A national service evaluation of performance of sleep-deprivation EEG

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Background

- Sleep-deprivation improves diagnostic yield of EEG, independent of the sampling effect of repeated EEG[1]

- Detection of epileptiform abnormalities is reported in between 24-57% of adult patients and 27-54% of paediatric patients with normal routine EEG[2,3,4,5,6,7,8]

[1]**Leach, J P, et al.** *2006, JNNP; 77, 1040-2*
[2]**Degen, R, Degen, H E and Reker, M.** *1987, Eur Neurol; 26, 51-9.*
[3]**Liporace, J, et al.** *1998, Epilepsy Research, 32, 357-62.*
[4]**Kubicki, S, Scheuler, W and Wittenbecher, H.** *in Epilepsy, Sleep and Sleep Deprivation (Epilepsy Res. Suppl. 2). Elsevier Science Publisher, 1991, 217-30.*
[5]**Scollo-Lavizzari, G, Pralle, W and Radue, E W.** *1977, Eur. Neurol; 15, 121-23.*
[6]**Shahar, E, et al.** *2010, European Journal of Paediatric Neurology; 14, 308-12.*

Background

- Reasons for variation in reported diagnostic sensitivity include:
  - Heterogenous patient study groups
  - Variability in numbers of patients taking anti-epileptic medication
  - Variability in the practice of sleep-deprivation EEG
    - Duration of sleep-deprivation
    - Recording duration
    - Use of additional activation procedures
  - What constitutes epileptiform abnormalities

Duration of sleep deprivation

- Considerable variation in literature between 3 to 36 hours[9,10]
- One study using partial sleep-deprivation reports a similar diagnostic yield to other studies utilising total overnight sleep-deprivation[4]
- No studies have directly compared partial with total overnight sleep deprivation in the same patient population

[4]**Kubicki, S, Scheuler, W and Wittenbecher, H.** *in Epilepsy, Sleep and Sleep Deprivation (Epilepsy Res. Suppl. 2). Elsevier Science Publisher, 1991, 217-30.*

[9]**Molaie, M and Cruz, A.** 1988, Electroencephalogr. Clin. Neurophysiol; 70, 288-92.

[10]**Gandelman-Marton, R and Theitler, J.** 2011, Acta Neurol. Scand., 124, 202-5.

Duration of recording

- Activating effect of sleep-deprivation may be independent of the activating effect of sleep[11], as evidenced by TcMS studies finding increased cortical excitability in patients with epilepsy following sleep-deprivation[12,13]

- Most studies report detection of abnormalities during sleep, and one large retrospective study demonstrated detection of abnormalities was greatest during N2 sleep[14]

[11] **Founatin, N B, Kim, J S and Lee, S I.** 1998, J Clin Neurophysiol; 15, 69-75.
[12] **Manganotti, P, et al.** 2006, J Neurol Neurosurg Psychiatry; 77, 56-60.
[13] **Badawy, R A, et al.** 2006, Neurology; 67, 1018-22.
[14] **Peraita-Adrados, R, et al.** 2001, Neurophysiol Clin, 31, 34-9.

Additional activating procedures

- Sleep-deprivation activates photoparoxysmal responses[15], which may be more readily demonstrated after a short period of sleep[16] ?selective deprivation of REM sleep

- Performing HV may increase attainment of sleep in children[17], but no studies have directly assessed its role in detection of epileptiform abnormalities in sleep-deprivation EEG

[15] **Scollo-Lavizzari, G and Scollo-Lavizzari, G R.** 1974, Euro Neurol; 11, 1-21.
[16] **Elmali, A D, et al.** 2017, Neurophysiol Clin, 47, 239-45.
[17] **Kaleyias, J, et al.** 2006, Clin Neurophysiol, 117, 1582-4.

Seizure provocation

- Sleep-deprivation may provoke seizures in some patients and some centres will not perform sleep-deprivation EEG in suspected JME[18], for example

- Sleep-deprivation significantly improves detection of interictal abnormalities in patients with JME[19]

- No published figures on the occurrence of seizures in sleep-deprivation EEG in a heterogenous referral population

[18] **Giorgi, F S, et al. 2013**, Clinical Neurophysiology; 124, 2101-7.
[19] **Sousa, N A, et al.** 2005, Arq Neuropsiquiatr; 63, 383-88.

Proposed guidelines for sleep-deprivation EEG

- One research group[18] has proposed the following protocol for adult patients:
  - Wake at 02:00 and avoid stimulants
  - 2.5 hour EEG recording from 08:00 to 10:30
  - No further activation procedures performed
  - Avoid sleep-deprivation when high suspicion of JME
  - Report 40% of patients with previously normal EEGs demonstrated epileptiform abnormalities using this technique, significantly higher than for repeat routine EEG

[18] **Giorgi, F S, et al. 2013**, Clinical Neurophysiology; 124, 2101-

Rationale for service evaluation

Sleep-deprivation EEG is widely used and has been demonstrated to increase detection of interictal epileptiform abnormalities in adult and paediatric patients with epilepsy who have normal or non-specific routine EEGs.

However, there is variation in the performance of sleep-deprivation EEG and no evidence-based guidelines exist. In addition, there is a lack of evidence regarding the risk of seizure provocation that can be used to inform patients.

We performed a cross-sectional survey of current UK practice in performance of sleep-deprivation EEG.

Aims of service evaluation

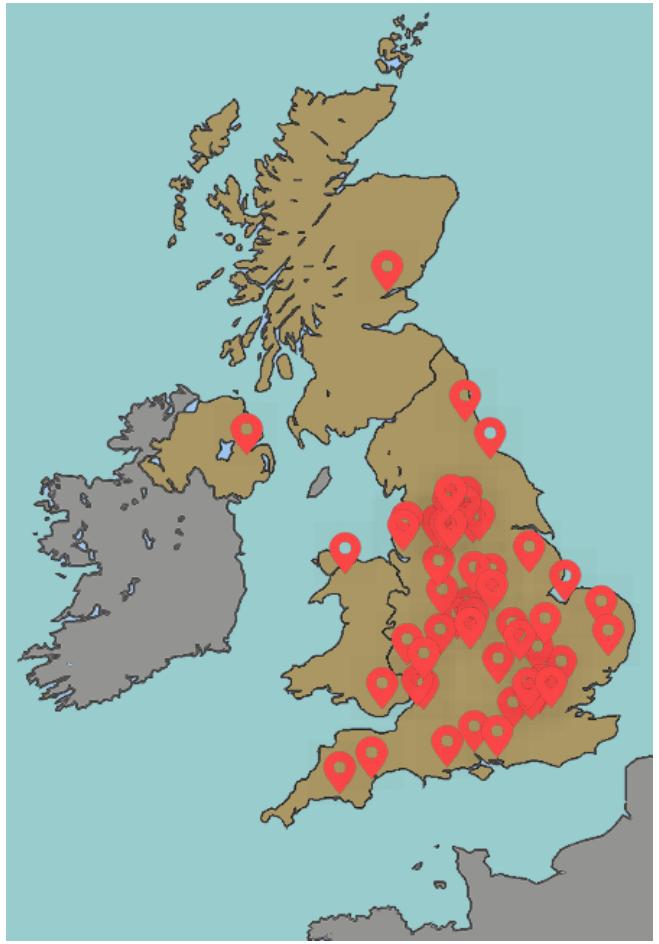
1. To assess consistency in practice across different UK centres

2. To determine the frequency of epileptic seizures occurring during sleep-deprivation EEG in a typical referral population

3. To assess the effect of several variables on the detection of epileptiform abnormalities

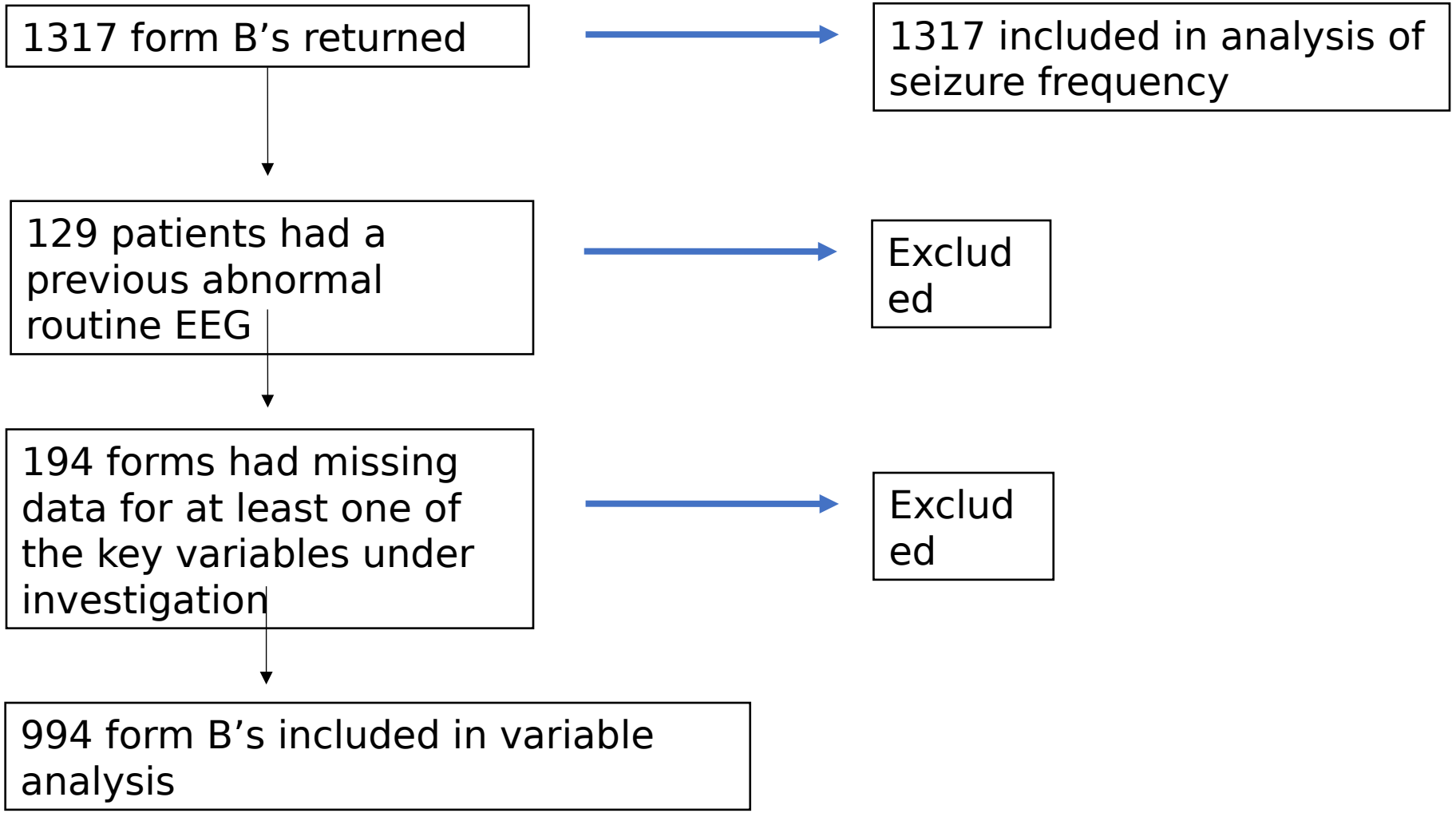
Methodology

- 55 UK Neurophysiology departments
- Form A: Survey
  - 52 responses
- Form B: Prospective study of every SDEEG between 1st Feb and 30th April 2018
  - 1317 responses from 55 centres



