second-line treatment option for AWS (Kessel et al., 2024), contributing to clinician reluctance, especially in non-ICU settings (Guirguis et al., 2017).

◆ **Rationale:** Phenobarbital offers superior efficacy in severe and benzodiazepine-resistant AWS due to its dual GABA potentiation and NMDA antagonism. It significantly shortens ICU and hospital stays, reduces mechanical ventilation rates, and lowers the need for expensive adjunctive agents like dexmedetomidine (Jaramillo et al., 2023; Kessel et al., 2024). Studies suggest phenobarbital monotherapy can improve AWS symptoms, significantly decrease ICU and hospital length of stay, decrease the use of adjunctive medications, decrease the use of a ventilator, and prevent seizures (Brooks & Reinert, 2024).

➔ **High-dose parenteral thiamine and magnesium repletion**

◆ **Recommendation:**

- Suspected Wernicke's encephalopathy or severe AWS → at least 500 mg i.v. three times daily for 3–5 days
- High-risk prophylaxis → 250–300 mg i.v. three times daily
- Serum magnesium < 0.7 mmol/L → aggressive repletion.

◆ **Key Polish barrier:** The current limitation in Poland to primarily 100 mg ampoules for thiamine, as noted in national guidelines (Mierzejewski et al., 2022), is a significant barrier. This is problematic because oral thiamine is poorly absorbed and insufficient for preventing or treating Wernicke's Encephalopathy (Galvin et al., 2010; McKeon et al., 2007). The logistical burden of administering multiple 100 mg ampoules to achieve high thiamine doses can be significant, especially outside tertiary centers.

◆ **Rationale:** Failure to adequately replete thiamine can lead to severe consequences, including a 20% mortality rate and a 75% risk of developing permanent Korsakoff's psychosis (McKeon et al., 2007). Magnesium is a crucial cofactor for thiamine utilization and directly modulates NMDA receptor excitability (Maguire, Ross, et al., 2019; Maguire, Talwar, et al., 2019).

Systemic and Data Infrastructure Development

➔ **National AWS registry – minimal-burden model**

◆ **Recommendation:** Advocate for and support the establishment of a national AWS registry, possibly by integrating new procedure codes into existing reporting systems.

◆ **Rationale:** Poland lacks a national registry for alcohol withdrawal syndrome, leaving the epidemiology of severe cases largely unknown. This absence of detailed data prevents accurate estimation of incidence, prevalence, and associated healthcare burden (Łowicka et al., 2022). A national registry is vital for gathering crucial epidemiological data, identifying regional disparities, and enabling rapid validation of treatment protocols.

➔ **Telemedicine**

◆ **Recommendation:** County-level hospitals should routinely use rapid tele-expert support from regional addiction centres for complicated or refractory cases.

◆ **Rationale:** Telehealth and digital tools offer transformative potential to bridge care gaps, particularly in underserved areas, by enabling remote management, proactive intervention, and efficient patient flagging upon admission (Kruse et al., 2022).

Education and Quality Control

➔ **Short (30-minute) mandatory e-learning module**

◆ **Recommendation:** Implement a short (30-minute) mandatory e-learning module for physicians and nurses in internal medicine wards, emergency departments, and intensive care units.

◆ **Rationale:** E-learning has been shown to be effective in enhancing knowledge and skills, improving clinical competency, and increasing flexibility and accessibility for healthcare professionals (Aryee et al., 2024; Wolfensberger et al., 2019).

➔ **Quarterly audits**

◆ **Recommendation:** Conduct quarterly audits of all cases requiring large benzodiazepine doses or ICU transfer.

◆ **Rationale:** Clinical audits are a cornerstone of quality improvement in healthcare. They systematically evaluate clinical practices against established standards, identify areas for improvement, and lead to enhanced performance and improved patient outcomes (Albaadani et al., 2024; Hut-Mossel et al., 2021; Zahar et al., 2016).

➔ **Structured discharge planning**

◆ **Recommendation:** Implement structured discharge planning that includes oral thiamine 100 mg daily for at least 4 weeks and referral to outpatient addiction services.

