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Discontinuation of Antiseizure Medication Before Versus After Hospital Discharge Following Acute Symptomatic Seizures Related to Neonatal Encephalopathy: A Retrospective Cohort Study and Caregiver Survey

Ahmed Ismaiel

ahmedhisham717@gmail.com

Children's Hospital at Montefiore Einstein https://orcid.org/0000-0003-1643-4519

James Barnett

Children's Hospital at Montefiore Einstein

Marianna Castellanos

Children's Hospital at Montefiore Einstein

Shana Yazdanpanah

Children's Hospital at Montefiore Einstein

Elissa Yozawitz

Children's Hospital at Montefiore Einstein

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Abstract

Objective

To evaluate clinical and family-centered outcomes after a practice shift toward discontinuing antiseizure medications (ASMs) before discharge for neonatal encephalopathy (NE)-related acute symptomatic seizures.

Study Design:

Single-center two-part study of infants ≥ 35 weeks' gestation with NE-related acute symptomatic seizures treated with ASMs (2016–2025). Outcomes and caregivers' completed surveys were compared between infants discharged on ASMs and those whose ASMs were discontinued before discharge.

Result

Among 58 infants, 34 were discharged on ASMs, and 24 had ASMs discontinued before discharge. Baseline illness severity was generally similar. Discharge on ASMs was associated with higher neurology-related emergency department visits (26% vs 4%), readmissions (47% vs 13%), ASM-related laboratory monitoring (63% vs 22%), and caregiver-reported treatment burden, including missed/delayed doses, pharmacy needs, costs, sleepiness, and feeding concerns.

Conclusion

These real-world data support guideline-aligned ASM discontinuation before hospital discharge after seizure resolution and highlight lower healthcare utilization and family burden.

Introduction

Neonatal encephalopathy (NE), including hypoxic-ischemic, infectious, and other acute encephalopathic etiologies, is a common cause of acute symptomatic neonatal seizures and antiseizure medication (ASM) exposure.[1,2] Phenobarbital remains the most commonly used first-line ASM, but prolonged exposure has raised concern because of potential adverse neurodevelopmental effects and limited evidence that maintenance therapy improves mortality, neurodevelopment, or later epilepsy after acute symptomatic neonatal seizures.[4–7]

The optimal duration of ASM therapy after neonatal seizure resolution has historically varied across centers. WHO guidance recommended considering ASM discontinuation after sustained seizure freedom, and more recent evidence has further challenged routine continuation after discharge.[3] In the Neonatal Seizure Registry, discontinuation before discharge was not associated with worse functional

neurodevelopment or increased epilepsy risk at 24 months,[8,9] and long-term follow-up to 5–8 years similarly showed no adverse association with childhood IQ, functional development, or post-neonatal epilepsy.[10] These data informed recent ILAE consensus-based recommendations supporting ASM discontinuation before discharge after cessation of acute provoked seizures when there is no concern for neonatal-onset epilepsy.[11]

Beyond neurologic safety, discharge on ASM may require daily medication administration, refills, and outpatient neurology follow-up, creating a potential burden for families. At our institution, practice shifted over time toward early ASM discontinuation before discharge for infants with NE-related acute symptomatic seizures. We conducted a two-part study to evaluate the clinical and family-centered impact of this practice shift during the first year of life.

Methods

Study Design

We conducted a two-part, single-center study to evaluate the impact of early ASM discontinuation before hospital discharge among neonates with NE-related acute symptomatic seizures. First, we performed a retrospective cohort study comparing infants discharged on ASMs with those whose ASMs were discontinued before NICU discharge. Second, we conducted a structured caregiver telephone survey to assess family experience after discharge, including medication-related burden, healthcare utilization, and caregiver confidence in recognizing seizures.

The study was conducted at Montefiore Einstein Weiler Hospital NICU, a tertiary level IV neonatal referral center and therapeutic hypothermia center in the Bronx, New York. Eligible infants were identified through an Epic electronic medical record report using ICD-10 codes for neonatal encephalopathy, hypoxic-ischemic encephalopathy, and neonatal seizures, followed by manual chart review to confirm eligibility.

