

Review Article

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Real-World Patterns of Anti-Seizure Medication Utilization in Epilepsy: A Scoping Review

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Abstract

Background: Epilepsy is a chronic neurological disorder affecting around 50 million people worldwide, regardless of sociodemographic factors. Studying antiseizure medication (ASM) utilization is essential to optimize treatment outcomes and reduce care gaps by ensuring timely access to effective therapies. **Objective:** This review aimed to evaluate real-world utilization patterns of anti-seizure medications (ASMs) among individuals diagnosed with epilepsy.

Methods: A scoping literature review was conducted using ScienceDirect, PubMed, and Google Scholar, covering studies from the past 20 years. Keywords included “anti-seizure medications,” “antiepileptic,” “epilepsy,” “drug utilization,” and “real-world evidence.” Duplicates were removed using Rayyan software. Only original English-language articles with full-text access were included. The review adhered to PRISMA-Scr guideline and was performed by a team of pharmacists and neurologists. Data extraction was independently carried out by two reviewers and summarized narratively with tables and diagrams.

Results: A total of 40 studies met the inclusion criteria, with 26 published in the last decade; 29 originated from Asian countries. Adult males (18–60 years) were the predominant population studied. Retrospective and prospective observational designs were most common. Monotherapy was generally preferred over polytherapy. Traditional ASMs like Sodium Valproate was most prescribed followed by Phenytoin, Carbamazepine, and Clobazam, though newer agents such as Levetiracetam, Lamotrigine, Pregabalin, and Gabapentin were also used.

Conclusion: Traditional ASMs continue to dominate, particularly in low- and middle-income countries, due to limited access to newer options. Further research is needed to address knowledge gaps in sex-specific responses, special populations, real-world use of new ASMs, and factors influencing discontinuation.

Keywords: Anti-seizure medications, Monotherapy, Levetiracetam, Phenytoin, Sodium Valproate, low- and middle-income countries

Abbreviations: ASM: Anti-Seizure Medications; ILAE: International League Against Epilepsy; IBE: International Bureau for Epilepsy; PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses; LMICs: Low- and Middle-Income Countries; WHO: World Health Organization; TDM: Therapeutic Drug Monitoring; ADR: Adverse Drug Reaction; QoL: Quality of life; GTCS: Generalized Tonic Clonic Seizure; ATC: Anatomical Therapeutic Chemical; DDD: Daily Defined Dose; EDL: Essential Drug List

Introduction

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures—defined operationally as two or more seizures occurring at least 24 hours apart. It affects around 5 million people annually, with a disproportionate burden in low- and middle-income countries (LMICs): 139 per 100,000 versus 49 per 100,000 in high-income countries. Nearly 80% of epilepsy cases occur in LMICs. While causes remain unknown in approximately 50% of cases, known risk factors include brain injury, infections, stroke, tumors, and genetic predisposition. The strongest predictors of recurrence are known etiology and abnormal EEG findings. People with epilepsy face a threefold higher risk of premature death and often experience stigma, discrimination, and financial hardship due to treatment costs and loss of productivity. Despite up to 70% of patients achieving seizure freedom with proper care [1], treatment gaps persist—particularly in LMICs—due to limited healthcare access, cultural beliefs, and reliance on traditional remedies [2]. Global initiatives led by the WHO, ILAE, and IBE aim to reduce the burden through awareness, policy, and improved care [3,4]. This scoping review examines real-world antiseizure medication (ASM) utilization, aiming to understand prescribing patterns, treatment strategies, adherence, and outcomes across diverse healthcare settings.

Methodology

Eligibility criteria

Inclusion Criteria

(1) Full-text peer-reviewed articles (2004–2024), in English. (2) Observational, cross-sectional, cohort, prospective, retrospective, database-based, or real-world studies. (3) Studies on epilepsy patients prescribed at least one ASM. (4) Focus on drug classes, monotherapy/polytherapy, and specific ASM use.