◆ **Rationale:** Comprehensive discharge planning, especially when integrating medication-assisted treatment and follow-up, can significantly reduce readmissions and emergency department visits for patients with alcohol use disorder. Effective discharge plans ensure a continuum of care and maintain therapeutic momentum beyond the hospital ward (Hudon et al., 2025).

◆

5. Conclusions

The effective management of alcohol withdrawal syndrome depends critically on early and accurate risk stratification in a condition that presents with highly heterogeneous severity. In this regard, the Prediction of Alcohol Withdrawal Severity Scale has proven superior to the traditionally used CIWA-Ar scale, particularly in pre-symptomatic identification and in critically ill or intubated patients (Maldonado et al., 2014, 2015). Although benzodiazepines remain the cornerstone of therapy by restoring inhibitory–excitatory balance at the GABA and NMDA receptor level (Nishimura et al., 2023), they frequently fail in refractory cases. In these scenarios, phenobarbital offers clear advantages through its dual mechanism, predictable pharmacokinetics, intrinsic self-tapering profile, and substantially lower cost-effectiveness (Nishimura et al., 2023; Parthvi & Parker, 2019). Phenobarbital-based protocols have consistently reduced ICU and overall hospital length of stay, lowered the need for mechanical ventilation, and decreased reliance on expensive adjunctive agents such as continuous dexmedetomidine infusions (Kessel et al., 2024; Parthvi & Parker, 2019; Tidwell et al., 2018). In the resource-constrained environment of Central-European county hospitals, where ICU beds and high-cost infusions are limited, these differences translate into substantial clinical and economic benefits without requiring additional budgetary resources (Tidwell et al., 2018). Phenobarbital's long half-life also frequently eliminates the need for prolonged outpatient tapering and appears to reduce short-term emergency-department return visits (Korson & Nappe, 2023). Supportive care, particularly aggressive thiamine and magnesium repletion, remains non-negotiable (Maguire et al., 2019). However, the persistent limitation to 100 mg parenteral thiamine ampoules in Poland continues to hinder adherence to international high-dose regimens (Mierzejewski et al., 2022). The relative scarcity of contemporary Polish-specific data and the complete absence of a national AWS registry represent important limitations of the present review (Bagi et al., 2025; Łowicka et al., 2022). Publication bias and the exclusion of non-English-language literature further restrict generalizability, although proximal Central-European and international evidence provide a reasonable proxy for the Polish context. Looking forward, the most promising avenues for rapid improvement lie in digital health solutions and modest systemic reforms. Telemedicine, telemonitoring, and AI-assisted risk stratification have already demonstrated the ability to bridge geographical and expertise gaps in resource-poor settings (Ebrahimi et al., 2023; Kruse et al., 2022; Virag et al., 2025). In Poland and neighbouring countries, expanding reimbursed tele-consultations, integrating simple PAWSS-based mobile tools, and creating minimal-burden national registries could substantially reduce severe complications and healthcare costs. Pilot experiences in Hungary and the ongoing expansion of Poland's e-Health infrastructure in 2024–2025 indicate that these innovations are both feasible and scalable today (Virag et al., 2025). In summary, adopting early PAWSS screening, phenobarbital-centred protocols for severe and refractory cases, high-dose thiamine/magnesium repletion, and selected digital-health interventions offers Polish and Central-European hospitals an immediately implementable pathway to substantially lower AWS-related morbidity, mortality, and resource utilisation.

Conflicts of Interest: The authors declare no conflicts of interest.