Eligible subjects were neonates admitted or transferred to the Weiler Hospital NICU between 2016 and 2025 with NE, acute symptomatic seizures, receipt of at least one ASM dose, gestational age ≥35 weeks, and survival to 1 year of age. NE was defined clinically as altered neurologic function in the neonatal period attributed to hypoxic-ischemic, infectious, or other acute encephalopathic etiologies. Infants were excluded if they had major congenital anomalies or had genetic neonatal-onset epilepsy. Infants were categorized by ASM status at NICU discharge. Study size was determined by the number of eligible infants; no formal sample size calculation was performed.

Variables and Outcomes

The primary exposure was ASM status at discharge. Healthcare utilization outcomes through 1 year included neurology-related emergency department (ED) visits, neurology-related hospital readmissions,

and ASM-related laboratory monitoring. Neurology-related ED visits included visits for seizure-like movements, medication concerns, or other neurologic concerns. Neurology-related readmissions included admissions for neurologic evaluation, video EEG monitoring, or seizure management. ASM-related laboratory monitoring included drug levels or laboratory evaluation for potential medication-related adverse effects in outpatient or ED settings.

Neurological outcomes included epilepsy diagnosis and clinically documented neurodevelopmental or neurologic concerns by 1 year of age. Epilepsy diagnosis was based on outpatient neurology documentation by the treating neurologist. Neurodevelopmental outcome was abstracted from outpatient neurology and/or general pediatric follow-up documentation and included documented developmental delay, abnormal muscle tone, focal motor abnormality, or other clinically significant neurologic or developmental concerns.

Baseline perinatal, neurologic, and treatment variables included gestational age, sex, size for gestational age, ethnicity, delivery mode, 10-minute Apgar score, delivery room resuscitation beyond positive pressure ventilation, Sarnat stage when applicable, therapeutic hypothermia, EEG background severity, seizure type and onset, number and type of ASMs, response to initial ASM, ASM duration, MRI/MRS findings, and neurologic examination at discharge.

Neuroimaging and EEG Definitions

Brain MRI and MRS findings were abstracted from clinical radiology reports and classified as normal or abnormal. MRI was considered abnormal if the report described parenchymal brain injury, including hypoxic-ischemic injury, restricted diffusion, abnormal signal intensity, stroke, hemorrhage, or other clinically relevant intracranial injury. MRS was considered abnormal if the report described metabolic abnormalities, including elevated lactate or reduced N-acetylaspartate. At our institution, post-cooling brain MRI with MRS is generally obtained at 5–7 days of life.

EEG background severity was categorized from clinical EEG reports as normal, mild/moderate abnormality, or severe abnormality. Severe EEG background included burst suppression, severe discontinuity, flat or markedly depressed background, or severely abnormal activity.

Caregiver Survey

Caregivers of eligible infants were contacted after chart review and invited to participate in a structured telephone survey (Supplemental Figure 1). Informed consent was obtained before the interview. The survey focused on the first month after discharge from the NICU or rehabilitation facility and assessed medication administration burden, perceived ASM side effects, missed or delayed doses, pharmacy needs, costs, medical contacts, caregiver confidence in recognizing seizures, clarity of the discharge plan, perceived support, seizure-related concerns, and seizure recurrence during the first year of life.

Questions were read as written, with clarification provided only if requested. Spanish-language surveys were supported by a native Spanish-speaking study team member or certified medical interpreter. Open-ended responses were recorded in the caregivers' own words and reviewed by the study team. Survey responses and study data were stored in password-protected files on a secure institutional server.

Statistical Analysis

Baseline characteristics and study outcomes were compared between discharge ASM groups. Continuous variables were summarized using mean with standard deviation when normally distributed or median with interquartile range when not normally distributed. Categorical variables were summarized using frequencies and percentages. Univariable comparisons used chi-square or Fisher exact tests for categorical variables and t-tests or Wilcoxon rank-sum tests for continuous variables, as appropriate. Statistical significance was defined as a two-sided p-value <0.05.

Multivariable regression was not performed because of the limited number of outcome events and risk of model overfitting. A subgroup analysis compared infants who developed epilepsy by 1 year with those who did not to evaluate differences in baseline characteristics. Survey data were analyzed descriptively. Scaled responses were grouped as 0–1 (low/minimal), 2–3 (moderate), and 4–5 (high/severe) for presentation. Missing data were handled using available-case analysis; variables with missing data were not imputed.

Ethical Approval

The Montefiore Einstein Institutional Review Board approved the study (IRB #2016-7132), including an amendment to add the caregiver survey. Informed consent was obtained for caregiver survey participation. The study was performed in accordance with the Declaration of Helsinki.

