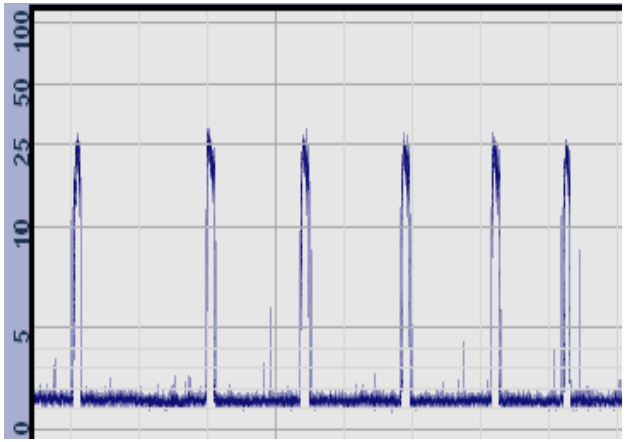
Why we need guidelines for neonatal seizures

Linda de Vries, Lauren Weeke, Kees van Huffelen, Mona Toet



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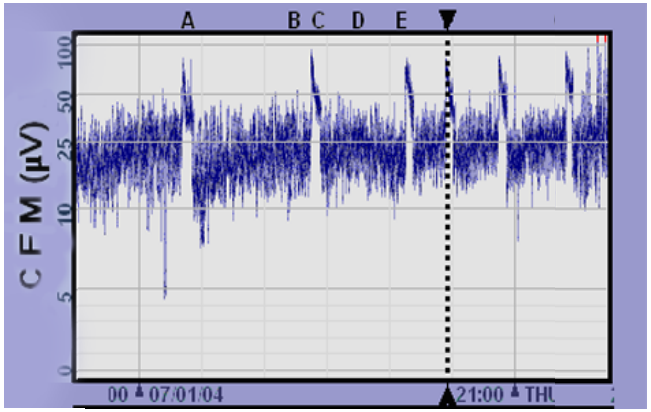

To discuss

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- Who needs monitoring and treatment
- How should we monitor
- How should we treat seizures
- How long should we treat for

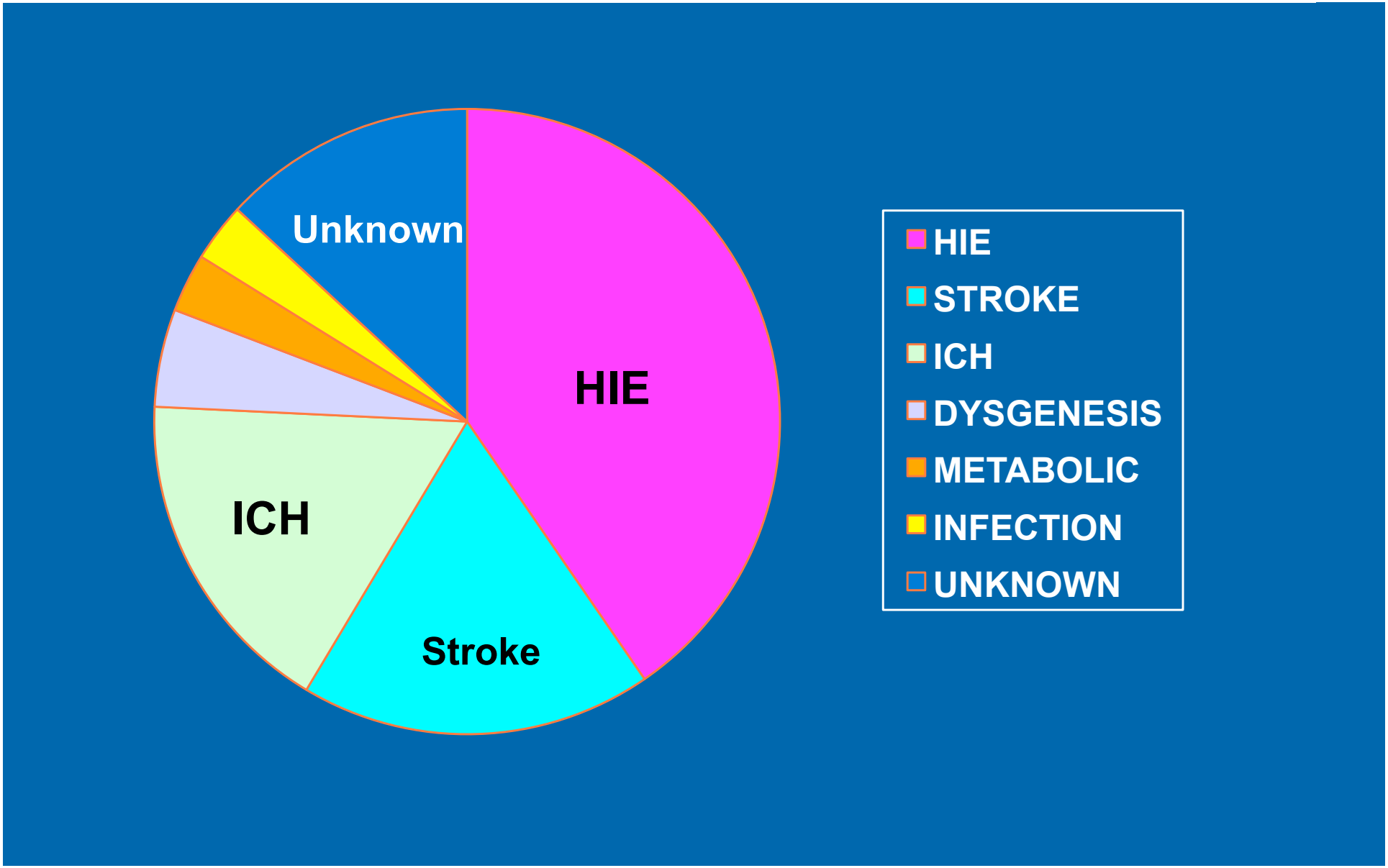
Table 1. Aetiologies and incidence of neonatal seizures in full-term infants.

	Tekgul *et al.* 2006	Mastrangelo *et al.* 2005	Yildiz *et al.* 2012	Ronen *et al.* 1999	Weeke *et al.* 2014
HIE	40%	37.1%	28.6%	40%	46%
ICH	17%	4.8%	17%	18%	12.2%
Stroke	18%	11.3%	-	1 case	13.5%
Infection	3% (CNS only)	9.7%	7.2% (+sepsis)	20% (+ sepsis)	7.6% (+sepsis)
Cerebral dysgenesis	5%	11.3%	4.5%	10%	2.9%
Metabolic disorders	1%	11.3%	10.7%	19% (including hypoglycaemia)	9% (including hypoglycaemia)
Unknown/ idiopathic	12%	1.6%	8.9%	14%	6.3%

HIE: hypoxic-ischaemic encephalopathy; ICH: intracranial haemorrhage.

The Current Etiologic Profile and Neurodevelopmental Outcome of Seizures in Term Newborn Infants

Tekgul et al; Pediatrics 2006; 117(4):1270-80



Murray et al;
Arch Dis Child, FFN 2007

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Electrographic Seizures
n=9 children
526 seizures

Clinical signs present on Video
n=179 seizures
(34%)

Staff detected
n=48/526
of all seizures
(9%)

and 48/179
of all clinical seizures
(27%)

Staff overdiagnosed
Suspected but not EEG confirmed
n= 129/177
(73%)

Distribution of seizure duration among 851 seizures studied. 60% lasted <90 seconds

Shellhaas R.A. et al, Pediatrics 2007

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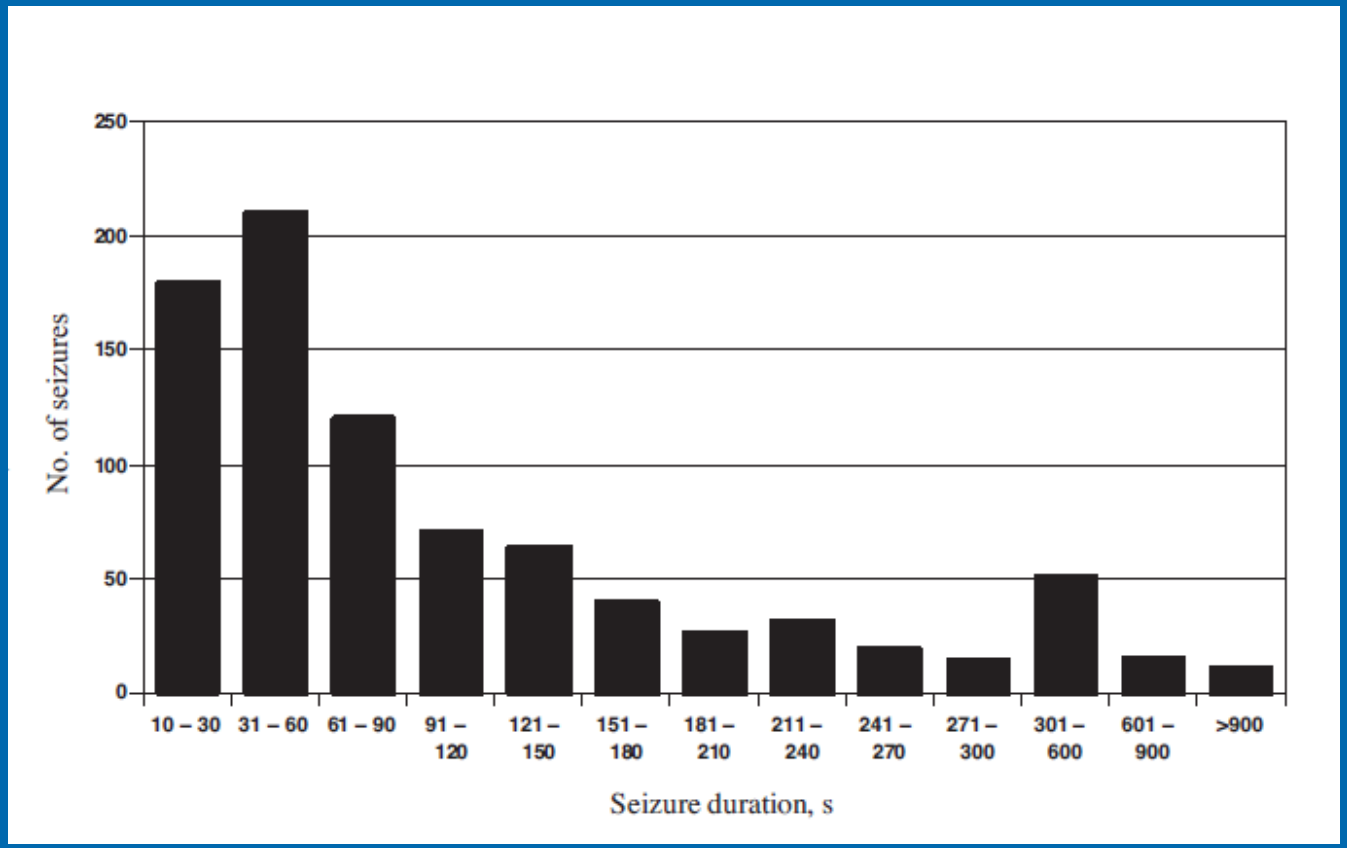

125 conventional EEGs from 121 neonates.