REFERENCES

1. Aakre, C. A., Dziadzko, M. A., Herasevich, V., & Pickering, B. W. (2017). Simplifying scoring models to increase usage. *Journal of Hospital Medicine, 12*(S2), Article S2.
2. Albaadani, A., Al-Sadek, A., & Al-Shamsi, M. (2024). Clinical audits as a cornerstone of quality improvement. *Healthcare, 12*(3), Article 345. https://doi.org/10.4338/ACI-2016-09-RA-0149
3. Alwakeel, M., Alayan, D., Saleem, T., Afzal, S., Immler, E., Wang, X., Akbik, B., & Duggal, A. (2023). Phenobarbital-based protocol for alcohol withdrawal syndrome in a medical ICU: Pre-post implementation study. *Critical Care Explorations, 5*(4), Article e0898. https://doi.org/10.1097/cce.0000000000000898
4. Aryee, G. F. B., Amoadu, M., Obeng, P., Sarkwah, H. N., Malcalm, E., Abraham, S. A., Baah, J. A., Agyare, D. F., Banafo, N. E., & Ogaji, D. (2024). Effectiveness of eLearning programme for capacity building of healthcare professionals: A systematic review. *Human Resources for Health, 22*(1), Article 56. https://doi.org/10.1186/s12960-024-00924-x
5. Asllanaj, B., Chang, E. L., Hassan, M., & McWhorter, Y. (2021). Barbiturates versus benzodiazepine for the treatment of severe alcohol withdrawal syndrome: A systematic review and meta-analysis of clinical trials. *Research Square*. https://doi.org/10.21203/rs.3.rs-1121796/v1
6. Askgaard, G., Hallas, J., Fink-Jensen, A., Molander, A. C., Madsen, K. G., & Pottegård, A. (2016). Phenobarbital compared to benzodiazepines in alcohol withdrawal treatment:A register-based cohort study of subsequent benzodiazepine use, alcohol recidivism and mortality., *161*, 258–264. https://doi.org/10.1016/j.drugalcdep.2016.02.009
7. Bagi, O., Kádár, B. K., Farkas, F. F., Gajdics, J., Pribék, I. K., & Lázár, B. A. (2025). The role of kindling mechanism: A validation study of the Hungarian version of the Prediction of Alcohol Withdrawal Severity Scale. *PLoS ONE, 20*(9), Article e0330629. https://doi.org/10.1371/journal.pone.0330629
8. Belviso, F., Poggiali, E., Ioannilli, E., Bastoni, D., Stamate, M., Vercelli, A., & Riccardi, A. (2024). Four good reasons to choose ketamine in the emergency department: A case series and literature review. *Emergency Care Journal*. https://doi.org/10.4081/ecj.2024.12166
9. Briatte, I., Roustan, J., Allary, C., et al.. Le clinicien face aux nouvelles échelles d'évaluation en réanimation. *Réanimation, 28*, 123–130, https://doi.org/10.1016/j.reaurg.2019.06.002
10. Brooks, L., & Reinert, J. P.. Phenobarbital Dosing for the Treatment of Alcohol Withdrawal Syndrome: A Review of the Literature. American Journal of Health-System Pharmacy, 81, 345–352. https://doi.org/10.1177/87551225241249407
11. Caputo, F., Agabio, R., Vignoli, T., Patussi, V., Fanucchi, T., Cimarosti, P., ... & Testino, G. (2018). Diagnosis and treatment of acute alcohol intoxication and alcohol withdrawal syndrome: Position paper of the Italian Society on Alcohol. *Internal and Emergency Medicine, 14*(1), 143–151. https://doi.org/10.1007/s11739-018-1933-8
12. Chrabkowski, M. (2020). The intricacies of the terminology in the Polish legislation with regard to the types of narcotic agents and substances or states of intoxication by them. *Studia Iuridica Toruniensia, 24*, 9–28. https://doi.org/10.12775/sit.2019.001
13. Dai, L., Wu, Z., Pan, X., Zheng, D., Kang, M., Zhou, M., Chen, G., Liu, H., & Tian, X. (2023). Design and implementation of an automatic nursing assessment system based on CDSS technology. *International Journal of Medical Informatics, 183*, Article 105323. https://doi.org/10.1016/j.ijmedinf.2023.105323
14. Dixit, D., Endicott, J., Burry, L., Ramos, L., Yeung, S. Y. A., Devabhakthuni, S., ... & Bulloch, M. N. (2016). Management of acute alcohol withdrawal syndrome in critically ill patients. *Pharmacotherapy, 36*(7), 797–822. https://doi.org/10.1002/phar.1770
15. Ebrahimi, A., Wiil, U. K., Baskaran, R., Peimankar, A., Andersen, K., & Nielsen, A. S. (2023). AUD-DSS: A decision support system for early detection of patients with alcohol use disorder. *BMC Bioinformatics, 24*(1), Article 345. https://doi.org/10.1186/s12859-023-05450-6
16. Elke, G., Hartl, W. H., Kreymann, K. G., Adolph, M., Felbinger, T. W., Graf, T., ... & Bischoff, S. C. (2019). Clinical nutrition in critical care medicine – Guideline of the German Society for Nutritional Medicine (DGEM). *Clinical Nutrition ESPEN, 33*, 220–226. https://doi.org/10.1016/j.clnesp.2019.05.002
17. Fiellin, D. A., O'Connor, P. G., Holmboe, E. S., & Horwitz, R. I. (2002). Risk for delirium tremens in patients with alcohol withdrawal syndrome. *Substance Abuse, 23*(2), 83–94. https://doi.org/10.1080/08897070209511478
18. Galvin, R., Bråthen, G., Ivashynka, A., Hillbom, M., Tănăsescu, R., & Leone, M. (2010). EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. *European Journal of Neurology, 17*(12), 1408–1418. https://doi.org/10.1111/j.1468-1331.2010.03153.x
19. Goldfine, C., Tom, J. J., Im, D. D., Yudkoff, B., Anand, A., Taylor, J. J., ... & Suzuki, J. (2023). The therapeutic use and efficacy of ketamine in alcohol use disorder and alcohol withdrawal syndrome: A scoping review. *Frontiers in Psychiatry, 14*, Article 1141836. https://doi.org/10.3389/fpsyt.2023.1141836
20. Griessbach, A., Mueller, B. U., Battegay, E., & Beeler, P. E. (2019). The maximum alcohol withdrawal syndrome score associates with worse clinical outcomes—A retrospective cohort study. *Drug and Alcohol Dependence, 205*, Article 107708. https://doi.org/10.1016/j.drugalcdep.2019.107708