Exclusion Criteria

(1) Animal studies, reviews, editorials, abstracts, commentaries, and qualitative research. (2) Studies on patients without ASM prescriptions or with comorbid psychiatric or cognitive disorders. (3) Articles not addressing ASM utilization or prescribing patterns. (4) Non-peer-reviewed or non-English articles, or those outside the time window.

Search strategy

Databases: PubMed, Science Direct, and Google Scholar.

Keywords: antiepileptic, anti-seizure medications, drug utilization, epilepsy, and real-world evidence (using Boolean operators and MeSH terms).

Only full-text articles in English were included; gray literature was excluded.

Selection of sources of evidence

The review followed Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) framework [5] and was con-

ducted by a team of pharmacists and neurologists. Following the search, all identified records were reviewed and duplicates excluded. Thereafter, titles and abstracts were assessed for inclusion. The remaining studies full texts were screened against the inclusion criteria and the reasons for exclusion were identified and recorded. This process was carried out using the reference management software 'Rayyan' [6]. Any discrepancy that may arise regarding evidence selection was resolved through discussion and consensus with a third reviewer.

Data charting process

A standardized extraction tool was used to collect: study details (authors, year, country, design), prescribing trends (age, sex, mono/polytherapy, drug switching), common ASMs, prescription errors, adverse effects, drug interactions, cost, adherence, quality of life, and seizure-free outcomes.

Result

The data screening and extraction process is illustrated in Figure 1. Out of 13,452 initial hits, 40 eligible studies were included after removing duplicates, non-English texts, inaccessible articles, and those not meeting quality or focus criteria.

Study Characteristics

From 13,452 articles, 40 were included. Most (75%) were published post-2014. Geographically, 22.5% came from high-income countries, and 77.5% from LMICs. Asia accounts for the majority of real-world ASM utilization studies (n=29) especially from India (Table 1) followed by Europe (n=6) (Table 2), and others (n=6) (Table 3), reflecting active clinical research and diverse prescribing trends. Study designs included cross-sectional (8), prospective (12), retrospective (12), cohort (6), population-based (3), and database studies (4). In 19 studies sample size <300 while >300 in 14 studies.

Drug utilization patterns

Monotherapy predominated globally, especially in Europe with polytherapy remaining more frequent in low-resource settings. Valproate remains the most widely prescribed anti-seizure medication globally, followed by Levetiracetam and Carbamazepine. Phenytoin and Lamotrigine maintain significant use, especially in resource-limited settings and pediatric populations. Traditional ASMs dominates in LMICs and newer ASMs were limited and more common in high-income countries. Valproate dominates usage in Asia and the Americas, while Levetiracetam and Lamotrigine are preferred in Europe and Oceania respectively. Africa shows predominant use of cost-effective Phenobarbitone due to accessibility factors. Overall, a shift toward safer and newer ASMs like levetiracetam and lamotrigine is evident.

Factors influencing drug utilization

Male predominance was observed in 25 studies. Special populations such as pediatrics (11), geriatrics (4), and pregnant women (3) were underrepresented. Most researches focus on generalized epilepsy. Adverse effects were reported in 7; cost analysis in 4; DDD

comparisons in 2 and seizure-free outcomes in 4 studies. Limited researches related drug interactions, prescription errors, and qual-

ity of life were noted. Generic prescribing was common, especially in India (up to 94%).