PMA ranged from 34 to 50 weeks.

78% (664/ 851) of the individual seizures were visible in the C3-C4 channel !!

How should we monitor; aEEG

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- Can be started in the level II unit
- Can be used during transportation (lifelines)
- Can be used for many days without need for maintenance when needles are used
- Many infants can be monitored simultaneously

How to monitor: cEEG

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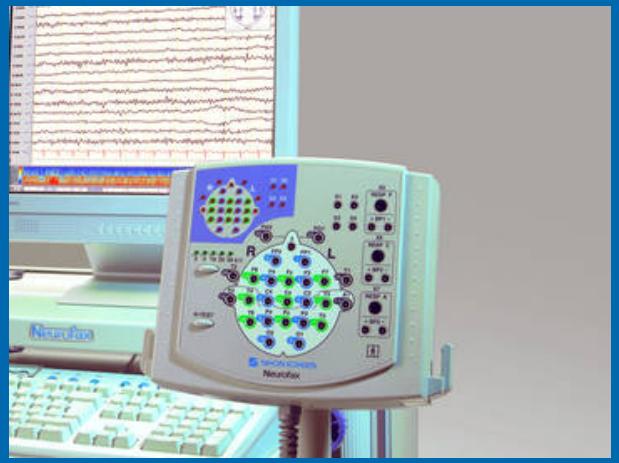
- More reliable to diagnose seizures
- Simultaneous video recording

- Mainly available in level III NICUs
- Few machines available to use simultaneously
- Not many units have access to 24 hr review



How do we treat neonatal seizures

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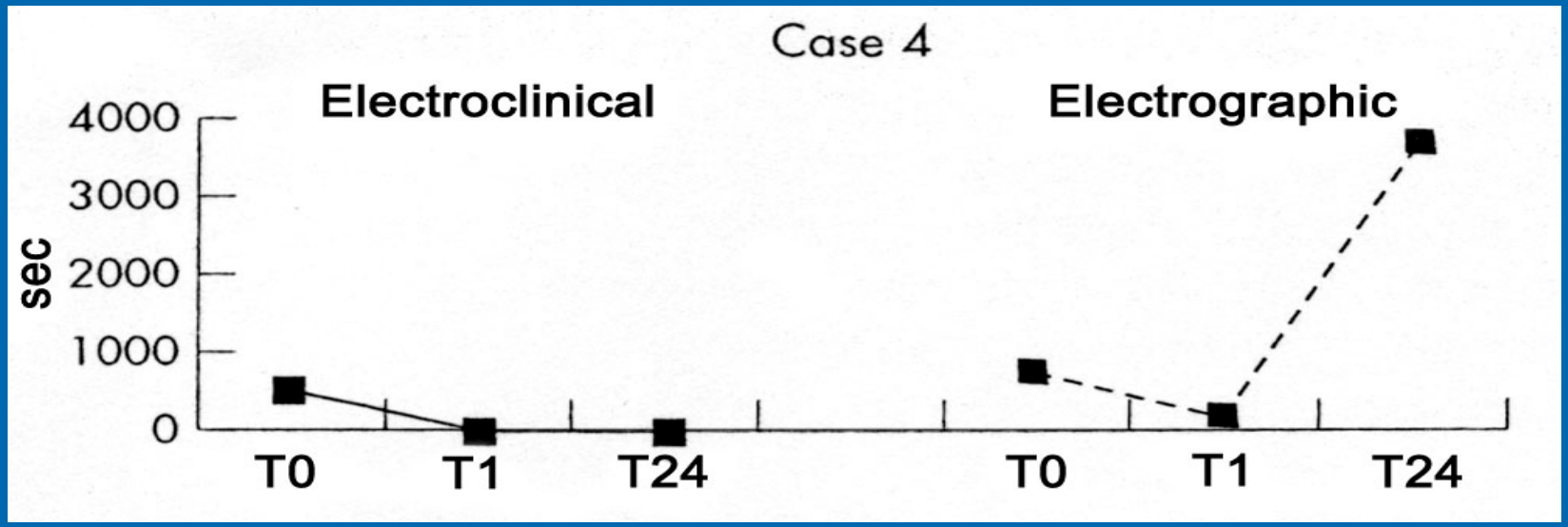
- Which drugs do we use (questionnaires)
- Do we treat clinical as well as subclinical seizures
- Differences per site
- Differences between Europe and USA
- Lack of RCTs



Boylan G et al, Arch Dis Child 2002

Which drugs do we use to treat neonatal seizures?

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NEUROLOGY 2005;64:776–777

Editorial

Neonatal seizures

After all these years we still love what doesn't work

Raman Sankar, MD, PhD; and Michael J. Painter, MD

Pediatr Neurol 2008

Original Articles

Off-Label Use of Antiepileptic Drugs for the Treatment of Neonatal Seizures

Faye S. Silverstein, MD* and Donna M. Ferriero, MD†

Seventy-three percent (40/55) recommended treatment of neonatal seizures with one or both of levetiracetam and topiramate; 47% (26/55) recommended levetiracetam; and 55% (30/55) recommended topiramate.

Neonatal seizures: multicenter variability in current treatment practices.

Bartha AI et al. Pediatr Neurol 2007

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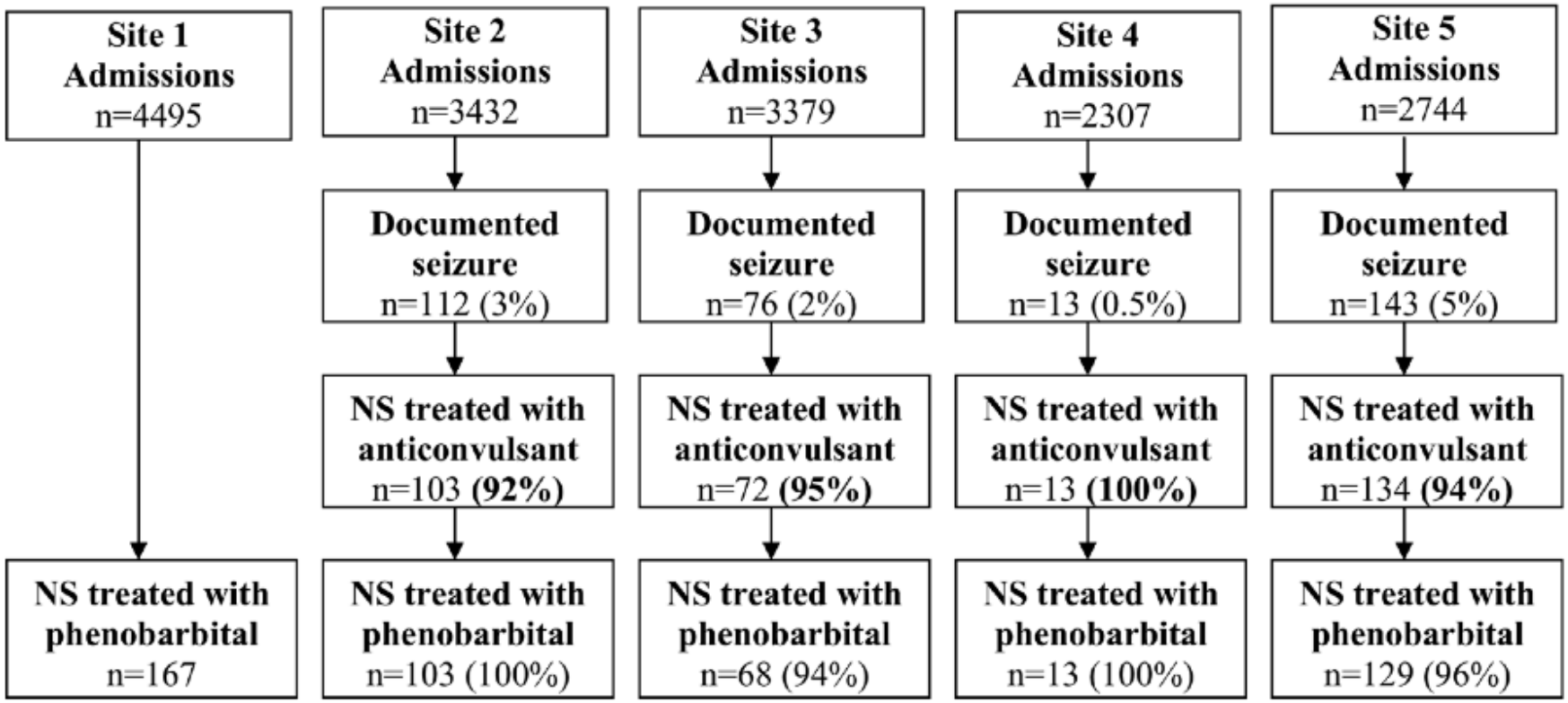

Figure 1. Flowchart of cohort formation. NS = neonatal seizure.

Second drug given to 46% in site 2-5

Neonatal seizures: multicenter variability in current treatment practices.

Bartha AI et al. Pediatr Neurol 2007

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Table 2. Variations in number of anticonvulsants used among sites

Number of Anticonvulsants	Site 1 (n = 167)	Site 2 (n = 103)	Site 3 (n = 68)	Site 4 (n = 13)	Site 5 (n = 129)	Total (n = 480)
1	126 (75%)	51 (50%)	30 (44%)	13 (100%)	65 (50%)	285 (59%)
2	31 (19%)	35 (34%)	28 (41%)	0	61 (47%)	155 (32%)
3	10 (6%)	13 (13%)	9 (13%)	0	3 (2%)	35 (7%)
4	0	4 (4%)	1 (1%)	0	0	5 (1%)
Median (range), by site*†	1 (1-3)	1 (1-4)	2 (1-4)	1	2 (1-3)	1 (1-4)

* Because of a policy at Site 4 that required all neonates who needed a second anticonvulsant to be transferred to an academic site, we did not compare the two community sites.