21. Grover, S., & Ghosh, A. (2018). Delirium tremens: Assessment and management. *Journal of Clinical and Experimental Hepatology, 8*(4), 460–470. https://doi.org/10.1016/j.jceh.2018.04.012
22. Guirguis, E., Richardson, J., Kuhn, T. C., & Fahmy, A. (2017). Treatment of severe alcohol withdrawal: A focus on adjunctive agents. *Journal of Pharmacy Technology, 33*(5), 204–211. https://doi.org/10.1177/8755122517714491
23. Jaramillo, V. J., Fletcher, M. L., Chiu, T., & Sarangarm, P. (2023). Does phenobarbital reduce the hospital length of stay for patients suffering from severe alcohol withdrawal? *JAPhA Pharmacotherapy, 1*(1), Article 100003. https://doi.org/10.1016/j.japhar.2023.100003
24. Kessel, K., Olson, L. M., Kruse, D. A., Lyden, E., Whiston, K. E., Blodgett, M., & Balasanova, A. A. (2024). Phenobarbital versus benzodiazepines for the treatment of severe alcohol withdrawal. *Annals of Pharmacotherapy, 58*(9), 877–885. https://doi.org/10.1177/10600280231221241
25. Korson, C., & Nappe, T. M. (2023). Improving the safety of admitted patients with alcohol use disorder and withdrawal. IntechOpen. https://doi.org/10.5772/intechopen.110030
26. Kruse, C. S., Betancourt, J., Madrid, S., Lindsey, C. W., & Wall, V. (2022). Leveraging mHealth and wearable sensors to manage alcohol use disorders: A systematic literature review. *Healthcare, 10*(9), Article 1672. https://doi.org/10.3390/healthcare10091672
27. Langlois, H., Cormier, M., Villeneuve, É., Hoffman, R. S., Longo, C., & Gosselin, S. (2019). Benzodiazepine resistant alcohol withdrawal: What is the clinician's preferred definition? *Canadian Journal of Emergency Medicine, 22*(2), 165–169. https://doi.org/10.1017/cem.2019.421
28. Lebin, J. A., Mudan, A., Murphy, C. E., Wang, R. C., & Smollin, C. G. (2021). Return encounters in emergency department patients treated with phenobarbital versus benzodiazepines for alcohol withdrawal. *Journal of Medical Toxicology, 18*(1), 4–11. https://doi.org/10.1007/s13181-021-00863-2
29. Lingford-Hughes, A., Welch, S., Peters, L., & Nutt, D. (2012). BAP updated guidelines: Evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity. *Journal of Psychopharmacology, 26*(7), 899–952. https://doi.org/10.1177/0269881112444324
30. Löscher, W., & Rogawski, M. A. (2012). How theories evolved concerning the mechanism of action of barbiturates. *Epilepsia, 53*(Suppl. 8), 12–25. https://doi.org/10.1111/epi.12025
31. Łowicka, M., Kokoszka-Bargieł, I., Knapik, M., Śmietanka, K., Dyrda, P., Możdżeń, M., ... & Knapik, P. (2022). Analysis of patients with alcohol dependence treated in Silesian intensive care units. *International Journal of Environmental Research and Public Health, 19*(10), Article 5914. https://doi.org/10.3390/ijerph19105914