Results

Participants

A total of 219 charts of infants with neonatal encephalopathy admitted to the NICU between 2016 and 2025 were reviewed for eligibility. After exclusions, the final analytic cohort included 58 infants, of whom 34 were discharged on ASM and 24 had ASM discontinued before NICU discharge (Figure 1).

Baseline Demographic and Clinical Characteristics (Table 1)

Most baseline markers of neurologic illness severity were similar between groups, including Sarnat stage among infants with available staging, EEG background severity, abnormal brain MRI/MRS findings, and abnormal neurologic examination at discharge. Vaginal delivery was more common among infants discharged on ASM.

Seizure and ASM Treatment Characteristics (Table 2)

Seizure type differed between groups, with clinical-only seizures more common in the ASM-discontinued group and electroclinical seizures more common among infants discharged with ASM. Infants discharged with ASM had longer inpatient NICU EEG monitoring than infants whose ASM was discontinued before discharge (median 5.5 days [IQR 4.0–6.0] vs 3.0 days [IQR 3.0–4.25], p=0.005) and received a greater number of ASMs during hospitalization (p=0.02). Day of life at seizure onset was similar between groups. Initial ASMs were phenobarbital (55/58), levetiracetam (2/58), and phenytoin (1/58). Response to initial ASM occurred in 25/34 (74%) infants discharged with ASM and 22/24 (92%) infants whose ASM was discontinued before discharge.

ASM exposure differed substantially between groups. During the first 60 days of life, infants discharged with ASM had a median ASM duration of 60 days [IQR 60–60] compared with 14.5 days [IQR 10–23.25] among infants whose ASM was discontinued before discharge (p<0.001). During the first year of life, median total ASM duration was 4.0 months [IQR 2.0–8.0] in the discharged-with-ASM group compared with 1.0 month [IQR 1.0–1.25] in the discontinued group (p<0.001).

Post-discharge Outcomes Through 1 Year (Table 3)

Infants discharged with ASM had higher neurology-related healthcare utilization. Neurology-related ED visits occurred in 9/34 (26%) infants discharged on ASM compared with 1/24 (4%) infants whose ASM was discontinued before discharge (p=0.03). Neurology-related readmissions occurred in 15/32 (47%) infants with known readmission status in the discharged-with-ASM group compared with 3/23 (13%) infants in the discontinued group (p=0.01). ASM-related laboratory monitoring was also more frequent among infants discharged with ASM (20/32, 63%) than among infants whose ASM was discontinued before discharge (5/23, 22%; p=0.005).

Epilepsy diagnosis by 1 year was more common among infants discharged on ASM (9/32, 28%) than among infants whose ASM was discontinued before discharge (1/23, 4%; p=0.03). Abnormal documented neurodevelopmental or neurologic concerns occurred in 26/34 (76%) infants discharged with ASM and 14/24 (58%) infants whose ASM was discontinued before discharge (p=0.16). Follow-up status was unknown for 3 infants for readmission, laboratory monitoring, and epilepsy status. Sarnat staging was available for 49 infants who underwent therapeutic hypothermia; the remaining 9 infants had infectious NE.

Epilepsy vs No Epilepsy Subgroup Analysis

A subgroup analysis comparing infants with and without epilepsy by 1 year showed no significant differences in most baseline clinical characteristics, including gestational age, Apgar score, sex, delivery mode, resuscitation, Sarnat stage, EEG background, or discharge neurologic examination (Supplemental Table 1). Infants who developed epilepsy were more likely to have electroclinical seizures and abnormal MRS findings; abnormal brain MRI approached statistical significance.

Caregiver Survey Results (Figure 2)

Of 58 eligible families, 31 completed the telephone survey, including 20 families of infants discharged on ASM and 11 families whose ASM was discontinued before discharge.

Among families discharged on ASM, most caregivers reported good medication adherence, with 14/20 (70%) reporting 0–1 missed or delayed doses per week; however, 6/20 (30%) reported two or more missed or delayed doses per week. Medication administration commonly involved more than one caregiver, with 16/20 (80%) families reporting two regular caregivers and 4/20 (20%) reporting more than two caregivers. Perceived ASM-related sleepiness was rated high/severe by 9/20 (45%) families. Feeding difficulty attributed to ASM was reported with more variability, including high/severe ratings in 4/20 (20%) families. Caregiver sleep disruption related to medication timing or seizure concerns was rated high/severe by 10/19 (53%) responding families. During the first month after discharge, 6/20 (30%) families reported calling a physician or presenting to the ED for ASM- or seizure-related concerns, and 6/20 (30%) reported out-of-pocket ASM-related costs.