† $P < 0.0001$ between all sites; $P < 0.0001$ between the two academic sites; and $P < 0.0001$ between academic and community-based settings.

ASM discharge	77%	82%	57%	92%	76%	75%

How good are we in treating neonatal seizures?

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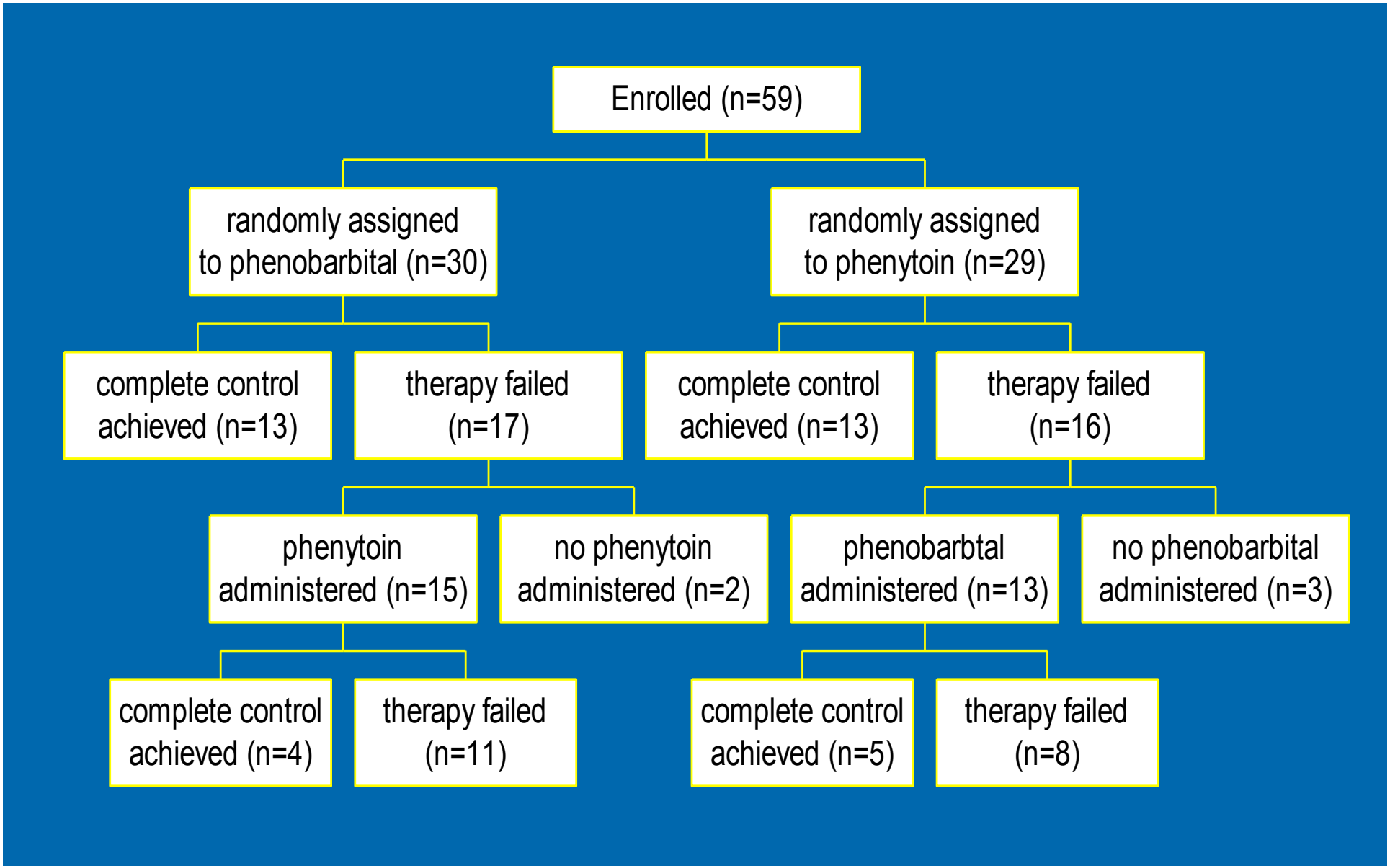
Comparison between phenobarbital and phenytoin;

Painter et al; NEJM 1999

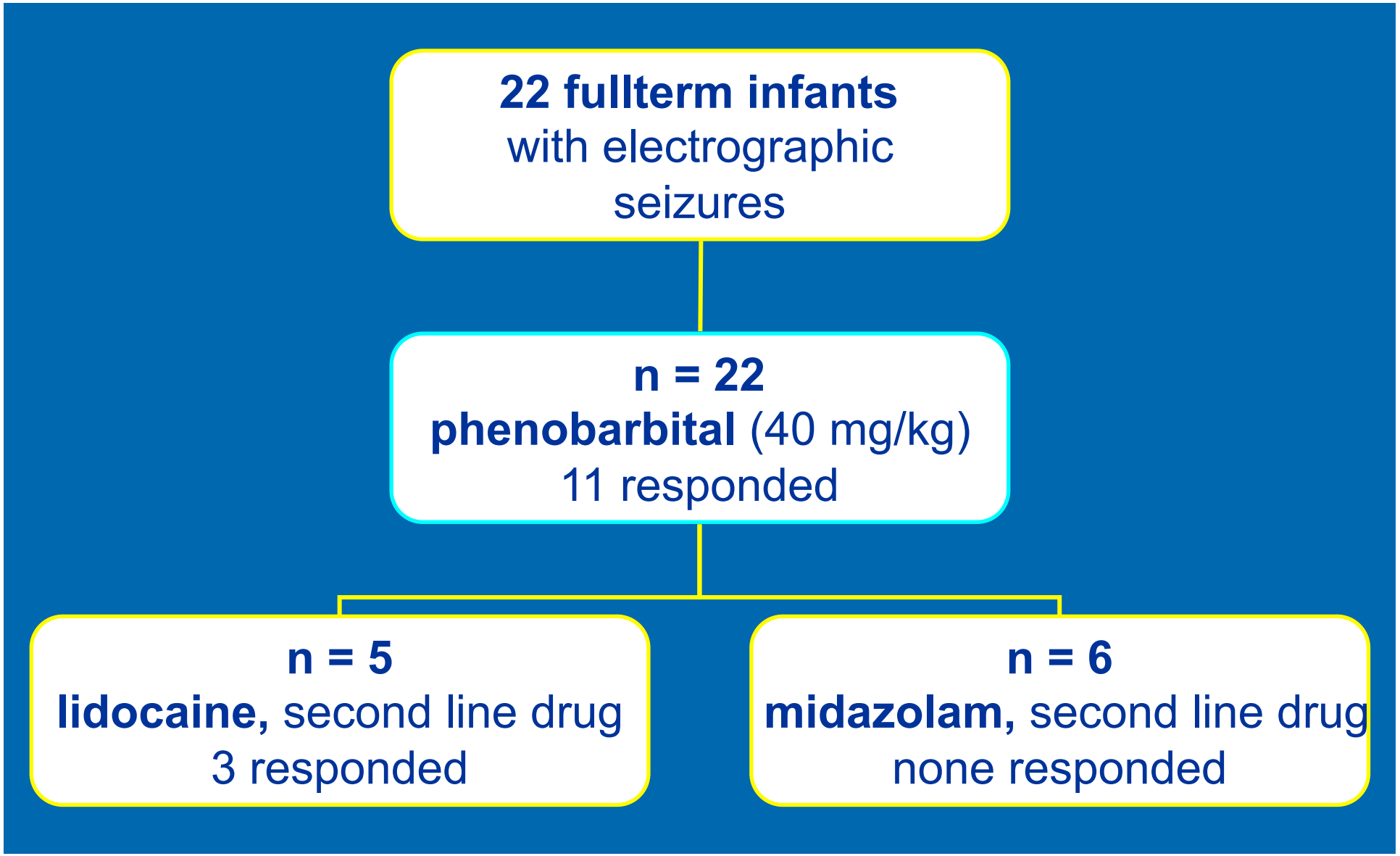


Comparison between phenobarbital and phenytoin;
Painter et al; NEJM 1999

- Randomised study for phenobarbital or phenytoin. When lack of seizure control, the second drug was added.
- 43% seizure control for phenobarbital and 45% for phenytoin treatment
- combined treatment resulted in seizure control in 57% when phenobarb was the first drug and 62% when phenytoin was the first drug.

Second-line anticonvulsant treatment of neonatal seizures: a video-EEG monitoring study;

Boylan GB et al Neurology. 2004;62:486-8



Should we treat Clinical *and* Subclinical Seizures?

Van Rooij LGM et al. Pediatrics 2010.