BSCN Joint National Audit Project ANS

Methodology

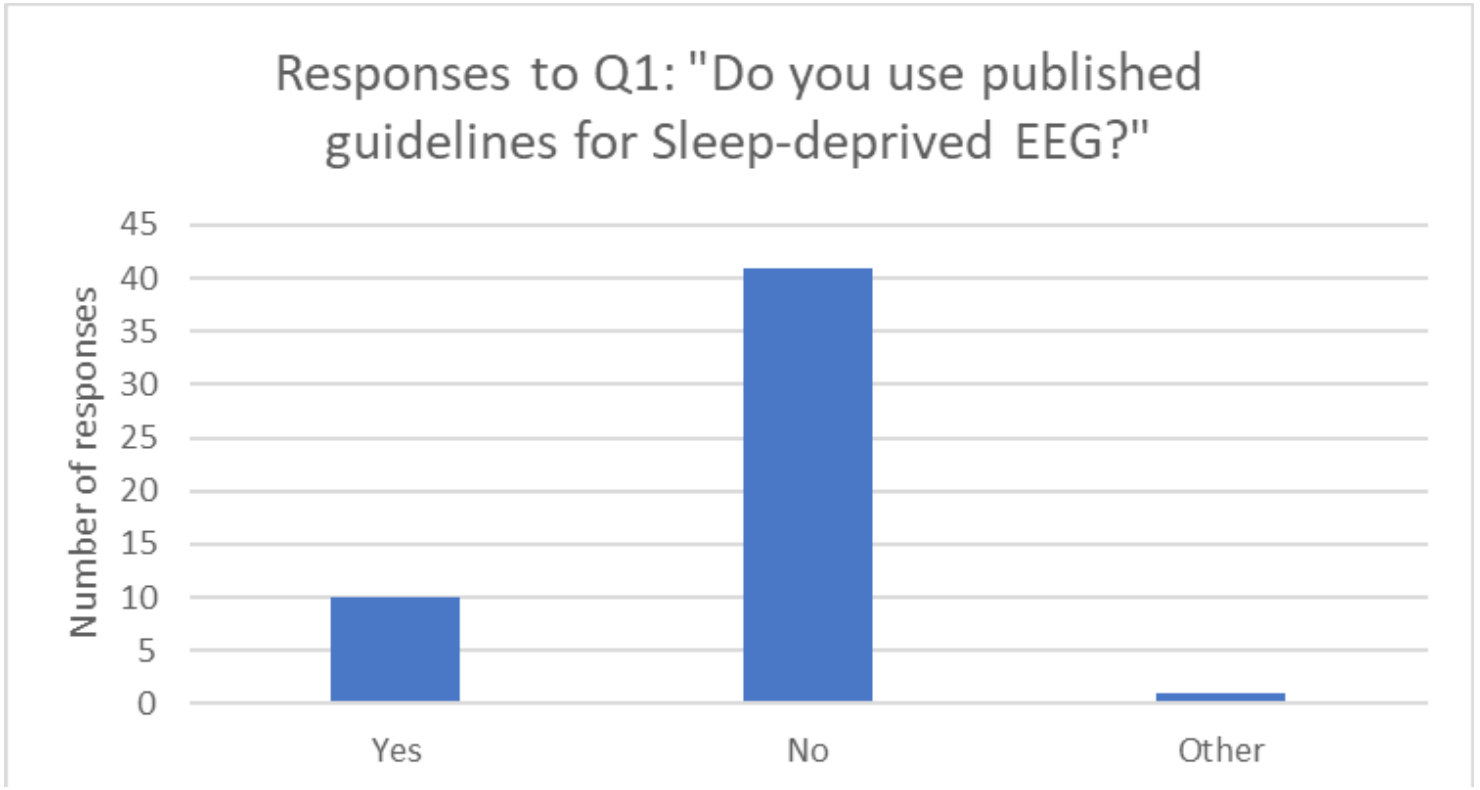


Methodology

- Relationship between identified variables and SDEEG outcome (i.e. “normal” or “abnormal”) was assessed
- Single variable analysis
  - Chi-square test for categorical variables
  - Mann-Whitney U test for continuous variables
- Multivariate analysis was performed using binary logistic regression modelling (stepwise and backward elimination)
  - Alpha <0.05 for inclusion/exclusion
- Analysis performed using Minitab 18 software

Part A

Part A: *Findings*

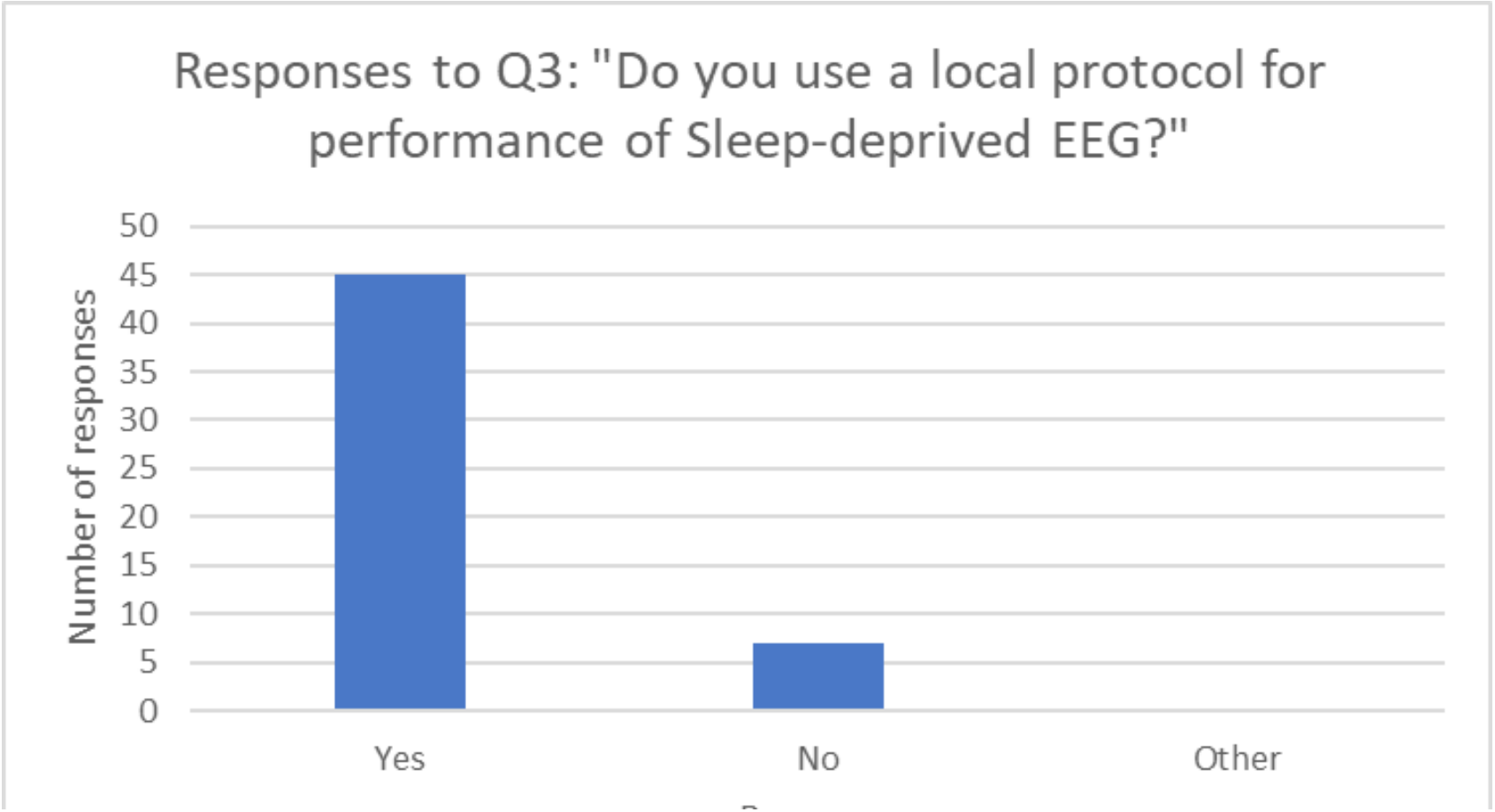


Response (N=52)

Protocols used (8 responses)

SUPPLEMENT 52 TO ELECTROENCEPHALOPAGRAPHY AND CLINICAL NEUROPHYSIOLOGY - RECOMMENDATIONSFOR THE PRACTICE OF CLINICAL NEUROPHYSIOLOGY: GUIDELINES OF IFCN
ANS; CLINICAL NEUROPHYSIOLOGY: EEG, PAEDIATRIC NEUROPHYSIOLOGY - SPECIAL TECH REPORT VOL 2, 1ST EDITION, 2003; EEG IN CLINICAL PRACTICE 2ND EDITION 1994;
RECOMMENDATIONS FROM: SMITH SJM (2005) EEG IN THE DIAGNOSIS AND CLASSIFICATION OF PATIENTS WITH EPIILEPSY; WHO (2012) - ROLE OF EEG IIN MANAGEMENT OF CONVULSIVE EPILESPY
ASET GUIDELINES
ANS/BSCN AUDIT/GUIDELINES
BRITISH BRAIN AND SPINE FOUNDATION; CURRENT PRACTICE OF EEG - 3RD EDITION, 2003
NICE GUIDELINES - EPILEPSIES, DIAGNOSES AND MANAGEMENT JUNE 2016 1.6.13
CH 22: RECORDING SLEEP AND WAKE: ELEMENTS USED TO GUIDE ELECTRODE PLACEMENT AND PSG CHANNELS

Part A: *Findings*



Local protocols (communication)

- Pre-appointment
  - Appointment letter sent with instructions for sleep deprivation (+/- consent form)
  - Inform patients of risk of seizures (written +/- phone-call)
  - Inform patient to take medication as usual
  - Avoid caffeine
  - Advise to be accompanied to appointment (and for 24hrs after)
  - Advise patient not to drive/cycle/work for the day of the appointment and avoid ‘unsafe’ situations e.g. bathing, boiling water, driving
- At the end of appointment
  - Advise patient of risk of seizure and encourage rest
  - Check well enough to leave

Local protocols (practicalities)