Among families whose infants were not discharged on ASM, concern about seizure recurrence after discharge was generally low, with 6/11 (55%) rating worry as minimal, 3/11 (27%) as moderate, and 2/11 (18%) as high. Most families in this group reported high confidence in recognizing seizures and knowing when to seek help (8/11, 73%) and high clarity of the discharge seizure plan (9/11, 82%). Three families (27%) sought medical advice for seizure concerns during the first month after discharge.

Caregiver-reported events concerning for seizures after discharge were reported by 13/20 (65%) families discharged on ASM and 2/11 (18%) families not discharged on ASM. Among infants discharged on ASM, ASM was discontinued without restarting in 10 infants, 5 remained on ASM through 1 year of age, and 5 restarted ASM after discontinuation. Among infants not discharged on ASM, 1 infant restarted ASM by 1 year.

Open-ended responses highlighted the emotional burden of seizure uncertainty, medication responsibility, and transition from NICU observation to home care. Caregivers described fear that seizures could occur unpredictably, worry about harm from recurrent seizures, stress about missed or incorrect doses, and uncertainty when seizures were electrographic-only without visible clinical signs. When asked what could have been improved, families most often requested clearer anticipatory

guidance, structured discharge education, and a formalized plan for what to do if concerning events occurred at home.

Discussion

In this single-center cohort study with caregiver survey, early discontinuation of ASM before discharge after resolution of NE-related acute symptomatic seizures was associated with lower post-discharge neurology-related healthcare utilization and less family-reported treatment burden. Infants discharged on ASM had higher rates of neurology-related ED visits, neurology-related readmissions, and ASM-related laboratory monitoring. Families also described practical challenges with medication administration, missed or delayed doses, pharmacy needs, costs, sleep disruption, and perceived side effects. In contrast, families whose infants were discharged without ASM did not report greater seizure-related worry and generally reported confidence in recognizing seizures and understanding the discharge plan.

These findings support current guideline-aligned practice with real-world, family-centered data. WHO guidance and recent ILAE consensus recommendations support discontinuing ASMs after resolution of acute provoked neonatal seizures when there is no concern for neonatal-onset epilepsy.[3,11] Prior multicenter studies have focused primarily on epilepsy and neurodevelopmental safety, showing no increase in epilepsy or adverse developmental outcomes after ASM discontinuation before discharge.[8–10,13] Our study extends this literature by showing that continued ASM exposure at discharge may also be associated with downstream utilization and family burden, including laboratory monitoring, urgent evaluations, and medication-management demands at home.

Early ASM discontinuation is clinically plausible for acute symptomatic neonatal seizures, as later epilepsy risk is likely driven more by the underlying brain injury, seizure burden, and evolving pathology than by continued prophylactic ASM exposure after seizure resolution.[4,7,12] Avoiding unnecessary maintenance therapy may therefore reduce exposure to medications such as phenobarbital, which remains effective for acute seizure control but has raised preclinical and clinical concern with prolonged use.[5,6].

The higher epilepsy rate in the ASM continuation group should be interpreted cautiously. Although baseline clinical severity measures were similar between groups, discharge ASM may have reflected clinicians' concern for infants perceived to be at higher risk for later epilepsy. This is supported by the subgroup analysis, in which infants who developed epilepsy were more likely to have prolonged electrographic seizures and abnormal MRS findings.

This study has limitations. The single-center design and relatively small sample size limited statistical power and precluded multivariable adjustment. Seizure classification was based on retrospective clinical documentation and EEG reports; as in prior neonatal seizure studies, clinical-only events may have included non-epileptic movements when EEG confirmation was not available before treatment. Neurodevelopmental outcomes were based on outpatient clinical documentation rather than standardized developmental testing. However, these clinical assessments often incorporated

documentation from early intervention services. Caregiver survey responses were also subject to recall and participation bias.

In conclusion, discontinuing ASM before discharge after resolution of NE-related acute symptomatic seizures was associated with lower neurology-related healthcare utilization and lower family-reported treatment burden. These findings support guideline-aligned early ASM discontinuation for appropriately selected infants and highlight the importance of structured discharge education and caregiver-centered seizure action planning.