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Results

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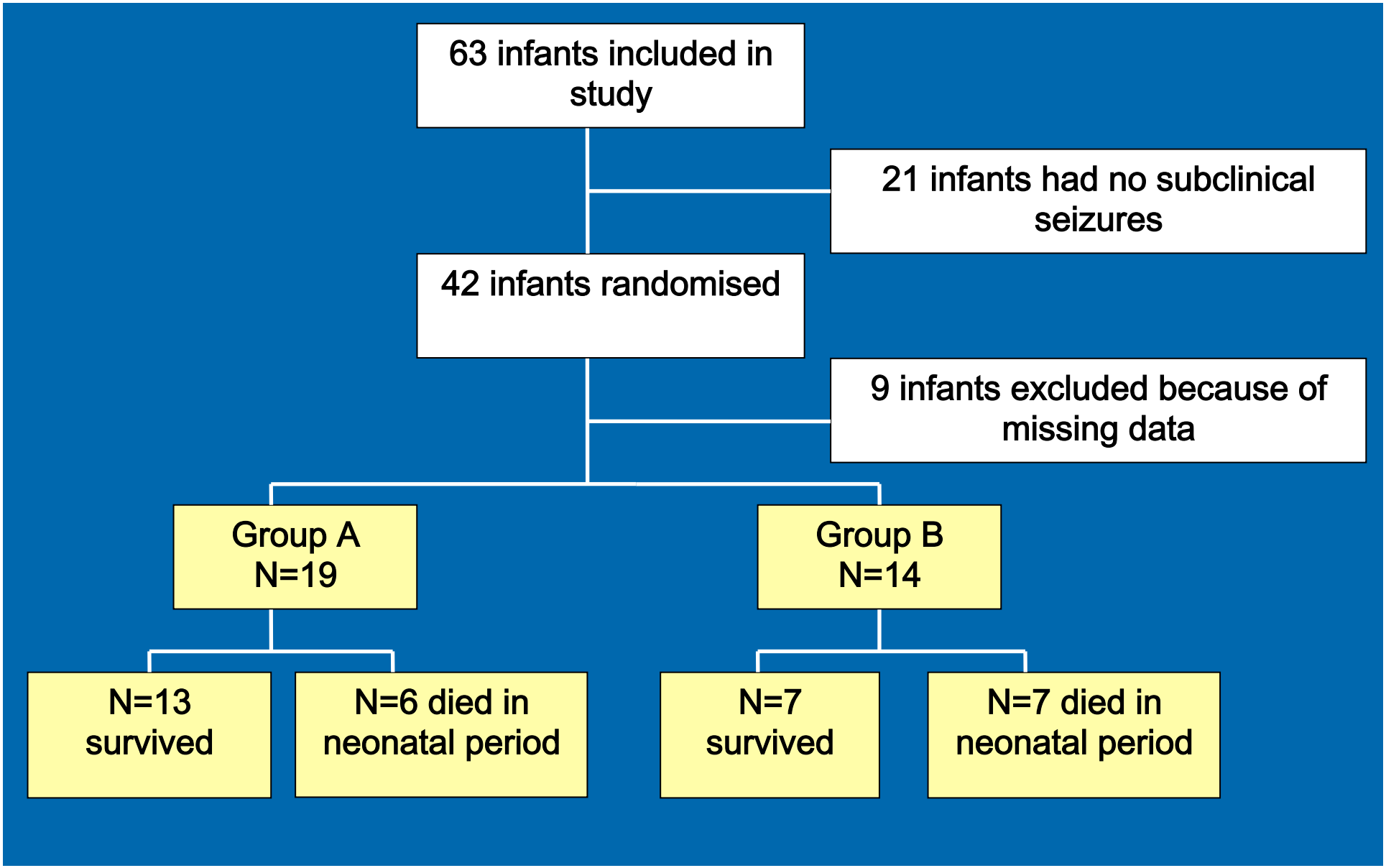

Results

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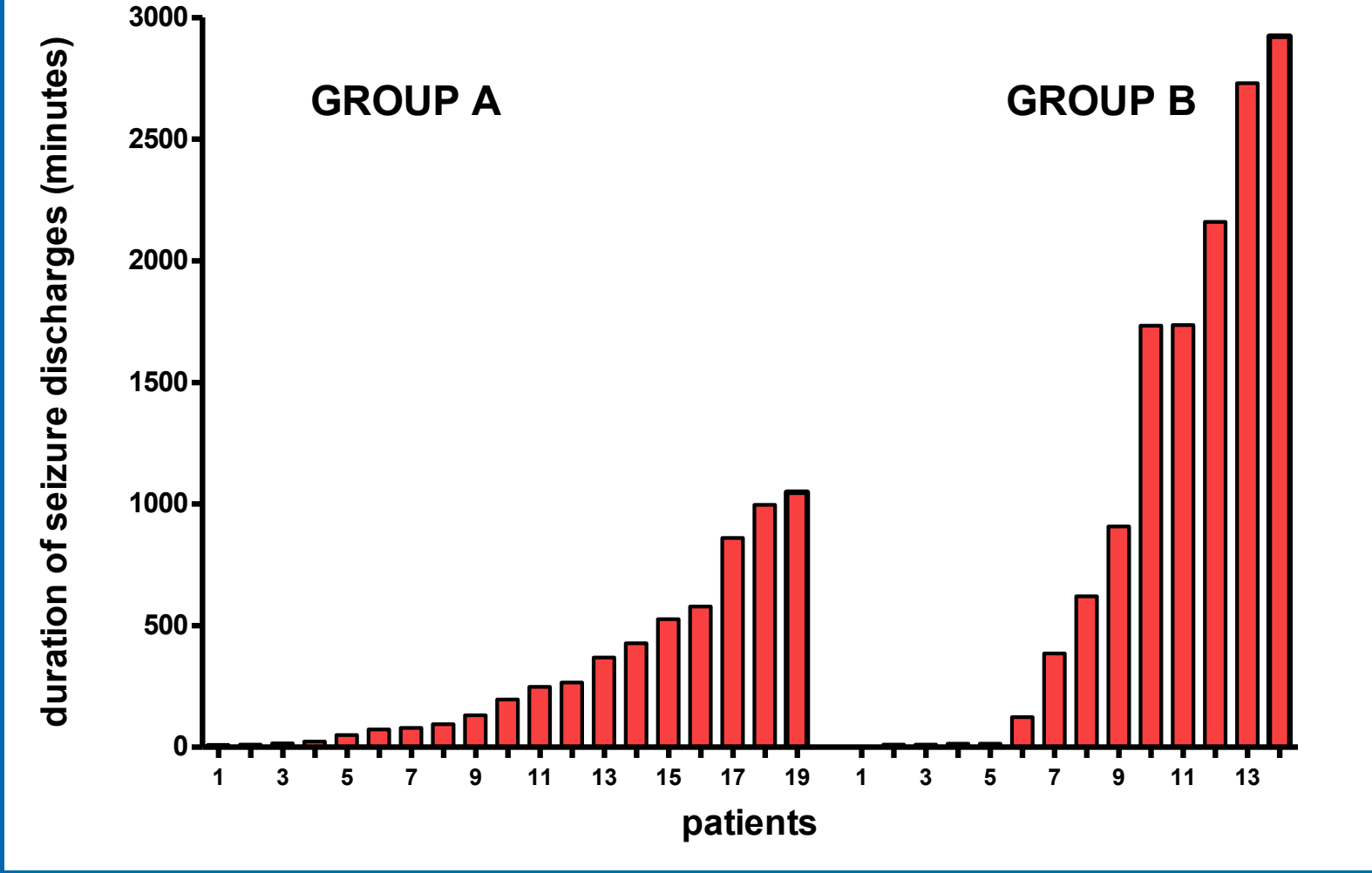

Results: MRI

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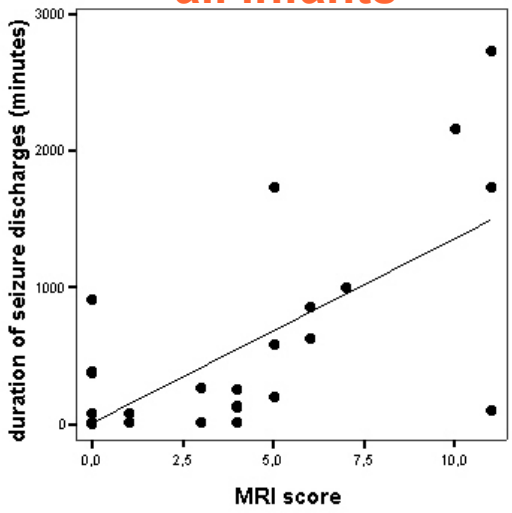
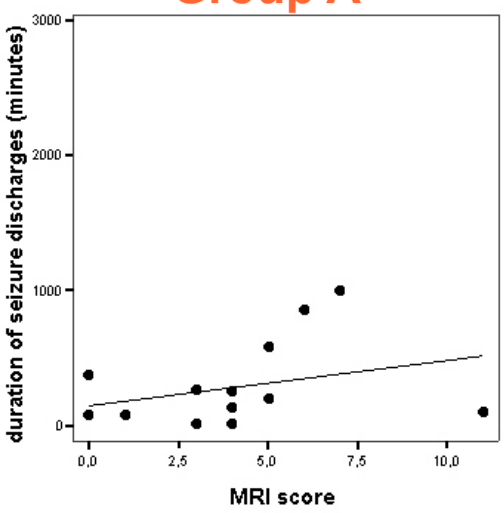
all infants