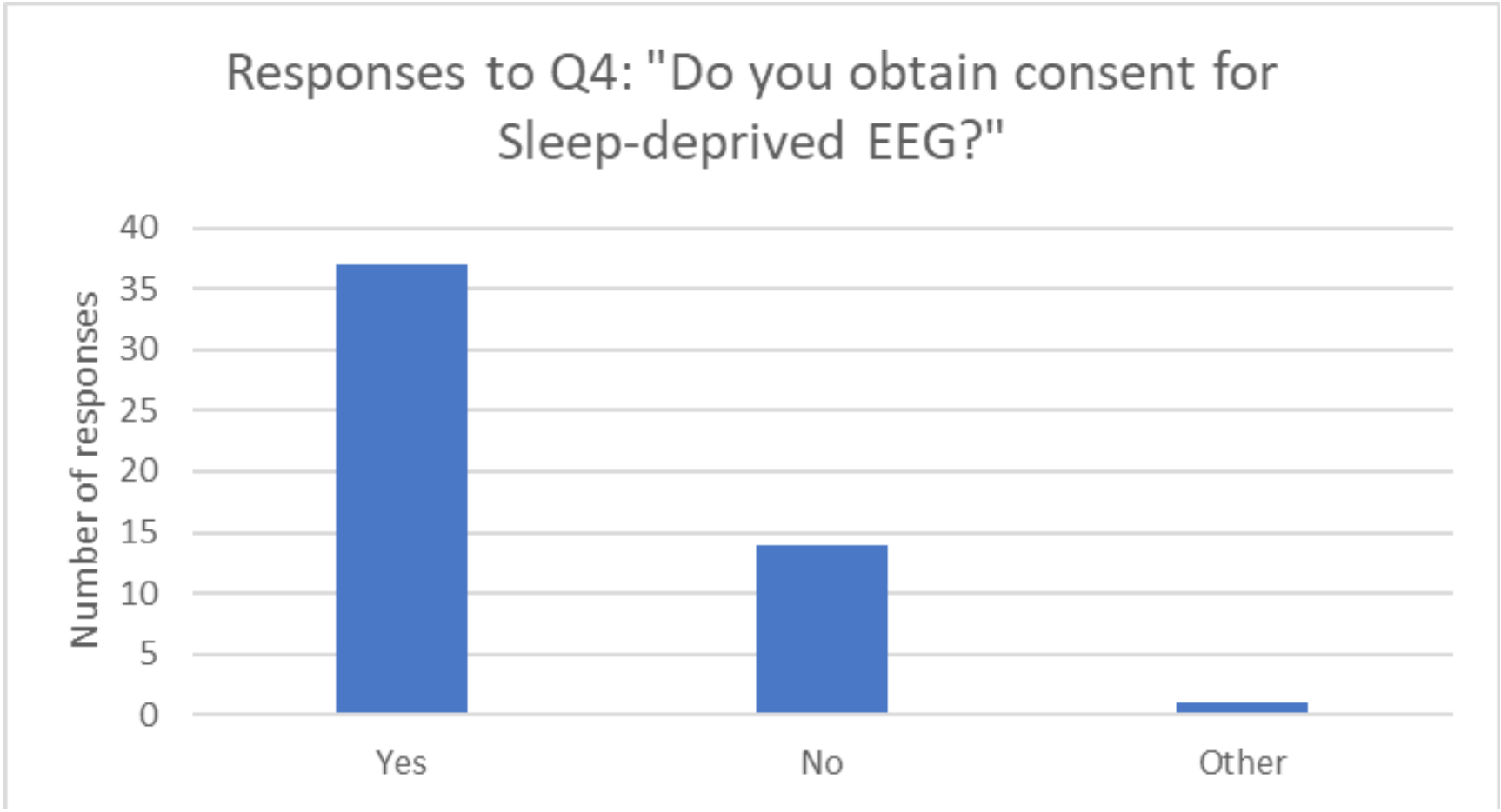
- Age guidance for amount of sleep deprivation
  - Use of total overnight sleep deprivation for adults most common
  - Often partial sleep deprivation in paediatrics
  - 2 centres specify partial deprivation in older age population (>65/>70 years)
- Specific appointment time for Sleep Deprived recording
  - 9am most frequent
  - 2.15pm also specified
- Duration of recording:
  - Time to sleep (up to 40’), period of sleep (10-60’); time recorded after wakening (5-10’)
  - Capture up to N3 sleep
- Longest appointment time 2.5 hours

Local protocols (activation procedures)

- *Caveats for activation procedures following sleep deprivation*
  - *PS not required if routine EEG in past 12/12*
  - *PS not performed if no routine EEG*
  - *'Discretionary'*
  - *PS not done 'unless specifically requested'*

- 6 centres do not perform PS following sleep deprivation

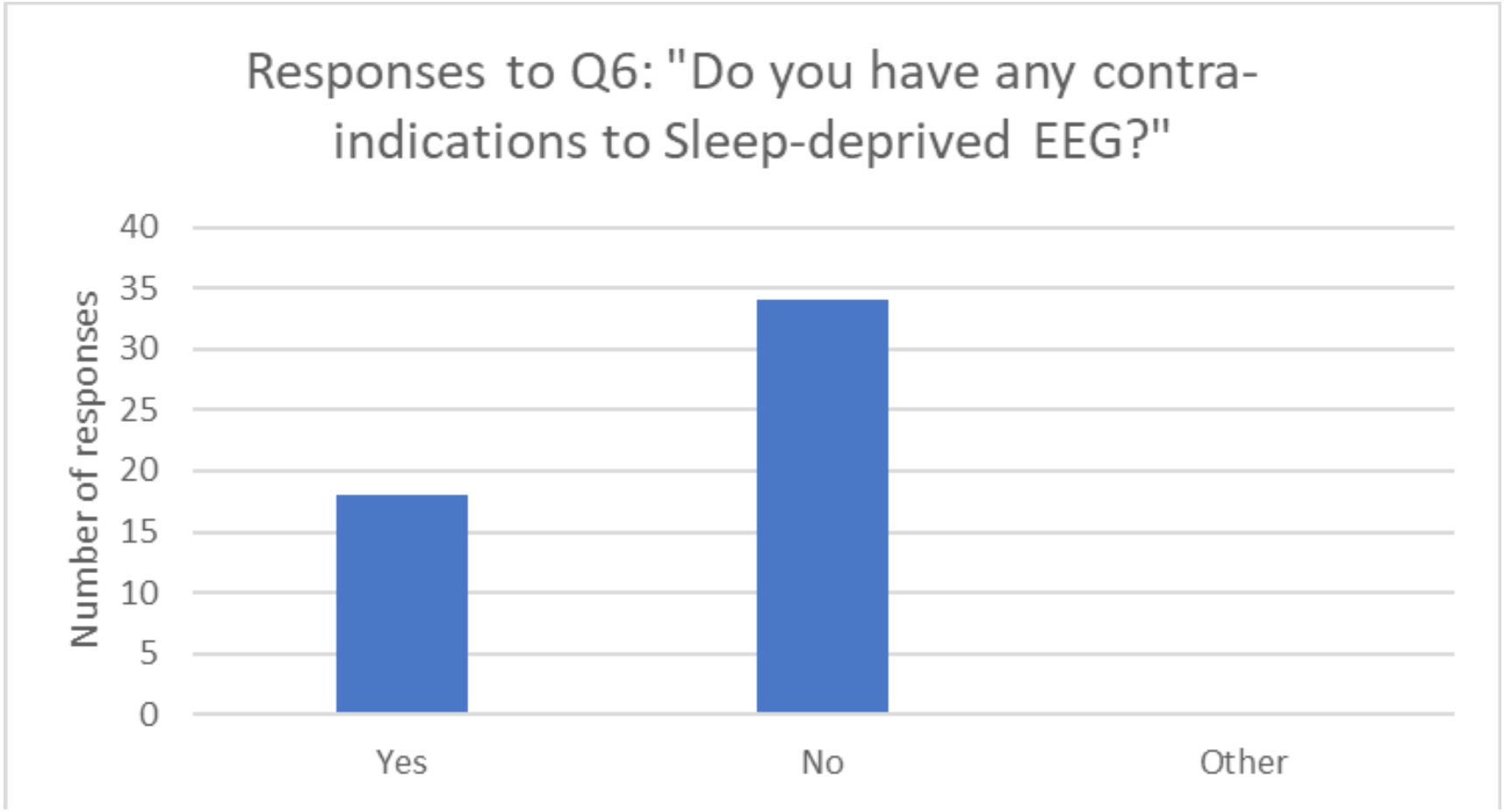
Part A: *Findings*



Consent

- ‘Implied’ consent (18/37 centres)
- Consent obtained by referrer (3/37 centres – one asks referrer to sign)
- Consent obtained when appointment booked by telephone (4/37 centres) as well as patient information sent
- Patient returns a signed consent form (1/37)
- Consent on the day of appointment for other activation procedures and video