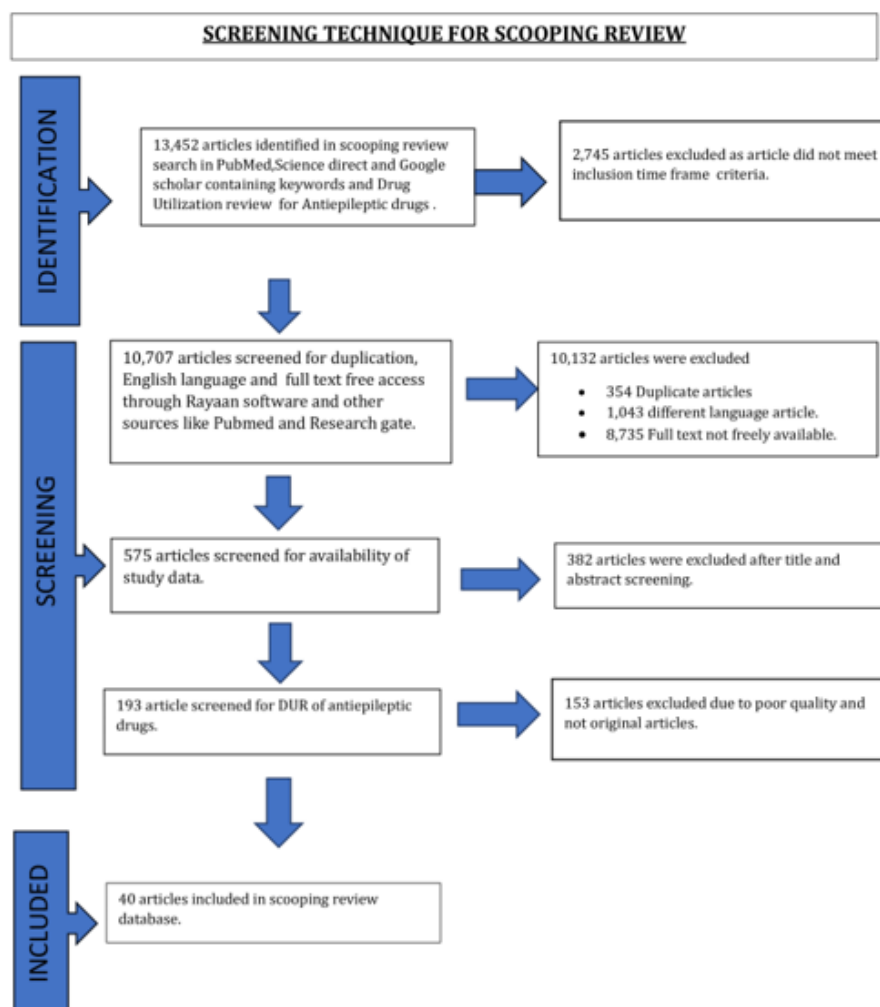


Figure 1: Data screening and extraction.

Table 1: Antiseizure medication utilization study from Asia (India, Malaysia, Hong Kong, Korea).

Author, Country, Study Design / Sample Size	Most Used Therapy & Commonly Used Drugs	Major Observations
Maity et al. 2011, India [7] Retrospective observational study (n=210)	Monotherapy (63.8%): Carbamazepine (52.8%), Valproate (37%), Phenytoin (19%), Phenobarbital (10.9%); common combinations Valproate+-Carbamazepine, Valproate+Clonazepam.	Males 56%; 52.4% partial seizures; newer ASMs rare; TDM used in 20.5% for uncontrolled seizures/adverse effects.
Pal et al. 2011, India [8] Retrospective hospital-based study (n=529)	Dual therapy common (55.3%): Sodium Valproate (42.4%), Phenytoin (23.1%), Carbamazepine (21%).	59.1% male; 47.7% aged 1–14 yrs; mostly tonic-clonic and complex partial seizures; 86.5% used essential drugs; mild ADRs in females.
Haroon et al. 2012, India [9] Prospective study (n=134)	Polytherapy common (68.7%): Sodium Valproate (37.8%), Carbamazepine (31.1%), Phenytoin (20%); newer: Clobazam (50.6%), Levetiracetam (21%), Lamotrigine (18%).	Males 67.9%; 11–30 yrs common; newer ASMs costlier; QoL similar between old/new drugs.