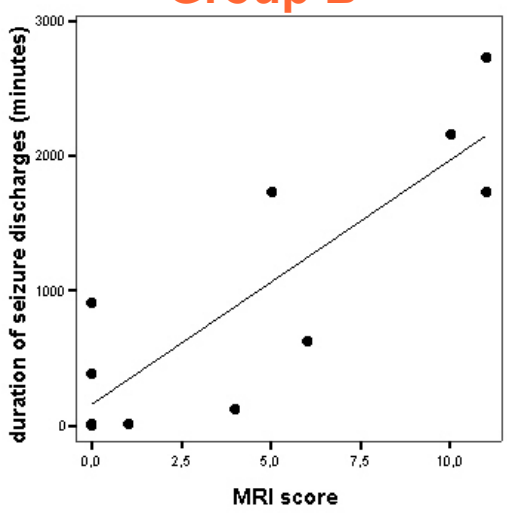
P < 0.001

Group A



P = 0.292

Group B



P = 0.001

Linear regression between seizure duration and MRI score

Treating EEG Seizures in HIE: A Randomized Controlled Trial

Srinivasakumar P et al; Pediatrics 2015,

University Medical Center Utrecht

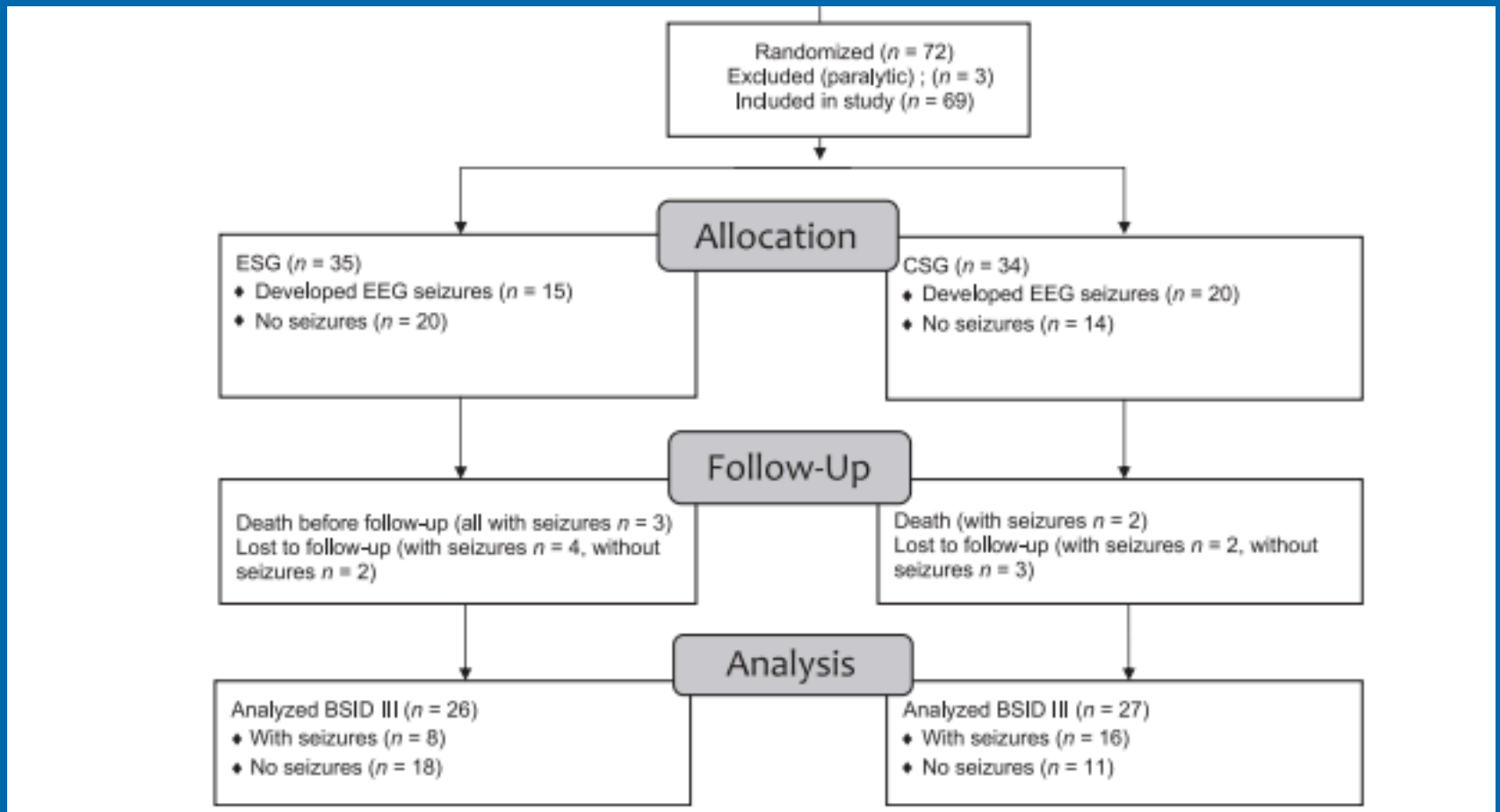


FIGURE 2
Consort flow diagram.

Treating EEG Seizures in HIE: A Randomized Controlled Trial

Srinivasakumar P et al; Pediatrics 2015,

University Medical Center Utrecht

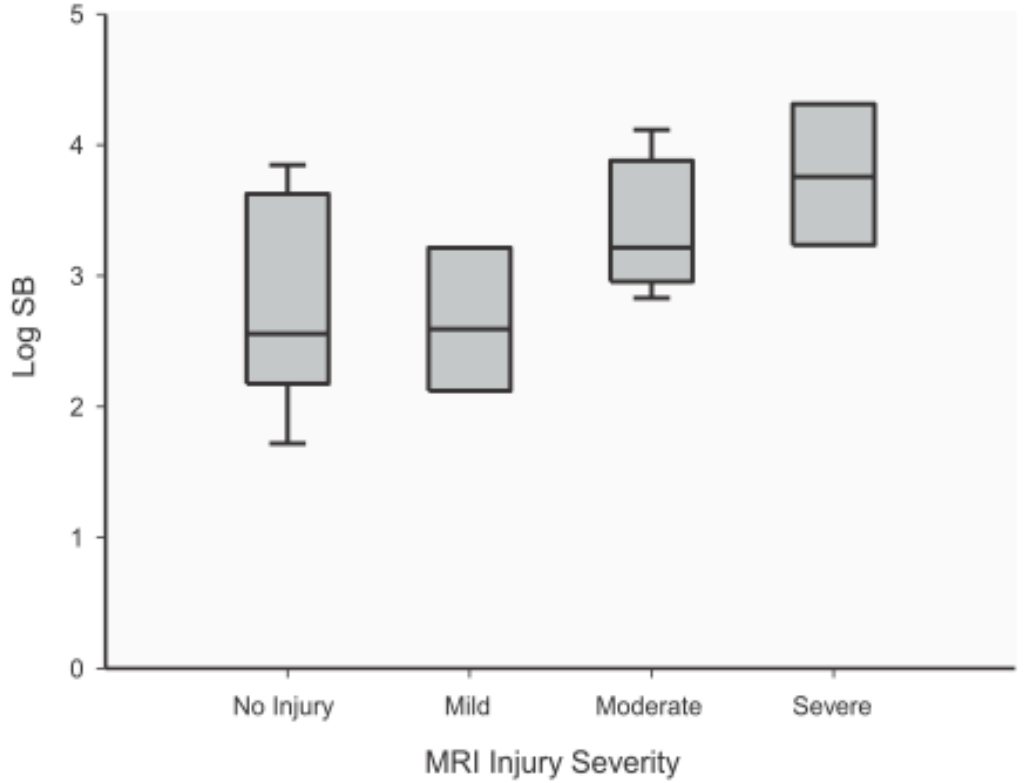


FIGURE 4

Overall trend of electrographic SB and severity of brain injury on MRI in the cohort. X-axis: Severity of brain injury on MRI; Y-axis: Log units of electrographic SB, $P < .03$ (no injury/mild versus moderate–severe).

Treating EEG Seizures in HIE: A Randomized Controlled Trial

Srinivasakumar P et al; Pediatrics 2015,

University Medical Center Utrecht

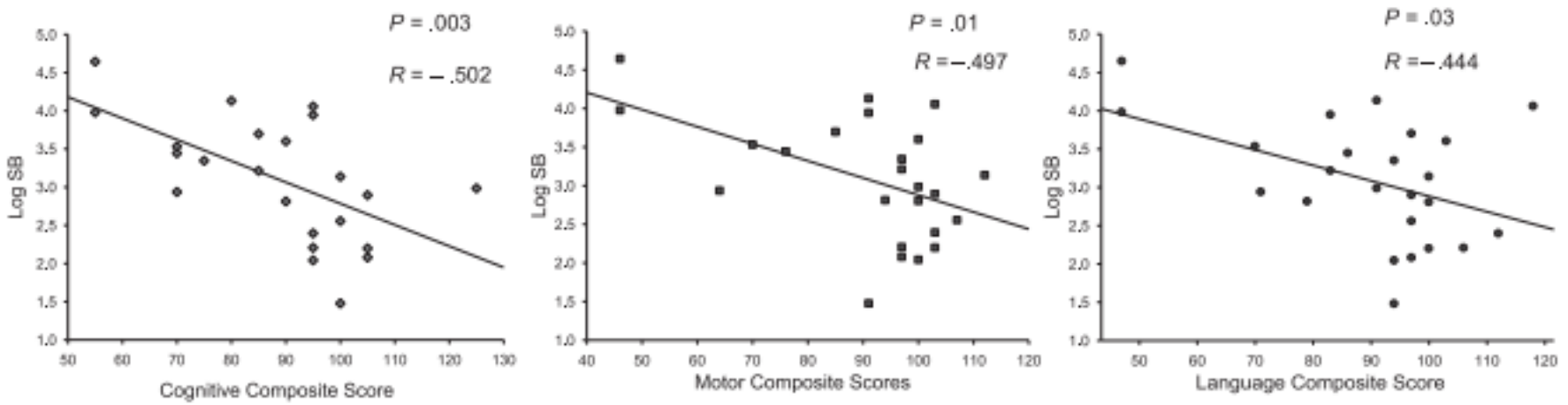


FIGURE 3
Correlation between electrographic SB and performance scores on BSID III. X-axis: Cognitive, motor, and language composite scores (BSID III); Y-axis: Log units of electrographic SB.

Conclusion: Treatment of electrographic seizures results in significant reduction in SB. SB is associated with more severe brain injury and significantly lower performance scores across all domains on BSID III.

Electrographic seizures are associated with brain injury in newborns undergoing therapeutic hypothermia.

Shah DK et al, Arch Dis Child Fetal Neon Ed 2014

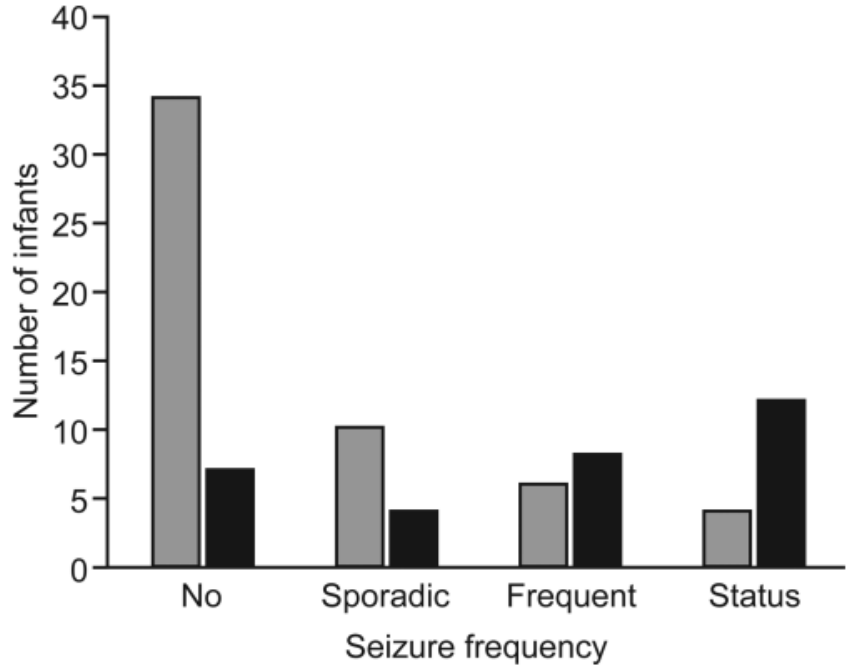


Figure 4 Numbers of infants with good (grey) and poor (black) MRI outcomes in seizure categories broken down into no seizures, sporadic seizures, frequent seizures and status epilepticus. Infants with severe (group 1 black) and non-severe (group 2 grey) patterns of cerebral injury on MRI.