Part A: *Findings*

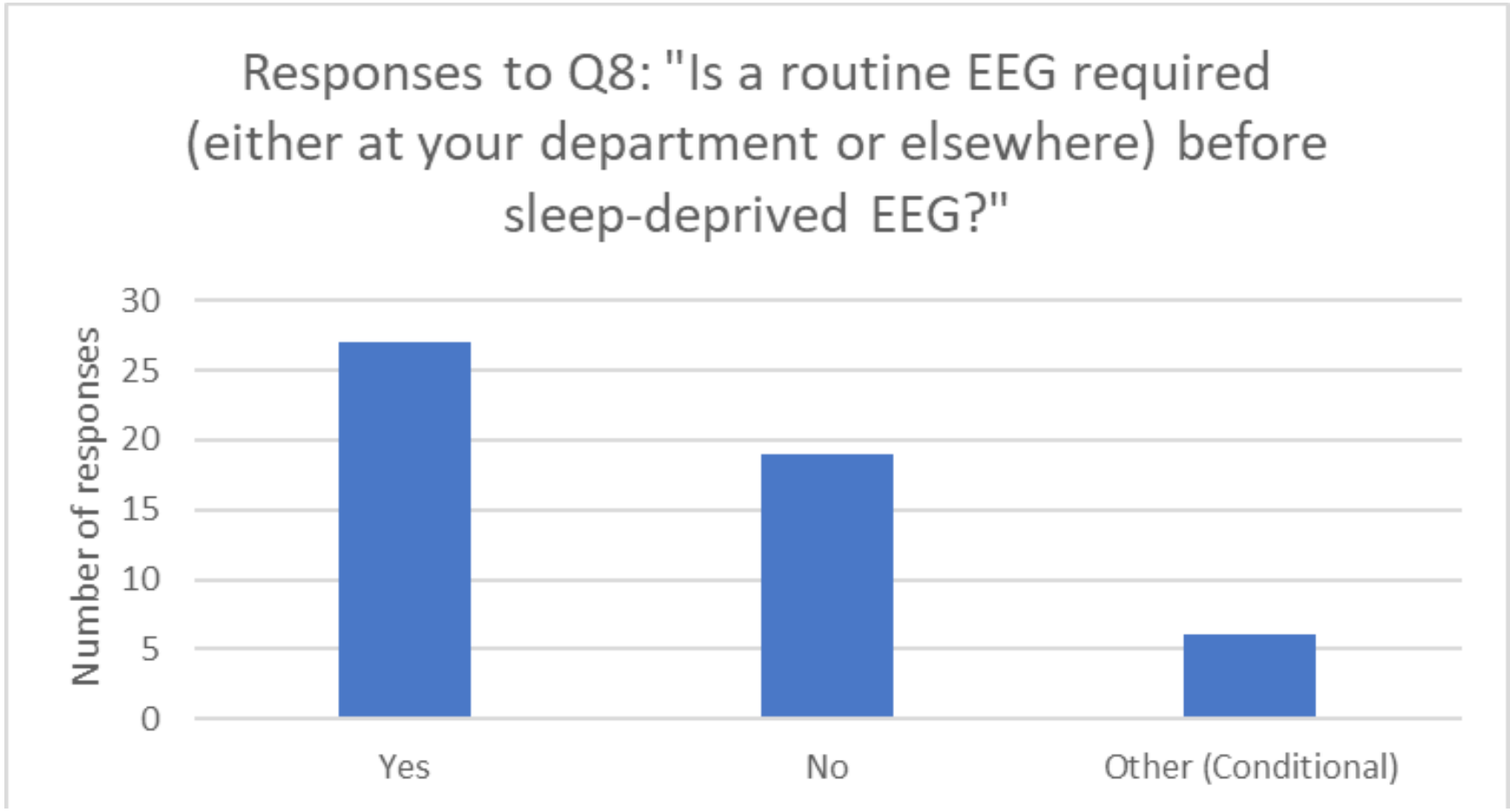


Contraindications

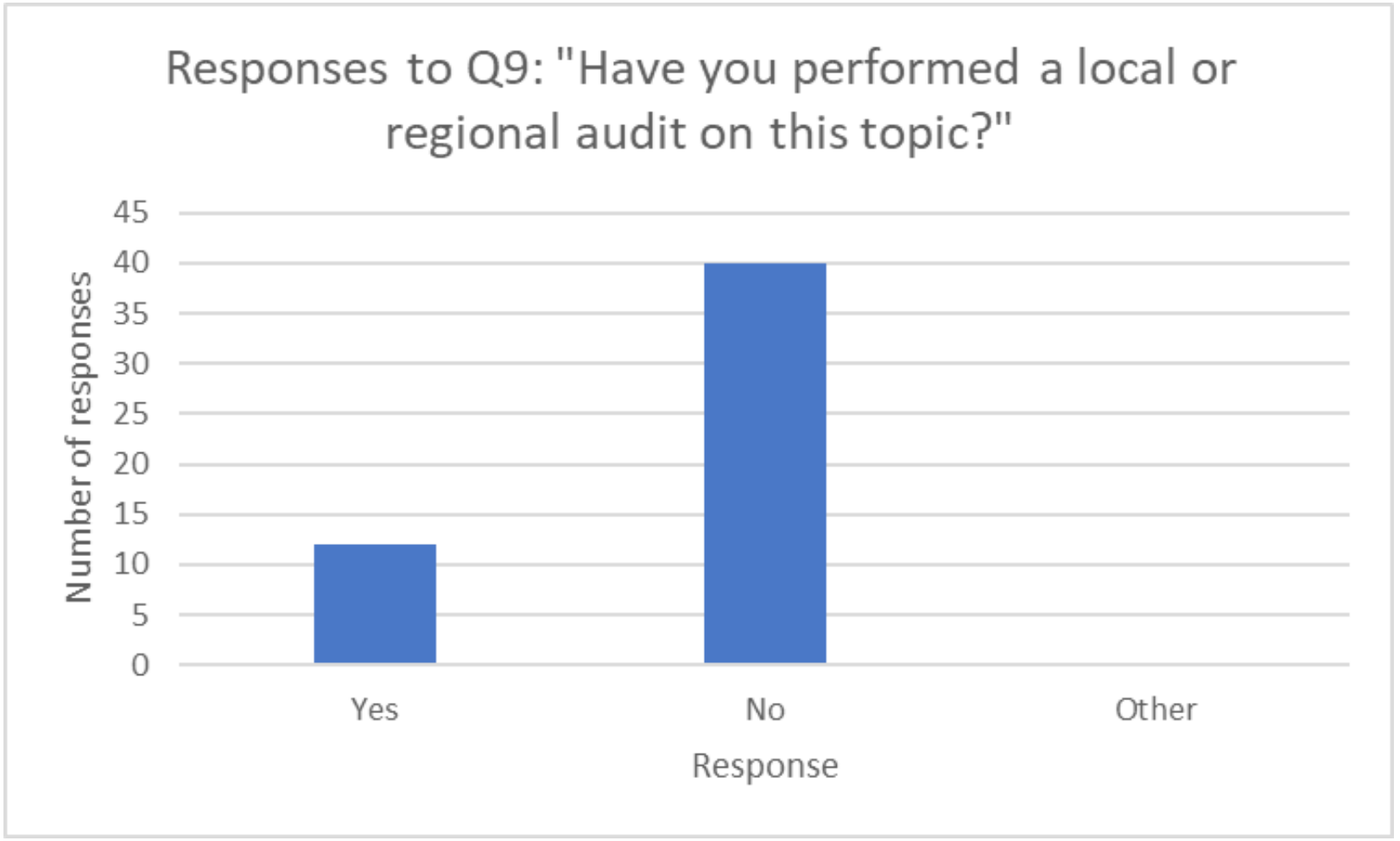
- **JME** (2 centres)
- **POORLY CONTROLLED/FREQUENT SEIZURES** (2 centres)
- **SUSPECTED IGE WITH H/O TC SEIZURES**
- **PATIENTS KNOWN TO HAVE SEIZURES FOLLOWING SLEEP DEPRIVATION**
- **PREVIOUS STATUS EPILEPTICUS** (2 centres)
- **PATIENT AGE** (3 centres)
  - Under 3 years
  - Over 65 years
  - Over 70 years
- **PREGNANCY** 5 centres (not an “absolute contraindication” in 1 centre)
- **MEDICAL HISTORY**: “medically unfit” , “encephalopathy”, “cardiac problems”, “sleep disorder”, “compliance difficulties”, “heavy alcohol consumption”

- **NO ROUTINE EEG** (3 centres)
- **PREVIOUS ABNORMAL EEG** (2 centres)
- **PHOTOPAROXYSMAL RESPONSE ON ROUTINE EEG**

Part A: *Findings*



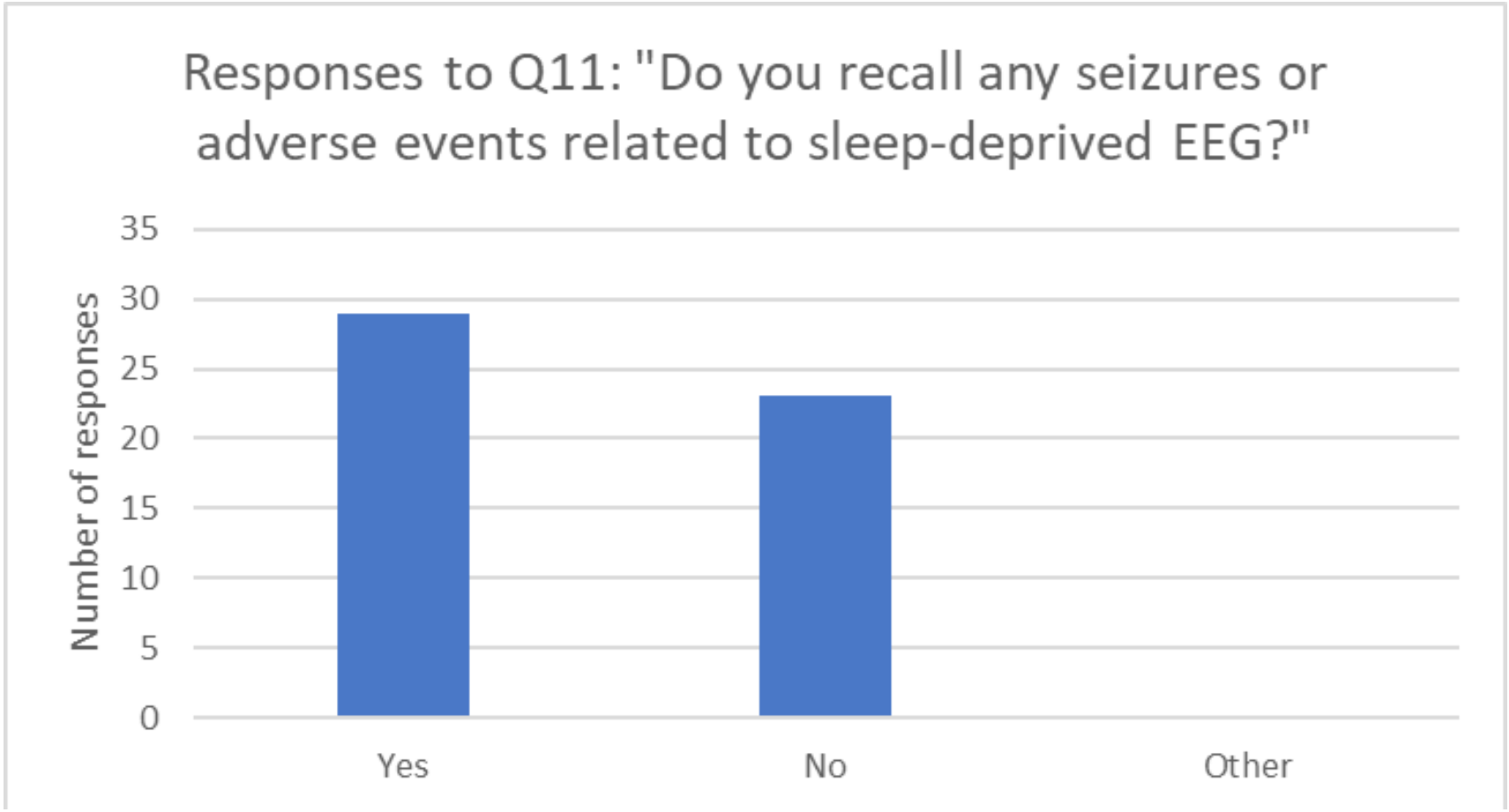
Part A: *Findings*



Recommendations from local audits

Physiologist student project (2008) comparing EEG and SDEEG outcome. SDEEG yield more information than routine EEG when performed first
Process and efficiency of sleep deprived EEG in achieving stage 2 sleep and test outcomes. Recommendations: Largely successful. Continue with partial sleep dep; increase use of melatonin in severely anxious patients
1. Consider total overnight SD to improve numbers that sleep 2. If total overnight SD choose an early appt (rather than 2.15pm) 3. Consider melatonin in children
‘Worth giving melatonin to children’
SDEEG increased rate of positive findings to 40% (*vs* 23.5% routine without sleep)
No recommendations; abnormality in 24% of 50 patients

Part A: *Findings*



Adverse events (27 centres)

Event	Centres reporting
GTCS	17
GTCS during photic stimulation	3
Partial seizures	2
Patient having seizure at home prior to appt	2
Partial status	2
NCSE	2
Myoclonic status	1
Myoclonic jerks	1

Changes to practice from adverse events

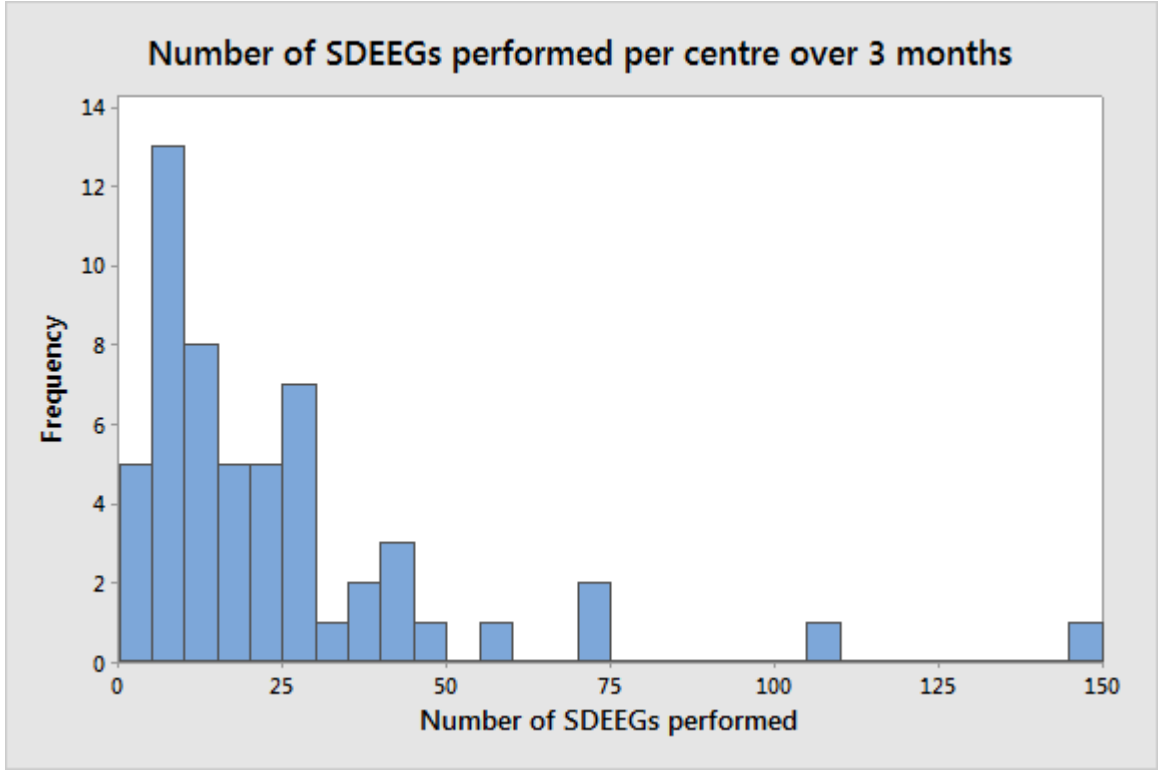
- No activation procedures carried out during SDEEG
- Routine EEG first for JME referrals
- Ambulatory EEG rather than SDEEG for JME referrals
- Routine EEG within 12 months before proceeding to SDEEG
- No SDEEG if patient having frequent clinical events
- Optimise patient information: Ensure patient information includes risks of seizures and asks patients not to drive and attend accompanied. Advise to rest afterwards
- Admit patient if there are concerns and sleep deprive on the ward overnight, then observe on the ward during the day