Vettikkadan et al. 2014, India [10] Prospective observational study (n=38)	Monotherapy (57.9%): Phenytoin (92.1%), Diazepam (36.84%), Sodium Valproate (7.89%).	Majority male (84.21%); frequent mild/moderate drug interactions (e.g., Phenytoin with Ranitidine/Diazepam).
Kousalya et al. 2014, India [11] Cohort study (n=170)	Monotherapy predominant (70.5%); Sodium Valproate most prescribed (37.02%).	Males 54.7%; idiopathic generalized seizures common; 9 ADRs and 30 prescriptions with interactions.
Mistry et al. 2014, India [12] Cross-sectional single centre (n=430)	Monotherapy (73.5%): Carbamazepine (73.8%) in focal, Sodium Valproate (89.5%) in generalized seizures.	Children majority (69.8% boys); irritability and drowsiness noted as ADRs.
Ramya et al. 2015, India [13] Prospective observational study (n=181)	Monotherapy (72%): Phenytoin most used, followed by Sodium Valproate.	Females 56%; children 1–5 yrs common; seizure-free rate 74%; ADRs 6.6%.
George et al. 2015, India [14] Cross-sectional study (n=200)	Mono:Poly = 1:1; Clobazam (37%), Phenytoin (25.5%), Levetiracetam (23%), Oxcarbazepine (21.5%), Carbamazepine (21%).	Partial seizures (58%) common; polytherapy linked to more ADRs; no significant QoL differences between old/new ASMs.
Mane et al. 2015, India [15] Prospective observational study (n=275)	Phenytoin (24%), Valproate (16.36%) common.	Males 58.69%; GTCS most common; brand-name prescriptions predominated; high annual patient cost.
Newale et al. 2016, India [16] Cross-sectional observational study (n=973)	Levetiracetam (59.9%), Valproate (16.3%), Clobazam (14.8%), Phenytoin (13.6%).	Males 61.3%; generalized seizures 81.1%; seizure control achieved in 95%.
Patel et al. 2016, India [17] Prospective observational study (n=160)	Monotherapy 70.6%; pregabalin most frequently prescribed, followed by phenytoin.	64.4% males; 50.6% prescriptions for epilepsy, remainder for other indications.
Parveen et al. 2017, India [18] Prospective observational study (n=65)	Monotherapy 50.76%: Phenytoin (86%), Diazepam (20%), Sodium Valproate (18%), Carbamazepine (14%), Levetiracetam (12%), Midazolam (11%).	80% male; 20–29 yrs common; GTCS 66.1%; rural > urban.
Magar et al. 2018, India [19] Cross-sectional observational study (n=593)	Monotherapy 53% and polytherapy 47%; Phenytoin (32%), Carbamazepine (25%), Valproate (21%).	55% male; age 21–40 yrs common; GTCS 55.7%; comorbidities in 30%.
Chandrarathna et al. 2019, India [20] Retrospective study (n=100)	Polypharmacy 98%: Phenytoin (40%), Sodium Valproate (38%), Midazolam (23%); Levetiracetam (32%) among newer ASMs.	GTCS 79%; 42% generic prescribing; 66% injectable formulations; 38% co-prescribed antibiotics.
Raphel et al. 2019, India [21] Prospective study (n=30)	Monotherapy oral 38%: Clobazam (43.24%), Levetiracetam (32.43%) in pediatric cases.	Partial adherence to guidelines in pediatric prescribing.
Singh et al. 2019, India [22] Prospective observational study (n=100)	Dual therapy 56%: Clobazam (31%), Phenytoin (19.7%).	Mostly males 56% aged 11–30; older ASMs used in 78%; compliance 73%; low ADRs.
Christian et al. 2020, India [23] Prospective observational cross-sectional (n=132)	Monotherapy 31% and dual therapy 41%: Midazolam (41%), Phenytoin (25%), Sodium Valproate (13%), Clobazam (13%).	Majority boys 56% aged 2–12 yrs; febrile convulsions 40%.
Sori et al. 2020, India [24] Retrospective study (n=386)	Monotherapy 68.39%: Levetiracetam (42.48%); polytherapy 31.6% (Levetiracetam+Carbamazepine 12%).	Males 56.47%; GTCS 63.98%.
Guttula et al. 2020, India [25] Prospective study (n=200)	Monotherapy 74.5%: Phenytoin (41.6%), Clobazam (24.8%), Sodium Valproate (23.5%); Dual and triple therapy combinations reported.	Males 58.5%; children 56% (2–12 yrs).
Kardani et al. 2021, India [26] Cross-sectional observational (n=120)	Polytherapy 52.5%; common drugs Carbamazepine (30%), Phenytoin (25%), Levetiracetam (21%).	56% male; focal epilepsy 63%; 80% prescriptions by generic name; highest adherence with monotherapy.
Mandal et al. 2021, India [27] Prospective cross-sectional observational (n=102)	Polytherapy 69.7%; Clobazam (53.9%), Valproic acid (51.9%).	Males 55.9%; mean age 29.7 yrs; most doses below ATC-DDD.
Khoshdel et al. 2022, India [28] Prospective observational (n=100)	Monotherapy 83.7%: Valproic acid (36.7%), Carbamazepine (17.1%).	66% male; generalized seizures 60%; prescription issues (missing generics 31%, legibility 15%).
Rai et al. 2022, India [29] Retrospective observational (n=331)	Monotherapy 75.53%: Sodium Valproate (46.1%), Phenytoin (30.13%), Carbamazepine (10%).	67.3% male; GTCS 68%; 95% prescriptions used generics; majority from WHO/national EDL.