What this study adds

Electrographic seizures as captured on aEEG with concurrent 2-channel EEG are associated with cerebral injury on MRI independent of aEEG background and Apgar at 10 min. Seizures are most common on the first day after birth with a significant rebound during rewarming.

Neonatal seizures

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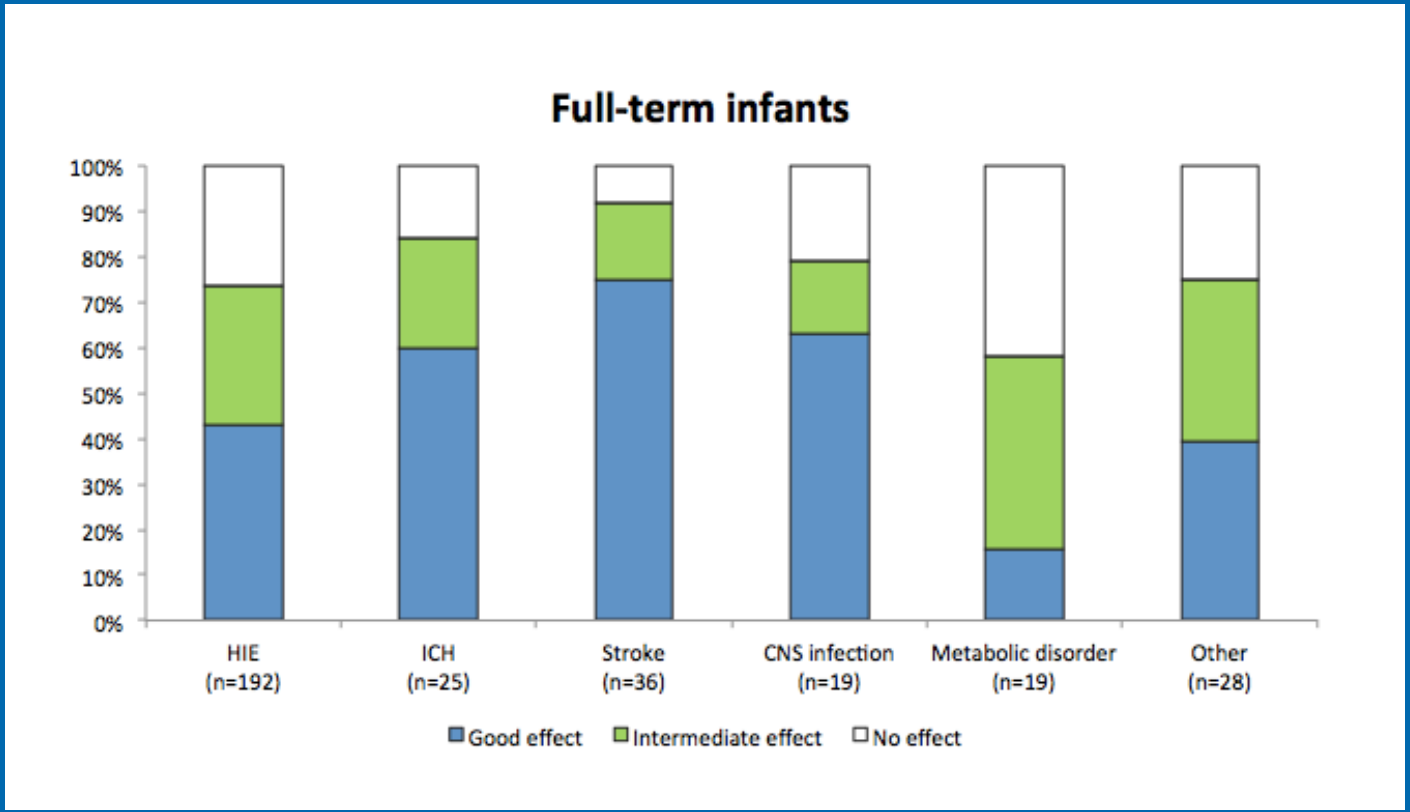
	1st AED	2nd AED	3rd AED	
Europe (1) (n=13 centres)	Phenobarbitone	Midazolam	**Lidocaine**	
International (2) (n=193 neurologist/ neonatologists, mainly US)	Phenobarbitone	Phenytoin	Levetiracetam	***Lidocaine 1-6%***

- Lidocaine is a sodium channel blocker
- No evidence based guidelines for treatment
- Lidocaine effective (60-90%)

1) Vento M et al. Acta Paediatr 2010
2) Glass H et al. Pediatr Neurol 2012

Boylan et al. Neurology 2004, **Hellström-Westas et al.** Acta Pediatr Scan 1988, **Hellström-Westas et al.** Acta Pediatr 1992, **Lundqvist et al.** Acta Pediatr 2013, **Malingre et al.** Eur J Pediatr 2006, **Radvanyi-Bouvet et al.** 1990, **Rey et al.** Ther Drug Monit 1990, **Shany et al.** J Child Neurol 2007, **van den Broek et al.** ADC FN 2013

Lidocaine response rate in aEEG-confirmed neonatal seizures: Retrospective study of 413 term and preterm infants. *Weeke et al, Epilepsia 2016*



- Seizure response to lidocaine was seen in ~70%.
  This was influenced by GA, underlying etiology, and timing of administration
- Lidocaine had a significantly higher response rate than midazolam as second-line AED, with a trend for a higher response rate as third-line AED

Neonatal Seizures: Treatment Practices Among Term and Preterm Infants.

Glass H et al, Pediatr Neurol 2012

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Table 3. Choice of anticonvulsants for preterm and term neonates

	Preterm			Term		
	First, n (%)	Second, n (%)	Third, n (%)	First, n (%)	Second, n (%)	Third, n (%)
Phenobarbitol	135 (72.2)	49 (26.2)	2 (1.1)	120 (70.9)	49 (27.2)	3 (1.7)
Lorazepam	41 (21.9)	26 (13.9)	23 (13.1)	42 (23.1)	19 (10.6)	26 (14.9)
Phenytoin	4 (2.1)	76 (40.6)	62 (35.2)	4 (2.2)	77 (42.8)	61 (34.9)
Levetiracetam	2 (1.1)	17 (9.1)	37 (21.0)	2 (1.1)	16 (8.9)	33 (18.9)
Midazolam	5 (2.7)	14 (7.5)	29 (16.5)	5 (2.7)	17 (9.4)	28 (16.0)
Topiramate	0 (0.0)	1 (0.5)	12 (6.8)	0 (0.0)	0 (0.0)	11 (6.3)
Lidocaine	0 (0.0)	4 (2.1)	7 (4.0)	0 (0.0)	2 (1.1)	11 (6.3)
Other	0 (0.0)	0 (0.0)	4 (2.3)	0 (0.0)	0 (0.0)	2 (1.1)

Survey among193 international neurologists, neonatologists, and specialists in neonatal neurology or neonatal neurocritical care to assess management practices for seizures in preterm and term neonates

How long do we use anti-epileptic medication for ?

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How long do we use ASM for?

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- Only during acute seizures
- Also following discharge home
- Which factors do we take into account?
  - ongoing seizure activity
  - neuro-imaging abnormalities
  - neuro-examination at discharge

Neonatal seizures: multicenter variability in current treatment practices.

Bartha AI et al. Pediatr Neurol 2007

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	ASM	No ASM	P value
Abn EEG	89 %	68 %	0.001
Brain imaging	72 %	39%	0.0001
2nd AED	37 %	26 %	0.03

Factors significantly associated with administration of ASM (overall 75%)

Treatment duration after acute symptomatic seizures in neonates: a multicenter cohort study.

Shellhaas RA et al, J Ped 2017

University Medical Center Utrecht

Table I. Clinical characteristics of 611 consecutive newborns with seizures at the 7 Neonatal Seizure Registry sites

Clinical characteristics	Overall n = 611	Site 1 n = 68	Site 2 n = 113	Site 3 n = 34	Site 4 n = 80	Site 5 n = 121	Site 6 n = 65	Site 7 n = 130	*P* value
Male sex	337 (55%)	39 (57%)	63 (56%)	21 (62%)	47 (59%)	59 (49%)	33 (51%)	75 (58%)	.7*
Term (>37 wk gestation)	519 (85%)	58 (85%)	95 (84%)	33 (97%)	64 (80%)	103 (85%)	54 (83%)	112 (86%)	.4*
EEG monitoring, h	66 (41, 99)	55 (25, 87)	66 (41, 107)	64 (40, 96)	63 (39, 102)	64 (37, 91)	86 (56, 106)	66 (41, 96)	.03†
Primary seizure etiology									.04*
Hypoxic-ischemic encephalopathy	231 (38%)	20 (29%)	46 (41%)	10 (29%)	29 (36%)	41 (34%)	31 (48%)	54 (41%)	
Ischemic stroke	101 (17%)	10 (15%)	16 (14%)	13 (38%)	14 (18%)	18 (15%)	6 (9%)	24 (18%)	
Intracranial haemorrhage	78 (13%)	7 (10%)	13 (12%)	1 (3%)	10 (13%)	17 (14%)	11 (17%)	19 (15%)	
Epilepsy†	80 (13%)	15 (22%)	17 (15%)	2 (6%)	11 (14%)	17 (14%)	7 (11%)	11 (8%)	
Deceased	110 (18%)	19 (28%)	20 (18%)	2 (6%)	17 (21%)	22 (18%)	14 (22%)	16 (12%)	.06*
Length of stay among survivors (d)	15 (10, 30)	11 (7, 20)	20 (10, 33)	10.5 (8, 14.5)	16 (11, 41)	10 (14, 35)	21 (14, 35)	13 (9, 34)	.05†
Discharge to home on antiseizure medication									
All subjects	428 (76%)	12 (27%)	76 (90%)	27 (90%)	49 (89%)	61 (71%)	39 (83%)	61 (74%)	<.0005*
Acute symptomatic etiology (n = 318)	233 (73%)	1 (4%)	57 (89%)	21 (91%)	32 (89%)	39 (65%)	33 (84%)	50 (71%)	<.0005*

Data are presented as N(%) or median (IQR).

*$\chi 2$.

†ANOVA.

‡Neonatal epilepsy includes epileptic encephalopathy, brain malformation, and benign familial neonatal epilepsy.

Treatment duration after acute symptomatic seizures in neonates: a multicenter cohort study.