- **20 departments reported no change in practice**

Part B

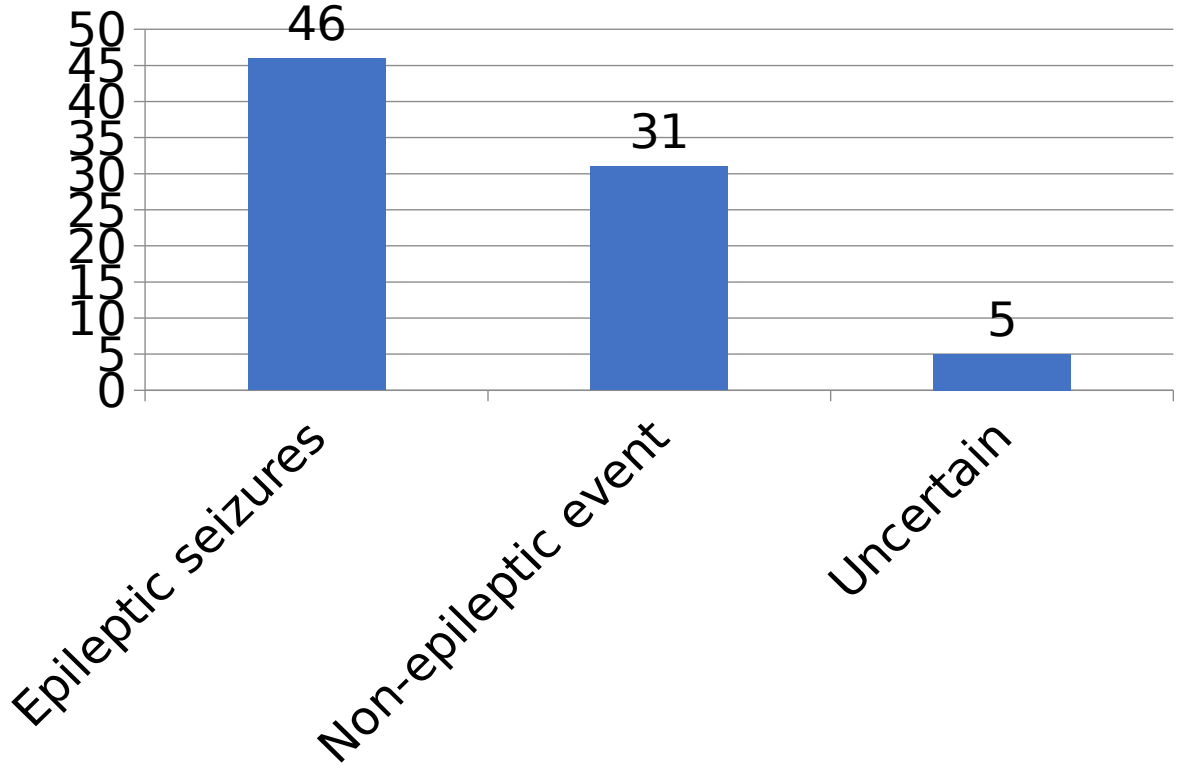
Results

- Total of 1317 SDEEGs performed in prospective study period
- 731 paediatric; 586 adult
- Median 5.7 SDEEGs per centre per month

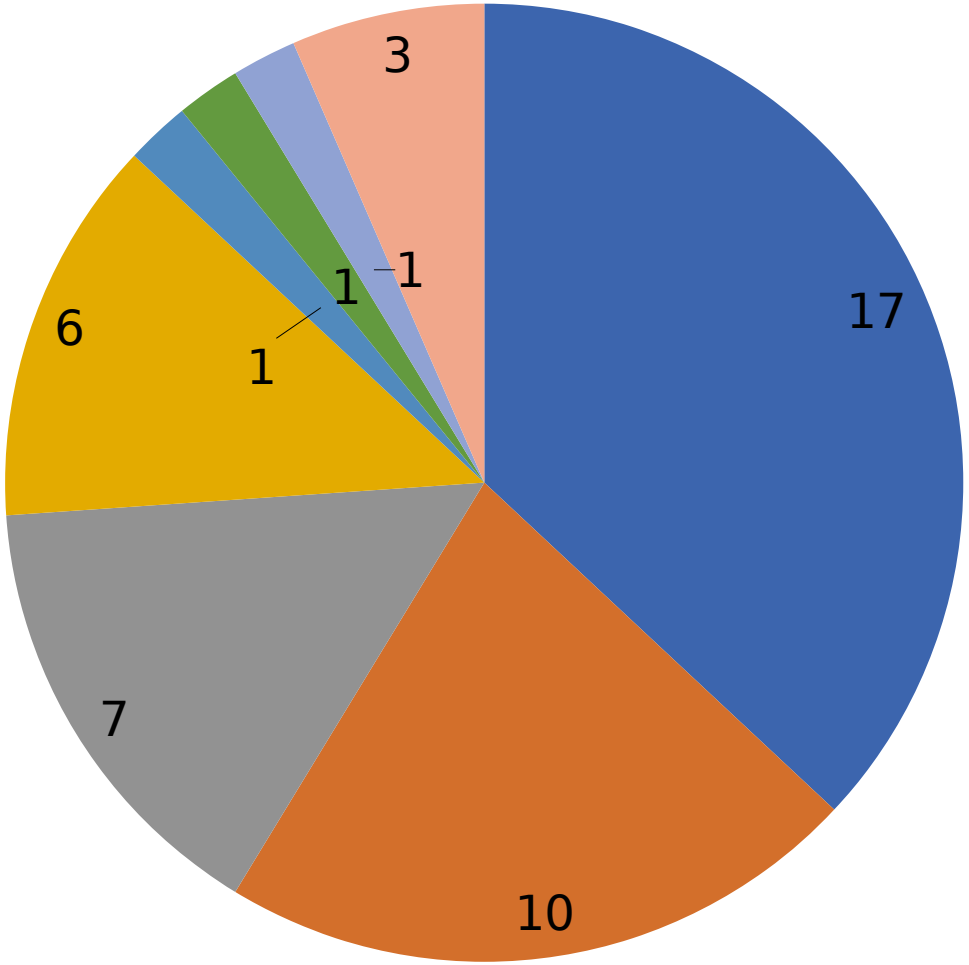


To determine the frequency of epileptic seizures occurring during sleep-deprivation EEG in a typical referral population

- Clinical event reported in 82 SDEEGs
- 46 seizures
  - 11 during HV
  - 5 during PS



Seizure type



- Generalised seizure - not otherwise specified
- Absence s ure
- Myoclonic jerk
- Focal seizure
- Drop attack
- Tonic seizure
- Subclinical seizure
- Not classified

In 3 instances (2 paediatric) the patient required monitoring or further assessment after the SDEEG

To determine the frequency of epileptic seizures occurring during sleep-deprivation EEG in a typical referral population

	This study		***ANS/BSCN NEAD Audit 2016***	
	Adult *(n=586)*	*Paediatric (n=731)*	Adult *(n=9775)*	*Paediatric (n=2693)*
Epileptic seizures	1.7%	4.9%	1.0%	6%

Overall, seizure frequency appears similar to a comparable, non-sleep deprived study population

0.2% of patients had seizures requiring further assessment or monitoring after completion of the SDEEG

NB: does not include any seizures that may have occurred after the patient left the department

To determine the effect of several variables on the detection of epileptiform abnormalities in SDEEG

- Patient-related variables
  - *Presence and type of epilepsy*
  - Age
  - Gender
  - Use of anti-epileptic medications at time of EEG

- Test-related variables
  - Sleep stage reached
  - Duration of overnight sleep deprivation (total or partial)
  - Recording duration
  - Time of day of EEG recording
  - Additional use of sedative medication
  - Use of additional activation procedures including HV and PS

To determine the effect of several variables on the detection of epileptiform abnormalities in SDEEG

- 994 studies (484 adults; 512 paediatrics)

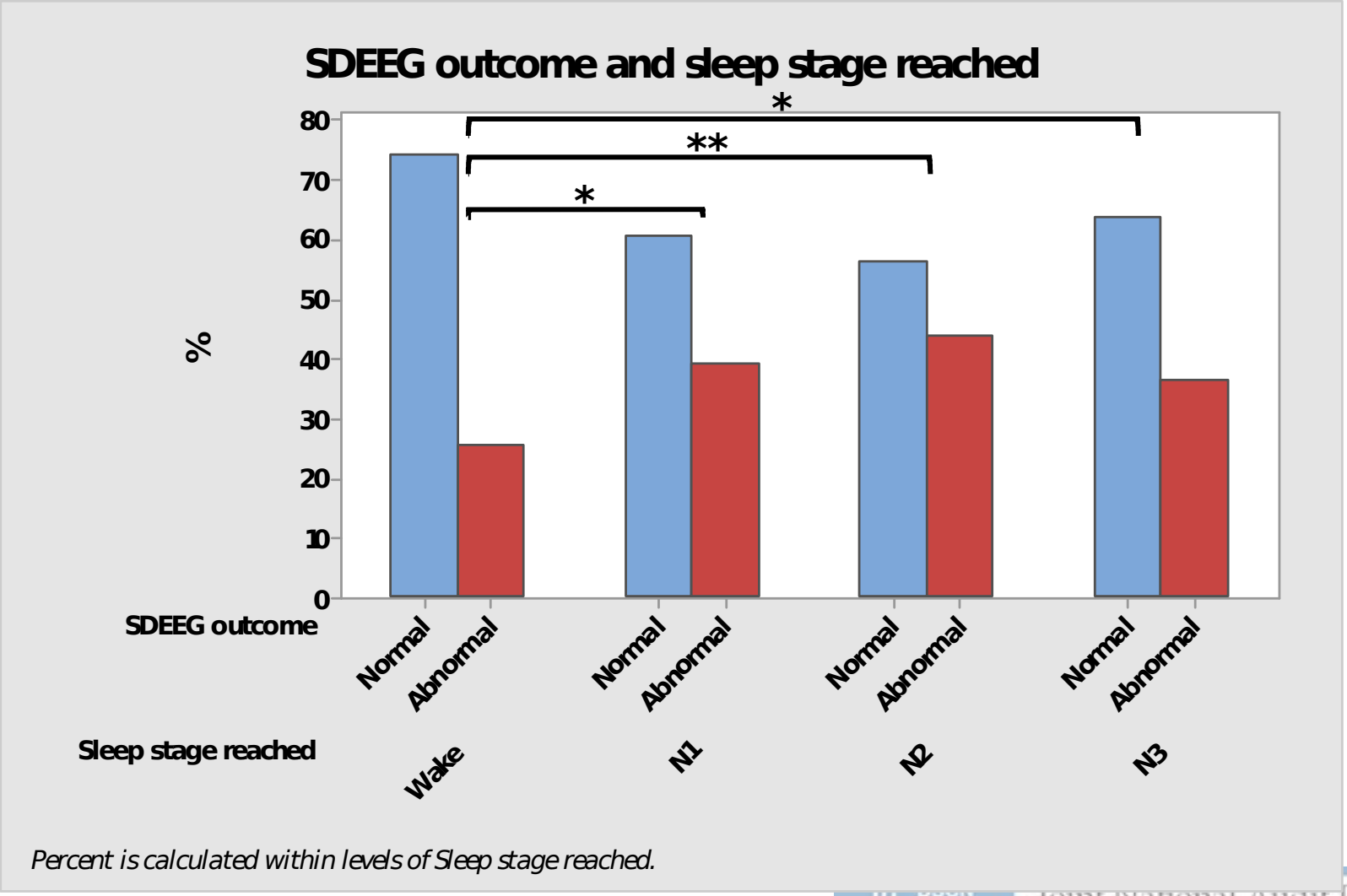
610 “normal” SDEEGs
containing no abnormality, non-specific changes or findings not supportive of diagnosis of epilepsy
384 “abnormal” SDEEGs
containing focal or generalised sharp waves or spike discharges other category with free-text option