Marurhi et al. 2023, India [30] Prospective questionnaire-based cross-sectional (n=200)	Monotherapy 54.5%: Phenytoin (47.8%), Lorazepam (19.1%), Sodium Valproate (8.7%).	70% male; age 21–30 yrs; high adherence; cost differences across ASMs.
Kuruva et al. 2024, India [31] Prospective observational study (n=126)	Monotherapy predominant: Levetiracetam (87%), Lacosamide (14.28%).	58.7% male; most patients aged 41–50 yrs (14.2%).
Hasan et al. 2010, Malaysia [32] Cross-sectional prospective study (n=70)	Monotherapy 54.3%: Sodium Valproate (36.8%), Carbamazepine (30.4%), Lamotrigine (10.4%).	62.9% male; partial seizures 47.2%; older ASMs (Carbamazepine) showed better seizure control.
Kwong et al. 2012, Hong Kong [33] Cohort (n=14,474)	Valproic acid most prescribed, then Carbamazepine and benzodiazepines; Phenobarbital common in youngest.	2005–2009: stable Valproate use; Carbamazepine declined 20%; Levetiracetam ↑4-fold; Oxcarbazepine ↑15-fold.
Kim et al. 2024, Korea [34] Retrospective population-based cohort (n=6,746)	Add-on: Lamotrigine, Levetiracetam, Oxcarbazepine showed better compliance and lower cost vs Carbamazepine, Topiramate, Valproate.	65.5% remained on index add-on; 76.8% adherence

ASM-Antiseizure medication; TDM-Therapeutic drug monitoring; ADR-Adverse drug reaction; QoL-Quality of life; GTCS-Generalized tonic clonic seizure; ATC-Anatomical therapeutic chemical; DDD-Daily defined dose, EDL-Essential drug list

Table 2: Antiseizure medication utilization study from Europe (Denmark, Croatia, Germany, UK, Sweden, Netherlands).