Shellhaas RA et al, J Ped 2017

University Medical Center Utrecht

Table II. Variables associated with medications continuation at the time of discharge to home among the 317 survivors of acute symptomatic seizures

			Univariable analyses*			Multivariable analyses†		
	n	Discharged with AED	RR	95% CI	*P*	OR	95% CI	*P*
EEG confirmed seizures								
Yes	266	206 (77%)	1.5	(1.2-2.0)	.0001	2.3	(0.97-5.4)	.06
No	51	26 (51%)						
Status epilepticus								
Yes	48	42 (88%)	1.2	(1.1-1.4)	.015	2.1	(0.6-7.3)	.2
No	269	190 (71%)						
Seizures refractory to initial loading dose								
Yes	196	160 (82%)	1.3	(1.1-1.5)	.0003	1.6	(0.8-3.2)	.2
No/unknown	115	71 (62%)						
Abnormal examination at discharge								
Yes	150	123 (82%)	1.3	(1.1-1.4)	.0008	2.0	(0.99-4.1)	.053
No	167	109 (67%)						

AED, antiepileptic drug; *RR*, relative risk.

*χ^2.

†Wald *P* value adjusted for each of the risk factors plus site, and etiology, which remain highly significant ($P < .0005$).

Early discontinuation of ASM in neonates with HIE.

Fitzgerald MP. Epilepsia 2017

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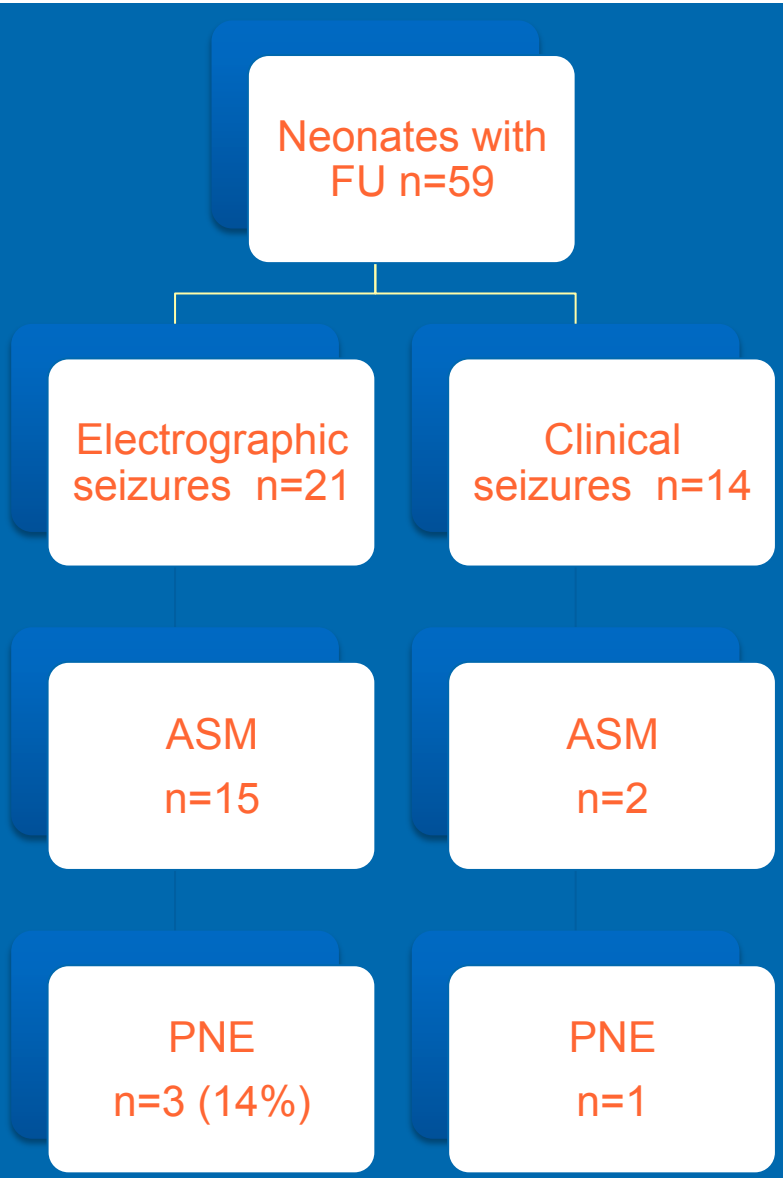

ASM continued:

- LOS: 27 versus 18d, p=0.02
- ES: 88% versus 33%, p<0.01
- abn brain MRI 61% versus 19%, p=0.03

PNE 11% including clinical sz

Early discontinuation of ASM in neonates with HIE.

Fitzgerald MP. Epilepsia 2017

University Medical Center Utrecht

Table 1. Clinical characteristics of the study cohort, stratified based on (1) the presence or absence of seizures during the follow-up period, and (2) antiseizure medication (ASM) on discharge. Continuous variables were analyzed with the Kruskal-Wallis test, whereas categorical variables were analyzed with Fisher's exact test

			Neonates with acute symptomatic seizures (n = 35)			Neonates with acute symptomatic seizures (n = 35)		
Variable	Full cohort (n = 81)	Follow-up cohort (n = 59)	Seizures in follow-up (n = 4)	No seizures in follow-up (n = 31)	p-Value	ASM on discharge (n = 17)	No ASM on discharge (n = 18)	p-Value
pH, cord blood, mean (SD)	6.93 (0.20)	6.96 (0.18)	6.69 (0.11)	7.00 (0.2)	**0.02**	6.89 (0.21)	7.00 (0.23)	0.40
pH, 1 h gas, mean (SD)	6.97 (0.14)	6.93 (0.15)	6.88 (0.14)	7.02 (0.14)	0.18	6.95 (0.13)	7.02 (0.16)	0.27
Apgar 1 min, median (IQR)	1 (1, 2)	1 (1, 2)	1 (0, 2)	1 (0, 2)	0.49	1 (0, 2)	1 (0, 2)	0.51
Apgar 5 min, median (IQR)	3 (2, 5)	3 (2, 5)	2 (1, 3)	2 (2, 5)	0.24	3 (1, 7)	2 (2, 3)	0.21
Apgar 10 min, median (IQR)	4 (3, 6)	4 (3, 6)	4 (3, 6)	4 (3, 6)	0.93	4 (3, 6)	4 (3, 5)	0.68
Admission length (days), median (IQR)	18 (11, 27)	19 (12, 27)	34 (27, 50)	18 (13, 26)	**0.02**	27 (16, 32)	18 (11, 23)	**0.02**
HIE severity, n (%)								
Mild	15 (19)	13 (22)	0 (0)	3 (10)	0.71	1 (6)	2 (11)	0.68
Moderate	45 (56)	36 (61)	2 (50)	20 (65)		10 (59)	12 (67)	
Severe	21 (26)	10 (17)	2 (50)	8 (26)		6 (35)	4 (22)	
EEG seizures, n (%)								
Yes	26 (32)	21 (36)	3 (75)	18 (58)	0.52	15 (88)	6 (33)	**<0.01**
No	55 (68)	38 (64)	1 (24)	13 (42)		2 (12)	12 (67)	
Mild	15 (19)	13 (22)	0 (0)	3 (10)	0.71	1 (6)	2 (11)	0.68
Moderate	45 (56)	36 (61)	2 (50)	20 (65)		10 (59)	12 (67)	
Severe	21 (26)	10 (17)	2 (50)	8 (26)		6 (35)	4 (22)	
EEG seizures, n (%)								
Yes	26 (32)	21 (36)	3 (75)	18 (58)	0.52	15 (88)	6 (33)	**<0.01**
No	55 (68)	38 (64)	1 (24)	13 (42)		2 (12)	12 (67)	

Early discontinuation of ASM in neonates with HIE.

Fitzgerald MP. Epilepsia 2017

University Medical Center Utrecht

Table 1. Clinical characteristics of the study cohort, stratified based on (1) the presence or absence of seizures during the follow-up period, and (2) antiseizure medication (ASM) on discharge. Continuous variables were analyzed with the Kruskal-Wallis test, whereas categorical variables were analyzed with Fisher's exact test

			Neonates with acute symptomatic seizures (n = 35)			Neonates with acute symptomatic seizures (n = 35)		
Variable	Full cohort (n = 81)	Follow-up cohort (n = 59)	Seizures in follow-up (n = 4)	No seizures in follow-up (n = 31)	p-Value	ASM on discharge (n = 17)	No ASM on discharge (n = 18)	p-Value
MRI injury distribution, n (%)								
Normal	35/72 (49)	28/57 (49)	1 (25)	13 (43)	0.08	3 (19)	11 (61)	**0.03**
Deep gray only	7/72 (10)	5/57 (9)	2 (50)	2 (7)		2 (13)	2 (11)	
Cortical only	20/72 (28)	19/57 (33)	0 (0)	11 (37)		6 (38)	5 (45)	
Cortical + deep gray	7/72 (10)	4/57 (7)	1 (25)	3 (10)		4 (25)	0 (0)	
Extensive injury	3/72 (4)	1/57 (2)	0 (0)	1 (3)		1 (6)	0 (0)	
Discharged on ASM, n (%)								
Yes	18/72 (22)	17 (29)	4 (100)	13 (42)	**0.05**	NA	NA	NA
No	63/72 (78)	42 (71)	0 (0)	18 (58)				
Length of ASM therapy after discharge (days), mean (SD)	144 (95)	144 (95)	121 (221)	120 (75)	0.08	NA	144 (95)	NA

Significant p-values are shown in bold.

Early discontinuation of ASM in neonates with HIE.

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Table 2. Summary of clinical characteristics for neonates with seizures in follow-up

Variable	Patient 1	Patient 2	Patient 3	Patient 4
Sex	Male	Male	Male	Male
Gestational age (weeks)	37	38	39	39
Race	Caucasian	Caucasian	Caucasian	Other
Apgar 1 min	0	3	0	1
Apgar 5 min	1	4	0	2
Apgar 10 min	3	4	3	7
NICU length of stay (days)	63	21	32	36
Hospital length of stay (days)	63	21	49	38
pH, cord blood	6.67	6.59	6.8	NA
pH, 1 h blood gas	6.8	7.04	6.8	NA
Acute symptomatic seizures	Yes (EEG)	Yes (EEG)	Yes (clinical)	Yes (EEG)
EEG background abnormality	Severe	Severe	Moderate	Severe
Number of seizures on cEEG	15	2	0	104
MRI injury distribution	Deep gray	Deep gray	Normal	Cortical + deep gray
HIE severity	Moderate	Severe	Moderate	Severe
ASMs on discharge	Phenobarbital	Phenobarbital	Phenobarbital	Levetiracetam
Age at seizure occurrence in follow-up (months)	48	4	16	15
Age at last follow-up (months)	54	46	48	21
Developmental delay at last follow-up	Global	Global	Gross motor	Global

Patient 3 had early clinical seizures and was started on phenobarbital prior to placement on cEEG. No electrographic seizures were captured; however, cEEG contained epileptiform abnormalities, as was a repeat EEG prior to discharge, thus phenobarbital was continued.