38.6% of patients without abnormality on routine EEG had epileptiform abnormalities on SDEEG

	Total		Normal SDEEG (%)	Abnormal SDEEG (%)	P value
Patient age					*p=0.029*
Adult	483		65.6	34.4	
Paediatric	511		57.3	42.7	
Patient gender					*p=0.215*
Male	475		59.4	40.6	
Female	519		63.2	36.8	
Taking AEDs (data missing for 35)					*p=0.067*
Yes	282		56.7	43.3	
No	677		63.1	36.9	
Use of sedative medication					*p=0.010*
Yes	159		52.2	47.8	
No	835		63.1	36.9	
Sleep stage reached					*p<0.001*
Wake only	179		74.3	25.7	
N1	815		58.5	41.5	
N2	708		58.2	41.8	
N3	182		63.7	36.3	
Sleep deprivation					*p=0.508*
Total	273		59.7	40.3	
Partial	721		62.0	38.0	

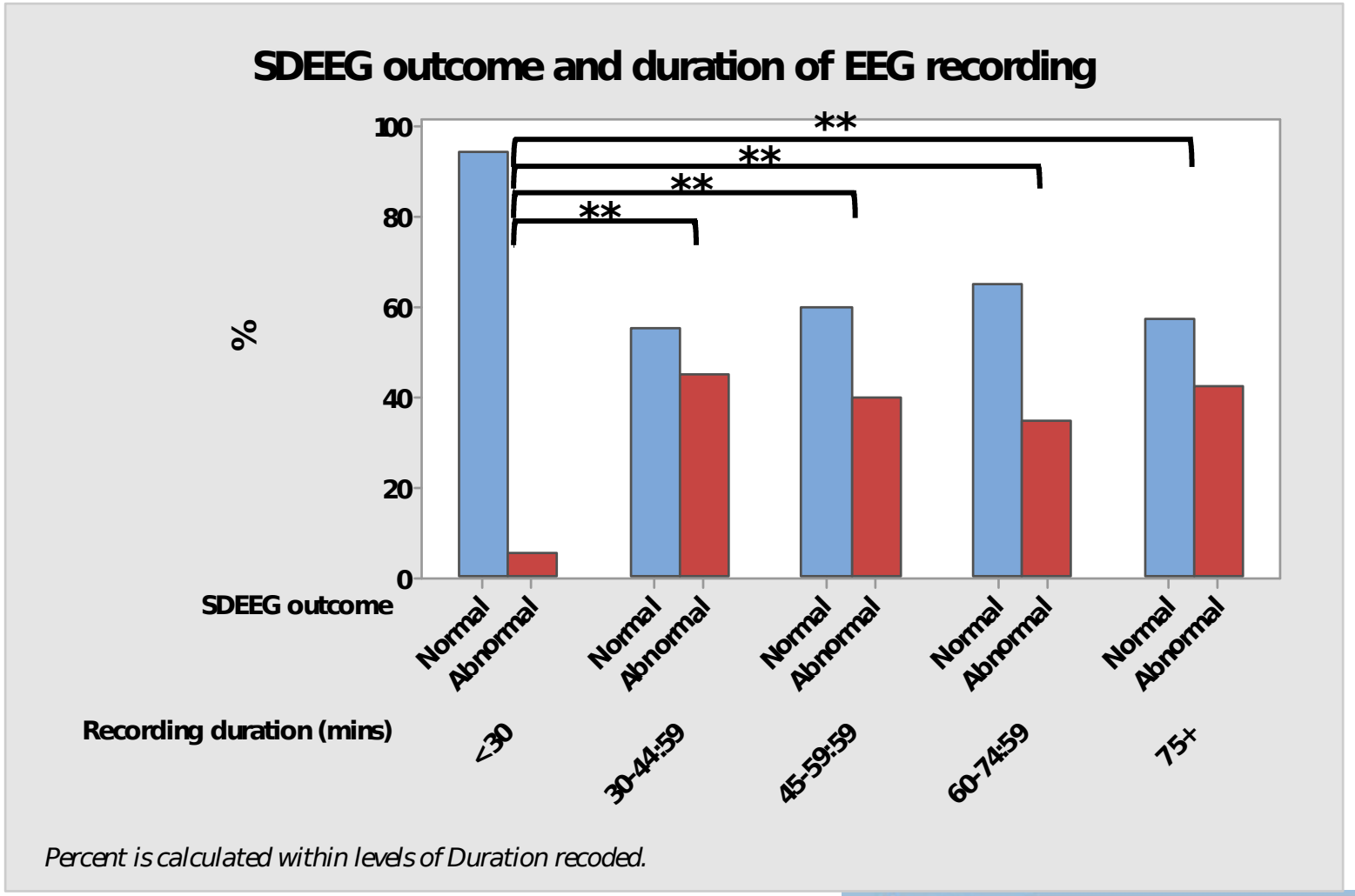
	Total		Normal SDEEG (%)	Abnormal SDEEG (%)	P value
Time of day of recording					*p=0.891*
08:00-09:59	518		61.8	38.2	
10:00-11:59	190		58.9	41.1	
12:00-13:59	203		62.6	37.4	
14:00-15:59	83		61.4	38.6	
Time patient woken					*p=0.936*
21:00-02:00	54		64.8	35.2	
02:01-04:00	88		60.2	39.8	
04:01-06:00	369		62.9	37.1	
06:01-11:00	163		61.3	38.7	
Duration of recording (mins)					*p<0.001*
<30	73		64.4	35.6	
30-44	306		56.9	43.1	
45-59	283		62.2	37.8	
60-74	248		65.7	34.3	
>75	84		59.5	40.5	
Included HV					*p=0.026*
Yes	533		58.2	41.8	
No	461		65.1	34.9	
Included PS					*p=0.009*
Yes	612		58.2	41.8	
No	382		66.5	33.5	