Declarations

Author Contributions

Ahmed Ismaiel conceptualized the study, designed the project, performed data collection and analysis, interpreted the data, drafted the manuscript, and revised the manuscript. James R. Barnett, Marianna Castellanos, and Shana Yazdanpanah contributed to project development, data collection and/or interpretation, and critical manuscript revision. Elissa G. Yozawitz supervised the study, contributed to study design and interpretation, and critically revised the manuscript. All authors reviewed and approved the final manuscript.

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No funding was received for this study.

Competing Interests

The authors declare no competing interests.

Data Availability

Data are available from the corresponding author upon reasonable request and subject to institutional review board requirements.

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Use of large language model

AI-assisted tools were used only for final writing refinement. These tools did not contribute to study design, data collection, data analysis, interpretation of results, or conclusions. All authors reviewed and approved the final manuscript.

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Tables

Table 1. Baseline Demographic and Clinical Characteristics

Variable	Total N=58	Discharged with ASM N=34	ASM discontinued before discharge N=24	P value
Male sex	28 (48%)	18 (53%)	10 (42%)	0.562
Vaginal delivery	20 (34%)	17 (47%)	3 (13%)	0.0073
Gestational age category				
35-36 weeks	5 (9%)	1 (3%)	4 (17%)	0.149
>=37 weeks	53 (91%)	33 (97%)	20 (83%)	
Birth location				
Inborn	36 (62%)	23 (68%)	13 (54%)	0.297
Outborn	22 (38%)	11 (32%)	11 (46%)	
Abnormal size for gestational age (SGA or LGA)	16 (28%)	9 (26%)	7 (29%)	>0.99
Sarnat stage				
Mild	10 (17%)	6 (17%)	4 (17%)	0.605
Moderate	25 (42%)	15 (42%)	10 (43%)	
Severe	14 (24%)	6 (17%)	8 (35%)	
Resuscitation beyond positive pressure ventilation	38 (66%)	22 (65%)	16 (67%)	>0.99
10-minute Apgar score, median (IQR)	6 (4-8)	6.5 (4.25-8)	6 (4-8)	0.292
EEG				
EEG background (Normal)	11 (19%)	5 (15%)	6 (26%)	0.638
EEG background - Mild/moderate abnormality	37 (64%)	23 (68%)	14 (61%)	
EEG background - Severe abnormality	10 (17%)	6 (18%)	4 (17%)	
Abnormal brain MRI	42 (72%)	26 (76%)	16 (67%)	0.59

Abnormal MRS	19 (33%)	14 (41%)	5 (21%)	0.38
Abnormal neurologic examination at discharge	30 (52%)	19 (56%)	11 (46%)	0.67

Abbreviations: ASM, antiseizure medication; EEG, electroencephalography; IQR, interquartile range; LGA, large for gestational age; MRI, magnetic resonance imaging; MRS, magnetic resonance spectroscopy; PPV, positive pressure ventilation; SGA, small for gestational age.

Table 2. Seizure and Antiseizure Medication Treatment Characteristics

Variable	Discharged with ASM N=34	ASM discontinued before discharge N=24	P value
Seizure type			**0.037**
Clinical seizures only	13 (38%)	17 (71%)	
Electroclinical seizures	16 (47%)	4 (17%)	
Electrographic seizures only	5 (15%)	3 (13%)	
Duration of inpatient EEG monitoring, days, median [IQR]	5.5 [4.0–6.0]	3.0 [3.0–4.25]	**0.005**
Day of life at seizure onset, median [IQR]	1.0 [1.0–2.0]	1.0 [1.0–1.25]	0.920
Number of ASMs used during hospitalization, median [IQR]	1.0 [1.0–2.0]	1.0 [1.0–1.0]	**0.02**
Response to initial ASM therapy	25 (74%)	22 (92%)	0.1
Duration of ASM during the first 60 days of life, median [IQR], days	**60 [60–60]**	**14.5 [10–23.25]**	**<0.001**
Total ASM duration during first year, months, median [IQR]	4.0 [2.0–8.0]	1.0 [1.0–1.25]	**<0.001**

Abbreviations: ASM, antiseizure medication; EEG, electroencephalography; IQR, interquartile range. Note: Continuous variables are reported as median [IQR]. Categorical variables are reported as n/N (%). P-values for continuous variables were calculated using the Mann-Whitney U test, and p-values for categorical variables were calculated using Fisher's exact test.