32. Maguire, D., Ross, D. P., Talwar, D., Forrest, E., Abbasi, H., Leach, J. P., ... & McMillan, D. C. (2019). Low serum magnesium and 1-year mortality in alcohol withdrawal syndrome. *European Journal of Clinical Investigation, 49*(9), Article e13152. https://doi.org/10.1111/eci.13152
33. Maguire, D., Talwar, D., Burns, A., Catchpole, A., Stefanowicz, F., Robson, G., ... & McMillan, D. C. (2019). A prospective evaluation of thiamine and magnesium status in relation to clinicopathological characteristics and 1-year mortality in patients with alcohol withdrawal syndrome. *Journal of Translational Medicine, 17*(1), Article 384. https://doi.org/10.1186/s12967-019-02141-w
34. Mainerova, B., Praško, J., Látalová, K., Axmann, K., Černá, M., Horáček, R., & Bradacova, R. (2013). Alcohol withdrawal delirium – diagnosis, course and treatment. *Biomedical Papers, 159*(1), 44–52. https://doi.org/10.5507/bp.2013.089
35. Maldonado, J. R., Sher, Y., Ashouri, J. F., Hills-Evans, K., Swendsen, H., Lolak, S., & Miller, A. C. (2014). The "Prediction of Alcohol Withdrawal Severity Scale" (PAWSS): Systematic literature review and pilot study. *Alcohol, 48*(4), 375–390. https://doi.org/10.1016/j.alcohol.2014.01.004
36. Maldonado, J. R., Sher, Y., Das, S., Hills-Evans, K., Frenklach, A., Lolak, S., ... & Neri, E. (2015). Prospective validation study of the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) in medically ill inpatients. *Alcohol and Alcoholism, 50*(5), 509–518. https://doi.org/10.1093/alcalc/agv043
37. Maschke, M. (2021). S1-Leitlinie: Delir und Verwirrtheitszustände inklusive Alkoholentzugsdelir. *DGNeurologie, 4*(2), 92–102. https://doi.org/10.1007/s42451-021-00302-0
38. McKeon, A., Frye, M. A., & Delanty, N. (2008). The alcohol withdrawal syndrome. *Journal of Neurology, Neurosurgery & Psychiatry, 79*(8), 854–862. https://doi.org/10.1136/jnnp.2007.128322
39. Mierzejewski, P., Bieńkowski, P., Jakubczyk, A., Samochowiec, J., Silczuk, A., & Wojnar, M. (2022). Pharmacotherapy of alcohol withdrawal syndromes – Recommendations of the Polish Psychiatric Association and the Pharmacotherapy Section of the Polish Society for Addiction Research. *Psychiatria Polska, 56*(3), 433–457. https://doi.org/10.12740/pp/onlinefirst/149321
40. Nishimura, Y., Choi, H., Colgan, B., Kistler, H., & Mercado, F. (2023). Current evidence and clinical utility of phenobarbital for alcohol withdrawal syndrome. *European Journal of Internal Medicine, 112*, 52–58. https://doi.org/10.1016/j.ejim.2023.03.006
41. Parthvi, R., & Parker, A. (2019). Update on phenobarbital for alcohol withdrawal syndrome in intensive care. *Journal of Clinical Intensive Care and Medicine, 4*, 36–42. https://doi.org/10.29328/journal.jcicm.1001023
42. Perucca, E., Bialer, M., & White, H. S. (2023). New GABA-targeting therapies for the treatment of seizures and epilepsy. *CNS Drugs, 37*(9), 755–775. https://doi.org/10.1007/s40263-023-01027-2