SDEEG outcome and sleep stage reached



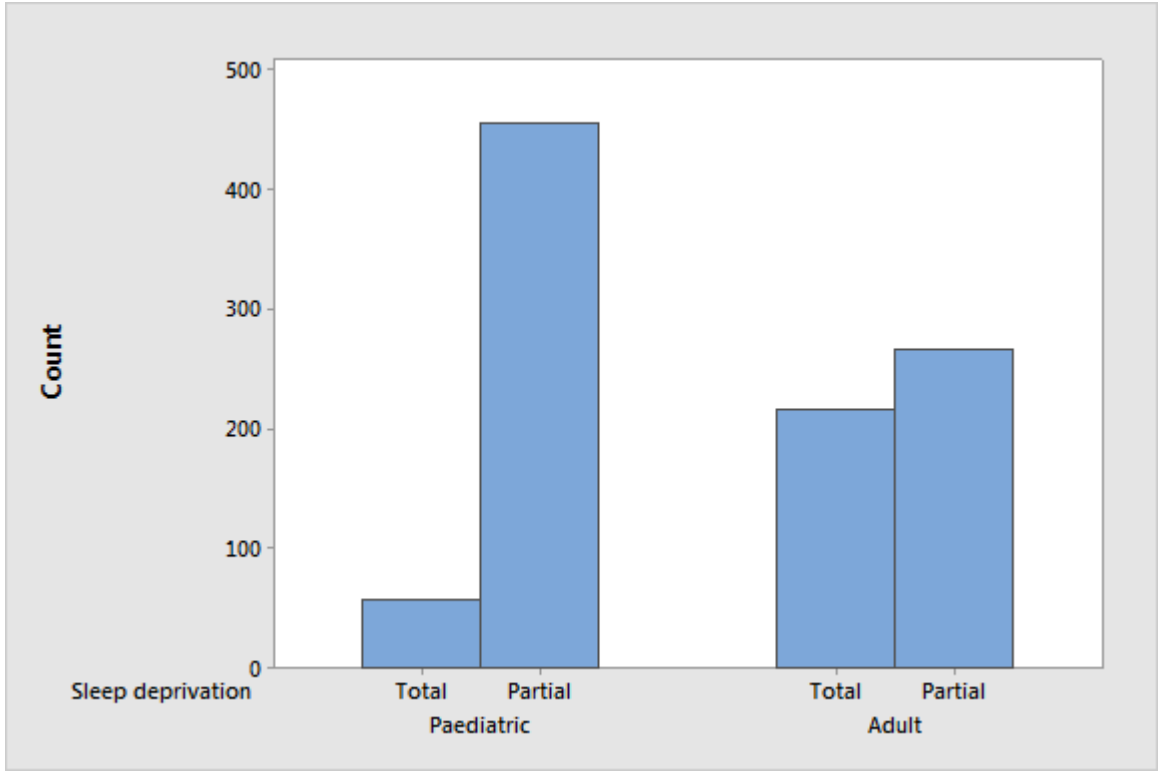
*p<0.05
**p<0.01

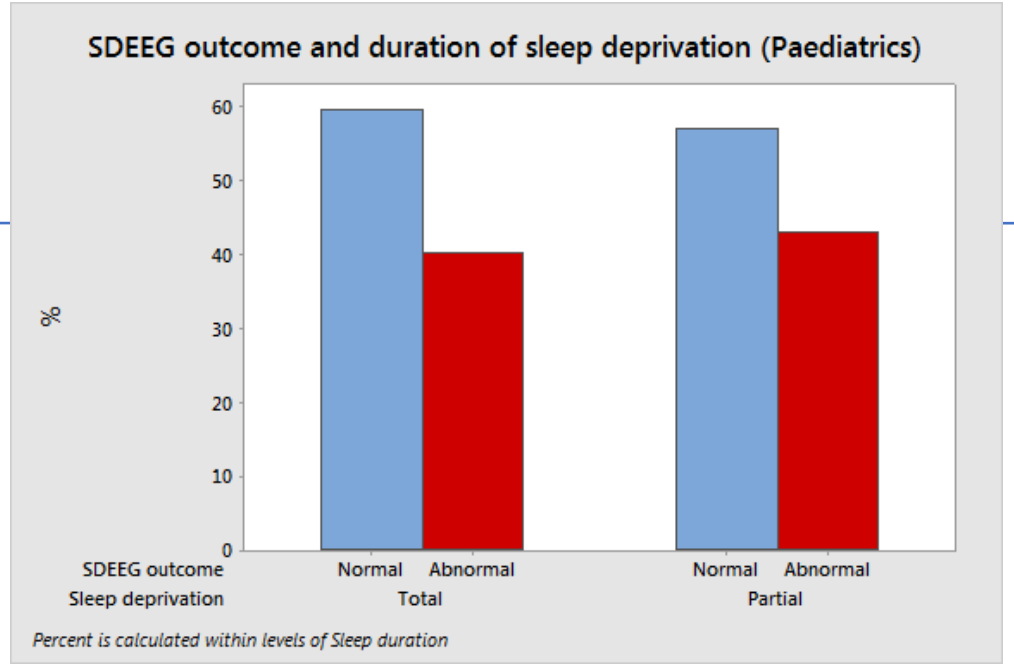
SDEEG outcome and duration of recording



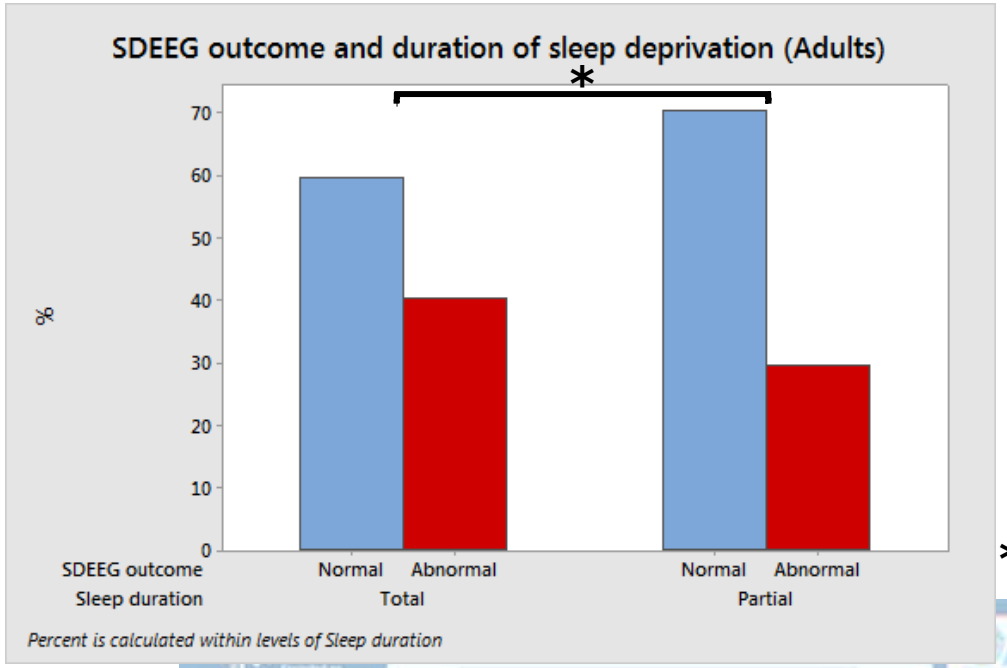
*p<0.05
**p<0.001

Partial *vs* total sleep deprivation



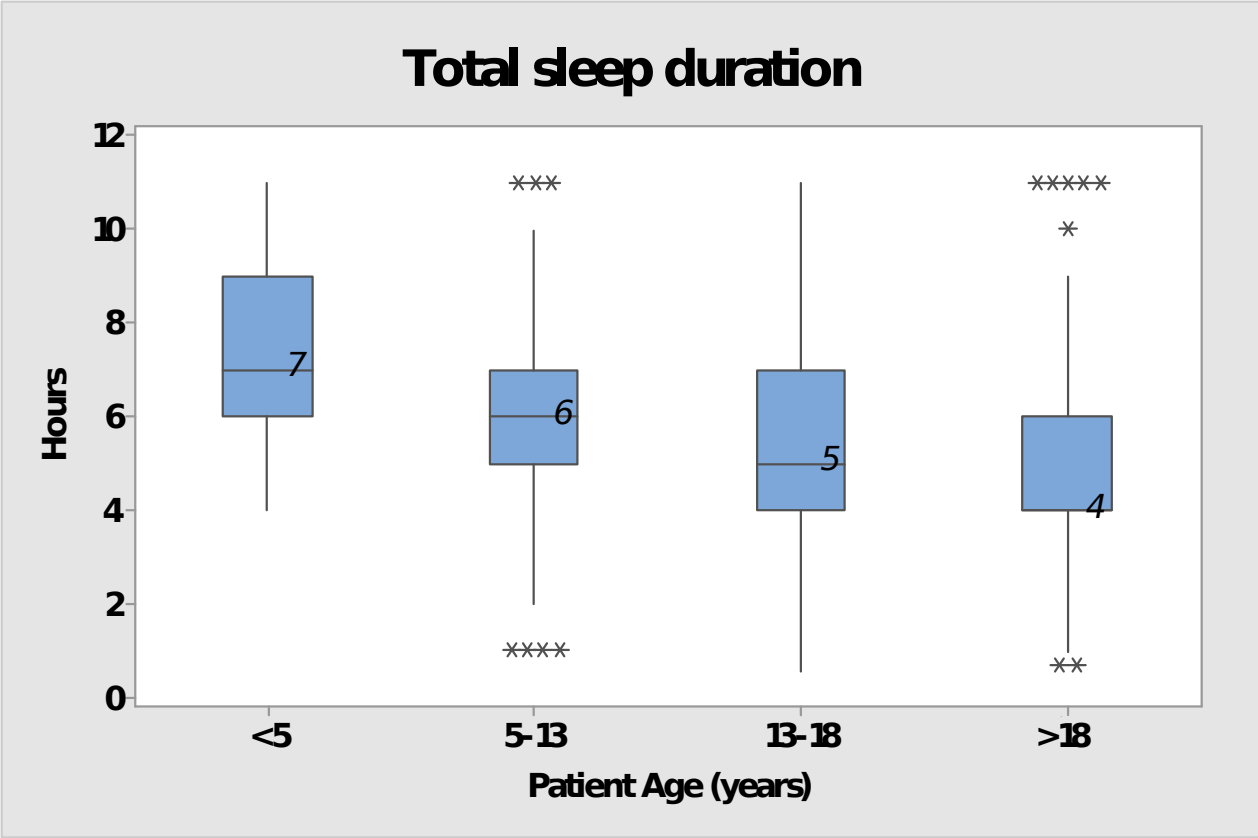


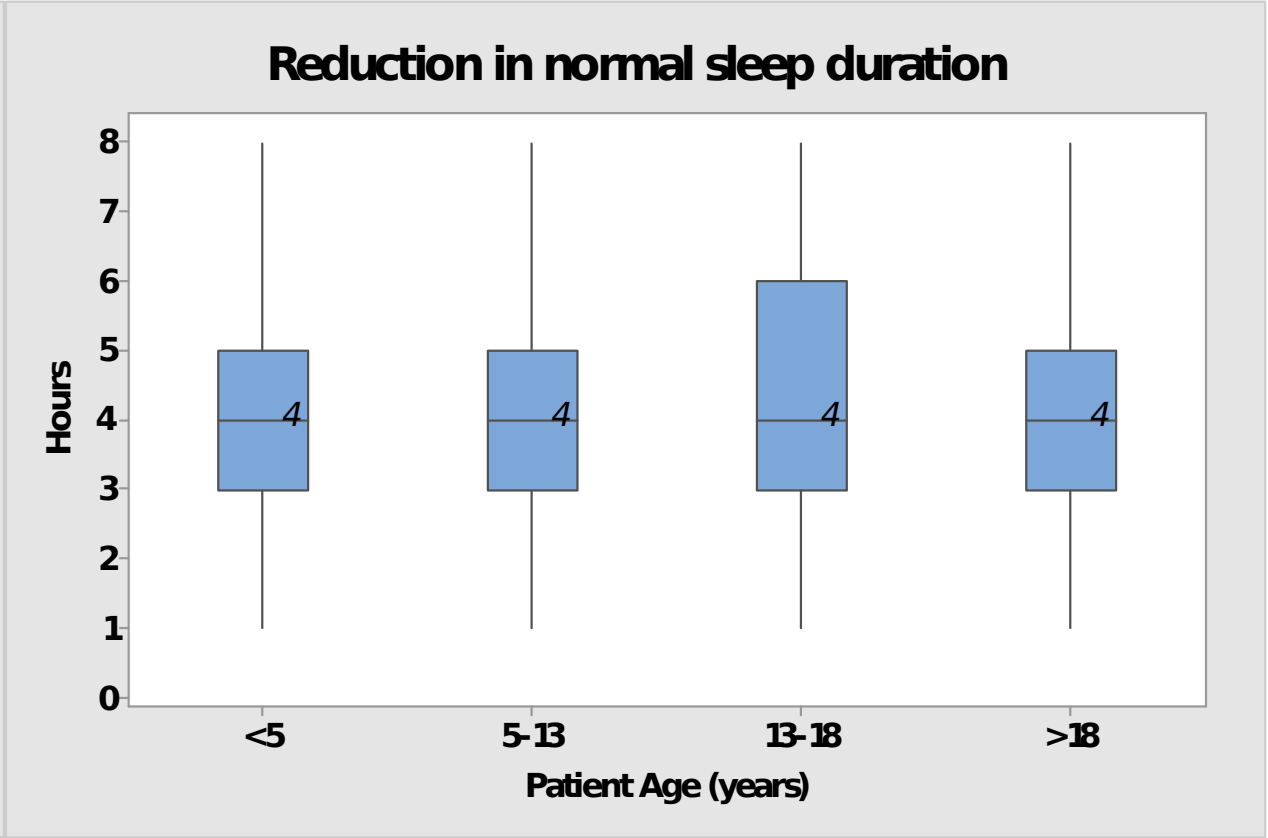
p=0.708



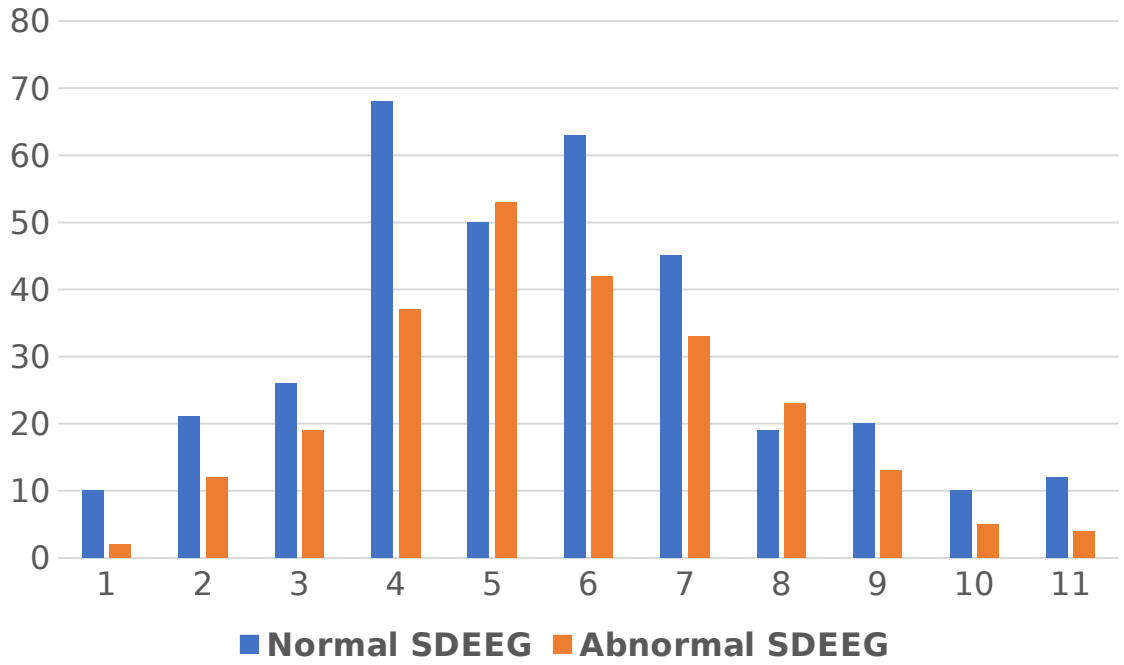
***p<0.05**

Partial sleep deprivation





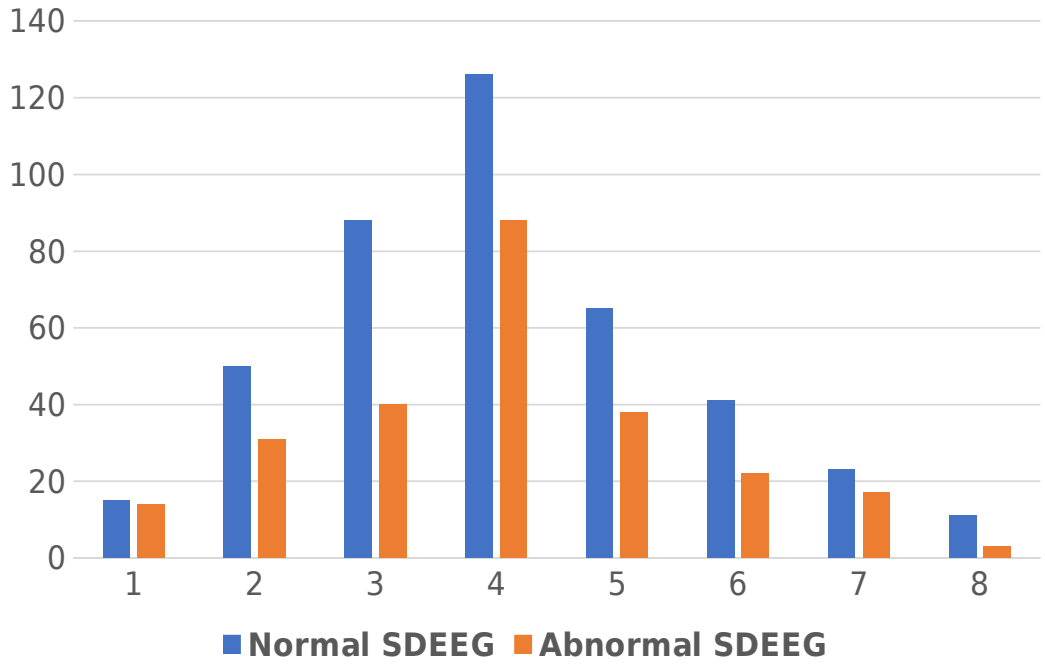