Table 3. Post-discharge outcomes through 1 year

Outcome	Total	Discharged with ASM (N=34)	ASM discontinued before discharge (N=24)	P-value
Neurology-related emergency department visit	10 (17%)	9 (26%)	1 (4%)	**0.035**
Neurology-related readmission	18 (33%)	15 (47%)	3 (13%)	**0.01**
No neurology-related readmission	37 (67%)	17 (53%)	20 (87%)	
Unknown readmission status	3(5%)	2(6%)	1(4%)	
ASM-related laboratory monitoring	25(45%)	20(63%)	5(22%)	**0.005**
No ASM-related laboratory monitoring	30(55%)	12(38%)	18(78%)	
Unknown laboratory monitoring status	3(5%)	2(6%)	1(4%)	
Epilepsy diagnosis by 1 year	10(18%)	9(28%)	1(4%)	**0.03**
No epilepsy diagnosis by 1 year	45(82%)	23(72%)	22(96%)	
Unknown epilepsy status	3(5%)	2(6%)	1(4%)	
Abnormal neurodevelopmental outcome at 1 year	40(69%)	26(76%)	14(58%)	0.16

Abbreviations: ASM, antiseizure medication; ED, emergency department. **Note:** Outcomes are reported as n/N (%). P-values were calculated using Chi-squared or Fisher's exact test.

Figures

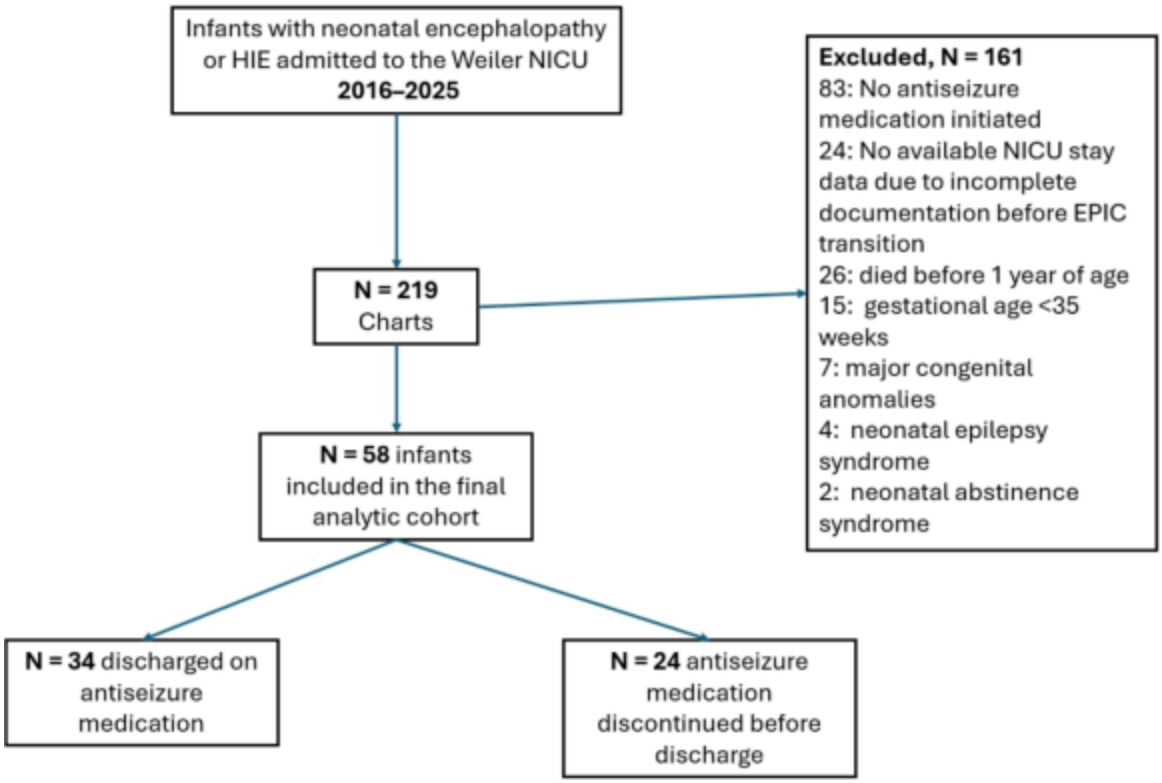


Figure 1

Study flow diagram showing chart screening, exclusions, and final analytic cohort categorized by ASM status at discharge.