Author, Country, Study Design / Sample Size	Most Used Therapy & Commonly Used Drugs	Major Observations
Tsiropoulos et al. 2006, [35] Denmark — Database cohort study (n=15,604)	Monotherapy 79–82%: Carbamazepine, Phenobarbital, Oxcarbazepine.	ASM use rose 9.3→12.1/1,000 (1993–2002); 19.7% decline for epilepsy; increased use for pain & mood disorders.
Bielen et al. 2009, Croatia [36] Population-based survey (n=966)	Monotherapy > polytherapy; Barbiturates (37%) and Carbamazepine (37%); Valproate higher in children (51%).	67.9% male; ASM use correlated with age; barbiturate prescriptions increased in older groups.
Hamer et al. 2012, Germany [37] Retrospective observational (n≈70,011,508)	Monotherapy 75%: Valproate (29.8%), Carbamazepine (26.4%), Lamotrigine (21.4%), Levetiracetam (16.9%); elderly more often Phenytoin/Primidone.	Prevalence 9.1/1,000; family physicians issued 44.5% prescriptions; ASM costs 1% of total meds.
Nicholas et al. 2012, UK [38] Cohort (n=63,586)	Monotherapy 72.6%: Carbamazepine, Valproates; rising Lamotrigine & Levetiracetam; declining barbiturates & Phenytoin.	Newer ASMs more in younger patients, especially women 15–44 yrs; older adults used long-established drugs.
Karlsson Lind et al. 2018, Sweden [39] Observational cross-sectional (n=68,013)	Monotherapy predominant (98%): Valproic acid (38%) in boys; Lamotrigine (34%) in girls.	ASM use slightly higher in boys; increased with age from preschool to adolescents.
Houben et al. 2022, [40] Netherlands Population-based data (1998–2019) (n=446,169)	In pregnancy: increased use of safer ASMs and newer ASMs with uncertain risk; high-risk ASMs declined (24.8→14.5/10,000); topiramate rose (0→6.7/10,000).	Rise in safest ASMs (0.7→18.0/10,000) and uncertain-risk ASMs (5.3→13.4/10,000) during pregnancy.

Table 3: Antiseizure medication utilization study from Africa (Ethiopia), Americas (Canada, Brazil, Colombia) and Multinational (Australia + Nordic cohort).

Author, Country, Study Design / Sample Size	Most Used Therapy & Commonly Used Drugs	Major Observations
Gurshaw et al. 2014, Ethiopia [41] Retrospective cross-sectional study (n=290)	Monotherapy 54.5%; Dual therapy 35.9%: Phenobarbitone (62.3%), Phenytoin (30.9%).	Male 58.6%; GTCS 80%; 56.7% seizure-free at 3-year follow-up.
Berhe et al. 2022, Ethiopia [42] Hospital-based cross-sectional (n=454)	Monotherapy 83.7%: Phenobarbitone (51.3%), Phenytoin (19.4%).	Majority male 58.6%; GTCS 93.3%; poor adherence and shorter therapy duration linked to uncontrolled seizures.
Freitas-Lima et al. 2013, Brazil [43] Cross-sectional retrospective survey (n=112)	Polytherapy 60.7%: Carbamazepine (72.3%), Clobazam (58.9%), Lamotrigine (36.6%).	ASM dosages 80–120% DDD; avg ASM load 3.3; 76% reported no adverse effects.

Machado-Alba et al. 2016, Colombia [44] Retrospective cross-sectional (n=373)	Monotherapy 65.4%: Valproic acid (53.1%), Carbamazepine (33.2%).	47.7% ASMs for epilepsy; 52.3% for other indications (neuropathic pain, affective disorders, migraine).
Shouman et al. 2022, Canada [45] Retrospective population-based cohort (n=273,492)	Among pregnant women: Clonazepam (45.9%), Gabapentin (18.4%), Carbamazepine (9.3%).	ASM use stable in epilepsy but increased in non-epileptic cases across 273,492 pregnancies.
Cohen et al. 2020 Multi-country (Denmark, Finland, Iceland, Norway, Sweden, New South Wales, Australia) [46] Nationwide prescription data (n=75,249)	Variation: Lamotrigine most used in Nordic countries; Clonazepam in the U.S.; Valproate in Australia. Polytherapy prevalence varied by country (Australia 15% vs Iceland 9%).	Analyzed ASM use in 4.9 million pregnancies; prevalence ranged 6.4–34.5 per 1000 across countries.