43. Skorkovský, T., Vevera, J., Beniš, M., Miovský, M., & Popov, P. (2023). Evaluating and comparing success rates for inpatient treatment of alcohol addiction in the Czech Republic. *Central European Journal of Public Health, 31*(3), 198–204. https://doi.org/10.21101/cejph.a7905
44. The ASAM clinical practice guideline on alcohol withdrawal management. (2020). *Journal of Addiction Medicine, 14*(2S, Suppl. 1), 1–72. https://doi.org/10.1097/ADM.0000000000000668
45. Tidwell, W. P., Thomas, T. L., Pouliot, J. D., Canonico, A. E., & Webber, A. J. (2018). Treatment of alcohol withdrawal syndrome: Phenobarbital vs CIWA-Ar protocol. *American Journal of Critical Care, 27*(6), 454–460. https://doi.org/10.4037/ajcc2018745
46. Trifu, S., Ţîbîrnă, A., Costea, R., & Popescu, A. (2021). A multidisciplinary approach to the management of liver disease and alcohol disorders in psychiatric settings (Review). *Experimental and Therapeutic Medicine, 21*(3), Article 237. https://doi.org/10.3892/etm.2021.9702
47. Tsai, G., & Coyle, J. T. (1998). The role of glutamatergic neurotransmission in the pathophysiology of alcoholism. *Annual Review of Medicine, 49*(1), 173–184. https://doi.org/10.1146/annurev.med.49.1.173
48. Vigouroux, A., Garret, C., Lascarrou, J.-B., Martin, M., Miailhe, A.-F., Lemarie, J., ... & Canet, E. (2021). Alcohol withdrawal syndrome in ICU patients: Clinical features, management, and outcome predictors. *PLoS ONE, 16*(12), Article e0261443. https://doi.org/10.1371/journal.pone.0261443
49. Virag, M., Kovács, R., Márovics, G., Tóth, L., Sandor, B., Vörös, P., ... & Maróti, P. (2025). Bridging healthcare gaps through specialized mobile healthcare services to improve healthcare access and outcomes in rural Hungary. *Scientific Reports, 15*, Article 12692. https://doi.org/10.1038/s41598-025-97447-9
50. Wai, J., Aloezos, C., Mowrey, W., Baron, S., Cregin, R., & Forman, H. L. (2019). Using clinical decision support through the electronic medical record to increase prescribing of high-dose parenteral thiamine in hospitalized patients with alcohol use disorder. *Journal of Substance Abuse Treatment, 99*, 117–121. https://doi.org/10.1016/j.jsat.2019.01.017
51. Wojnar, M., Bizoń, Z., & Wasilewski, D. (1999a). Assessment of the role of kindling in the pathogenesis of alcohol withdrawal seizures and delirium tremens. *Alcoholism: Clinical and Experimental Research, 23*(2), 204–208. https://doi.org/10.1111/j.1530-0277.1999.tb04100.x
52. Wojnar, M., Bizoń, Z., & Wasilewski, D. (1999b). The role of somatic disorders and physical injury in the development and course of alcohol withdrawal delirium. *Alcoholism: Clinical and Experimental Research, 23*(2), 209–214. https://doi.org/10.1111/j.1530-0277.1999.tb04101.x
53. Wojnar, M., Wasilewski, D., Matsumoto, H., & Cedro, A. (1997). Differences in the course of alcohol withdrawal in women and men: A Polish sample. *Alcoholism: Clinical and Experimental Research, 21*(8), 1351–1355. https://doi.org/10.1111/j.1530-0277.1997.tb04461.x