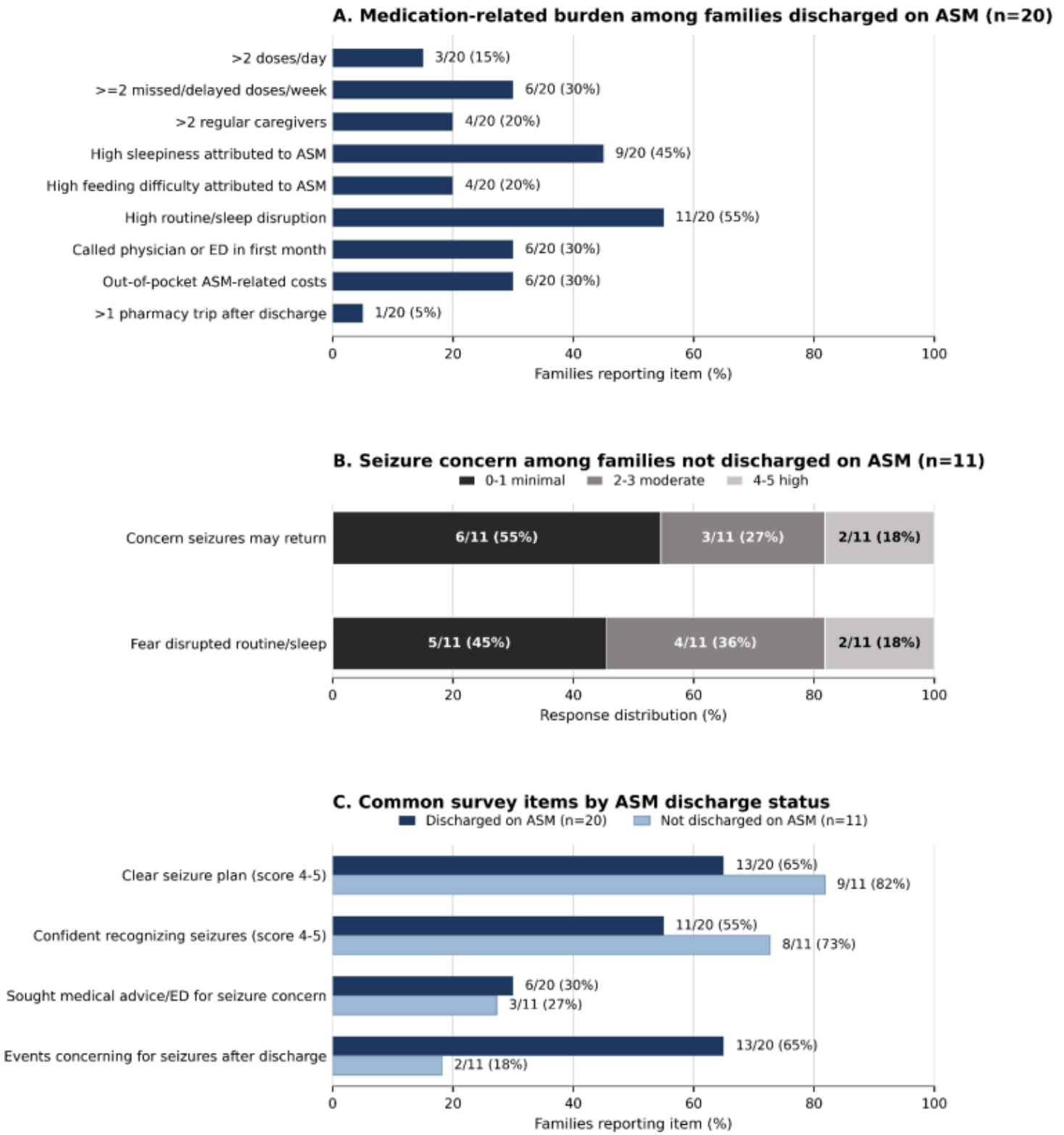


Figure 2

Caregiver-reported experience after discharge by antiseizure medication status. Panel A shows selected medication-related burden items among families discharged on antiseizure medication (ASM; n=20). Panel B shows scaled seizure concern and routine-disruption responses among families not discharged on ASM (n=11). Panel C compares survey items asked of both groups. Values are shown as n/N (%).

High scores were defined as 4-5 on a 0-5 scale unless otherwise specified. Abbreviations: ASM, antiseizure medication; ED, emergency department.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementalFigure1.docx
- SupplementalTable1.docx