Prediction of future epilepsy in neonates with HIE who received selective head cooling.

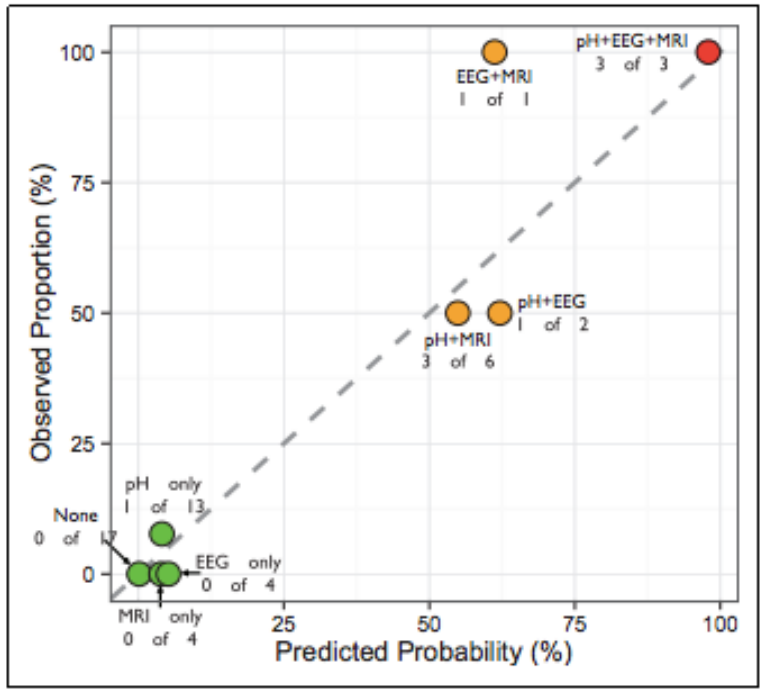
McDonough TL et al. J Child Neurol 2017

University Medical Center Utrecht

Table 2. Multivariable Logistic Regression Model to Predict Postneonatal Epilepsy (by Age 2).

Intercept (baseline probability)	0.1%	
Factor	Adjusted Odds Ratio [95% Confidence Interval]	*P*-Value (Wald)
Lowest pH ≤ 6.8 on DOL 1	30 [2.2-1900]	.04
EEG burst suppression DOL 4	39 [2.9-1800]	.02
MRI deep gray injury DOL 7-10	29 [3.1-850]	.01

Abbreviations: DOL, day of life; EEG, electroencephalograph; MRI, magnetic resonance imaging.



n= 80 with selective head cooling

n= 67 were 2 yrs, but only 50 had FU

Nine (18%) developed PNE

Early anatomic injury patterns predict epilepsy in head cooled neonates with HIE.

Jung DA et al Pediatr Neurol 2015

University Medical Center Utrecht

TABLE.
Anatomical Pattern of Injury on MRI and Outcome in Selectively Head-Cooled Neonates With Hypoxic-Ischemic Injury

Anatomical Pattern of Injury on MRI	Survived, No PNE	PNE	Infantile Spasms	Expire	Total
Normal	15	1	0	0	16 (22%)
Cortex and subcortical White matter	18	0	0	0	18 (25%)
Cortex and basal ganglia/thalamus	15	8	4	3	26 (35%)
Cortex, basal ganglia/thalamus and brainstem	0	4	4	9	13 (18%)
Total, n (%)	48 (66%)	13 (18%)	8	12 (16%)	73 (100%)

Abbreviations:
MRI = Magnetic resonance imaging
PNE = Postneonatal epilepsy
Patients include those with infantile spasms.

n=73, mean follow-up 41 m
18% developed PNE including 8 with infantile spasms
Risk of PNE was associated with BGT injury with/without brainstem involvement (12/39 versus 1/34, $p<0.003$)

Seizures and Antiseizure Medications are Important to Parents of Newborns With Seizures.

Hill E et al Pediatr Neurol 2017

University Medical Center Utrecht

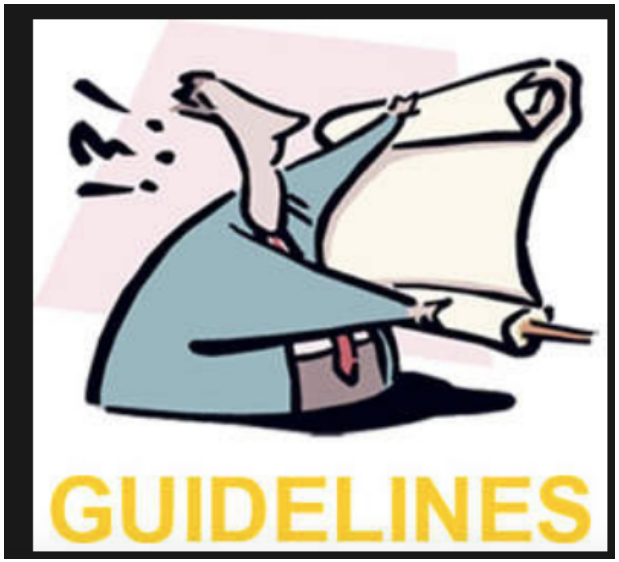
126 eligible respondents. Likert scale used.

- neonatal seizures had a major effect on their families (median 10 of 10; interquartile range 3; n 1⁄4 85).
- anti-seizure medications had a significant impact on their families (median 7 of 10; interquartile range 5.5; n 1⁄4 75).

TABLE 2.
Representative Responses to the Question, What are the Most Important Questions You Would Like Researchers to Answer About Neonatal Seizures and Their Treatment?

Themes	Representative Responses
Long-term impact of the medications	"How do you know the medication is less detrimental than the seizure?"
Long-term impact of the seizures	"How do seizures affect development?"
Unspecified long-term impacts	"Long-term consequences and predictability"
Medication effectiveness	"Why do some medicines work for a while, then not work anymore?"
Appropriate timing of medication discontinuation	"When a seizure is caused by a traumatic event, does the child need to continue on meds and for how long?"
Prevention or cause of neonatal seizures	"Why do they have them? Is there prenatal care to prevent it?"
Risk of future seizures	"I just wonder…are we over medicating these babies to prevent something that might never even happen."

YES !!
we do need guidelines



WHO guidelines 2011

University Medical Center Utrecht

TABLE 1- KEY RECOMMENDATIONS OF NEONATAL SEIZURES GUIDELINES

No.	RECOMMENDATIONS	*Strength*	*Quality of evidence*
1.	Clinically apparent seizures in the neonate should be treated if they last more than 3 minutes or are brief serial seizures.	*Strong*	*Not graded*
	In specialized care facilities where electroencephalography is available, all electrical seizures, even in the absence of clinically apparent seizures, should also be treated.	*Strong, context-specific*	*Not graded*
2.	In all neonates with seizures, hypoglycaemia should be ruled out and treated if present before antiepileptic drug treatment is considered.	*Strong*	*Not graded*
	If facilities for measuring glucose are not available, consider empirical treatment with glucose.	*Weak, context-specific*	
	If there are clinical signs suggestive of associated sepsis or meningitis, central nervous system infection should be rule out by doing a lumbar puncture, and treated if present with appropriate antibiotics.	*Strong*	
	If facilities for lumbar puncture are not available, consider empirical treatment with antibiotics for neonates with clinical signs of sepsis or meningitis.	*Weak, context-specific*	
	In all neonates with seizures, serum calcium should be measured (if facilities are available) and treated if hypocalcaemia is present.	*Strong, context-specific*	
	In the absence of hypoglycaemia, meningitis, hypocalcaemia or another obvious underlying etiology such as hypoxic-ischaemic encephalopathy, intracranial haemorrhage or infarction, pyridoxine treatment may be considered before antiepileptic drug treatment in a specialized centre where this treatment is available.	*Weak, context-specific*	
3.	Phenobarbital should be used as the first-line agent for treatment of neonatal seizures; phenobarbital should be made readily available in all settings.	*Strong*	*Very low*
4.	In neonates who continue to have seizures despite administering the maximal tolerated dose of phenobarbital, either a benzodiazepine, phenytoin or lidocaine may be used as the second-line agent for control of seizures (use of phenytoin or lidocaine requires cardiac monitoring facilities).	*Weak*	*Very low*
5.	In neonates with normal neurological examination and/or normal electroencephalography, consider stopping antiepileptic drugs if neonate has been seizure-free for >72 hours; the drug(s) should be reinstituted in case of recurrence of seizures.	*Weak*	*Very low*
6.	In neonates in whom seizure control is achieved with a single antiepileptic drug, the drug can be discontinued abruptly without any tapering of the doses.	*Weak*	*Not graded*
	In neonates requiring more than one antiepileptic drug for seizure control, the drugs may be stopped one by one, with phenobarbital being the last drug to be withdrawn.	*Weak*	
7.	In the absence of clinical seizures, neonates with hypoxic-ischaemic encephalopathy need not to be given prophylactic treatment with phenobarbital.	*Strong*	*Moderate*
8.	Where available, all clinical seizures in the neonatal period should be confirmed by electroencephalography.	*Strong, context-specific*	*Not graded*
	Electroencephalography should not be performed for the sole purpose of determining the etiology in neonates with clinical seizures.	*Strong*	
9.	Radiological investigations (ultrasound, computed tomography and magnetic resonance imaging) of the cranium/head should not be performed to determine the presence or absence of clinical seizures or to evaluate the efficacy of treatment with antiepileptic drugs in neonates.	*Strong*	*Not graded*
	Radiological investigations may be done as a part of the comprehensive evaluation of the etiology of neonatal seizures or to determine prognosis in neonates with seizures.	*Weak, context-specific*	

Conclusions

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- Over the recent decade more attention has been paid to brain monitoring, especially
  - continuous aEEG
  - cEEG with video
- Subclinical seizures are better recognized and more often treated
- Treatment strategies vary and new guidelines are needed