ASMs: Antiseizure medications, ATC: Anatomical therapeutic chemical, ADR: Adverse drug reaction, DDD: Daily defined dose, EDL: Essential drug list

Discussion

Epilepsy remains a major neurological disorder, with ASMs central to its management. Global ASM use varies due to healthcare infrastructure, economic factors, and prescribing habits [1]. Research has grown with newer drugs and increased awareness of epilepsy's burden. ASMs are more commonly prescribed to males, possibly due to biological and access-related factors, including neurosteroid and neurodevelopmental differences [47]. Data on pediatric, geriatric, and pregnant populations are limited due to ethical and regulatory challenges, despite concerns like cognitive side effects from drugs such as phenobarbital and topiramate in children [48]. High-income countries, including Germany [37] and the UK [38], increasingly use newer ASMs for women of reproductive age to avoid teratogenic risks.

Studies from the USA, UK, India, Ethiopia, and others include both adults and children, though geriatric data remain sparse. Generalized tonic-clonic seizures are most common. Monotherapy is preferred for its safety and adherence benefits, with high rates in Sweden (98%) [39], Ethiopia (83.7%) [42], and Denmark (79%) [35], and lower rates in India (30%) and Colombia (47.7%) due to case complexity or drug access. Polytherapy, used in refractory cases, increases adverse event risks [7,14].

Older ASMs like phenytoin, carbamazepine, valproate, Phenobarbital dominate in low- and middle-income countries due to cost and availability. In Ethiopia, phenobarbital makes up 51.3% of prescriptions [42]; phenytoin and valproate remain common in India [15,30]. High-income countries prefer newer ASMs like levetiracetam, lamotrigine, and clobazam [33,38], though their use is limited in LMICs. India shows high generic use (94%) [21], but treatment costs may reach 53% of per capita income [15]. There is a clear regional variation in ASM preferences, influenced by availability, economic constraints, and evolving clinical guidelines. The gradual shift toward newer-generation ASMs in high-income regions reflects a global trend toward improved safety and tolerability profiles.

Off-label ASM use for conditions like neuropathic pain and bipolar disorder is rising, especially in Denmark and Colombia [35,44], affecting availability and cost. Older ASMs remain common in elderly German patients [37] and Croatian children [36], while the UK favors lamotrigine in women of childbearing age [38]. These trends highlight global disparities and the need for more inclusive,

evidence-based epilepsy treatment.

Knowledge Gap

Sex-based differences in epilepsy and treatment response remain understudied, with gaps in ASM use among pediatric, geriatric, and pregnant populations due to ethical and practical barriers. Addressing these requires real-world data, adaptive trials, AI/ML tools, global collaboration, and regulatory support. Newer ASMs are underutilized despite their benefits, highlighting the need for long-term data on safety, cost-effectiveness, and quality of life. Rational prescribing, adherence studies, generic vs. branded comparisons, and standardized WHO indicators are crucial, especially in low-resource settings. Enhanced pediatric reporting and international cooperation can help reduce global treatment disparities.

Implications for Practice

This review highlights the need for personalized, evidence-based ASM prescribing that considers age, sex, comorbidities, drug access, and socioeconomic factors. Monotherapy should be prioritized, especially in primary care, to improve adherence and reduce adverse effects. While newer ASMs are more common in high-income countries, policy action is needed to improve access in low- and middle-income regions. Standardizing prescribing using WHO indicators and national essential medicine lists can promote equity and responsible use. Expanding research in special populations and strengthening patient education, adherence support, generic vs. branded assessments, supply stability, and off-label prescribing protocols are key to improving epilepsy care.

Limitations

This review is limited by study heterogeneity, uneven geographic representation, and scarce data on special populations. Most studies lack standardized WHO indicators and focus on prescribing trends over outcomes. As a scoping review, it does not assess study quality or causality. Exclusion of grey literature and limited patient-reported and long-term data may narrow the findings.

Conclusion

Global ASM use reflects clinical and economic disparities—newer drugs and monotherapy dominate in high-income countries, while older, affordable ASMs are common in low-resource settings. Limited data in vulnerable groups highlight the need for inclusive

research. Targeted efforts and long-term studies are essential to support rational ASM use worldwide.

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None.

Conflict of Interest

None.

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