Total sleep duration (in hours)



	Normal SDEEG	Abnormal SDEEG
Mean	5.5	5.7
Median	5.0	5.0

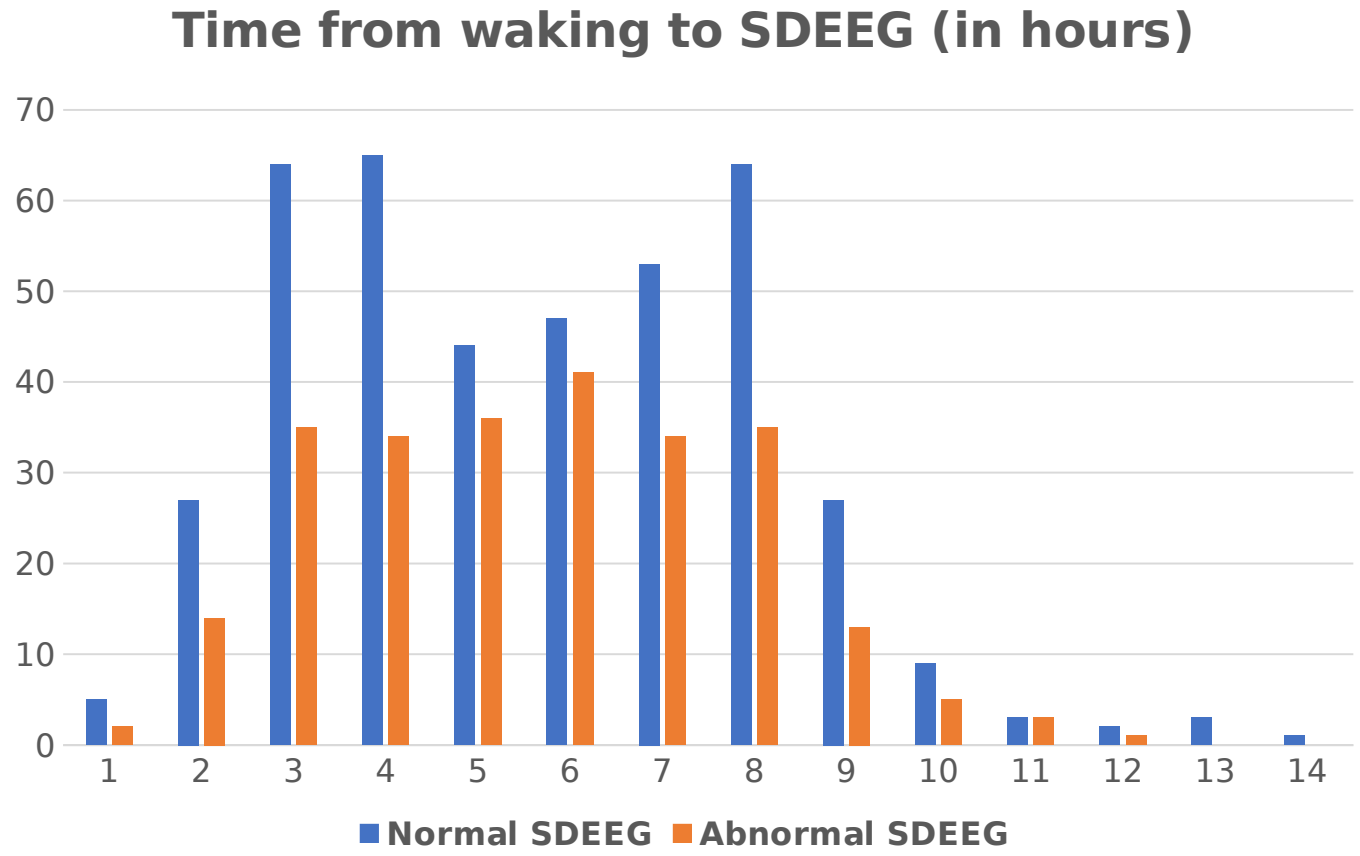
P-value=0.413

Reduction in normal sleep duration (in hours)



	Normal SDEEG	Abnormal SDEEG
Mean	4.1	4.0
Median	4.0	4.0

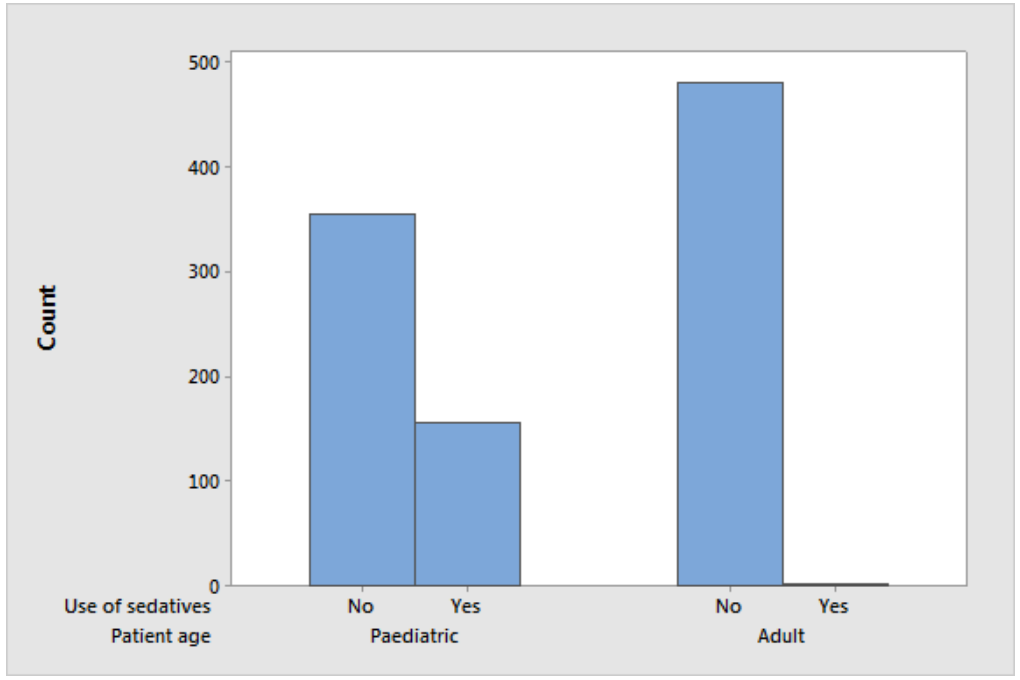
P-value=0.853

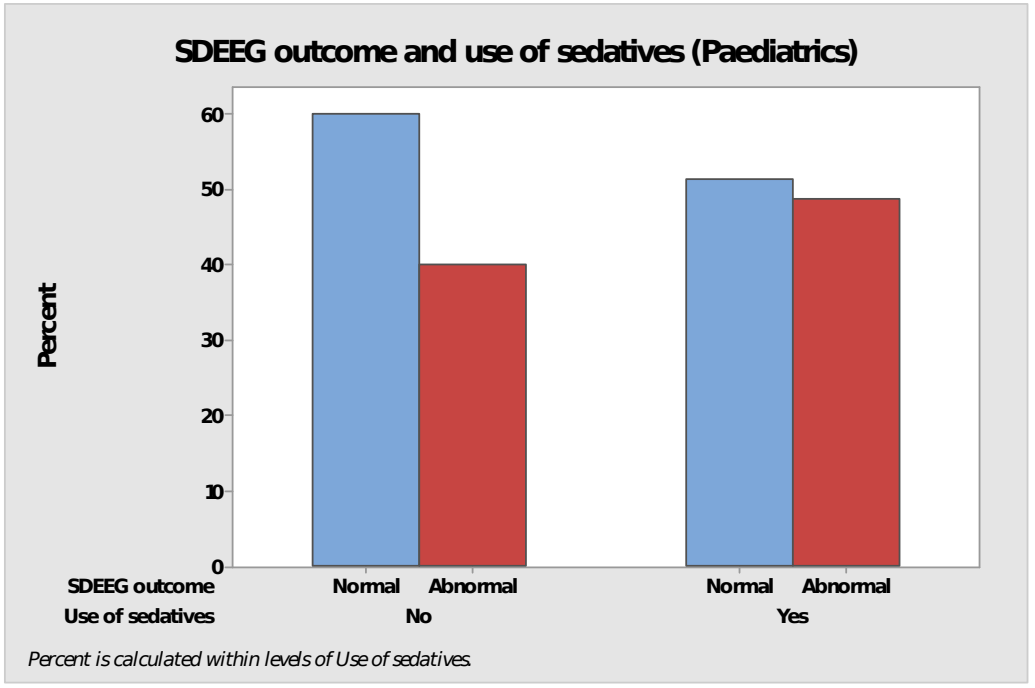


	Normal SDEEG	Abnormal SDEEG
Mean	5.7	5.6
Median	6.0	6.0

P-value=0.755

SDEEG outcome and use of sedation





p=0.067

Multivariate analysis

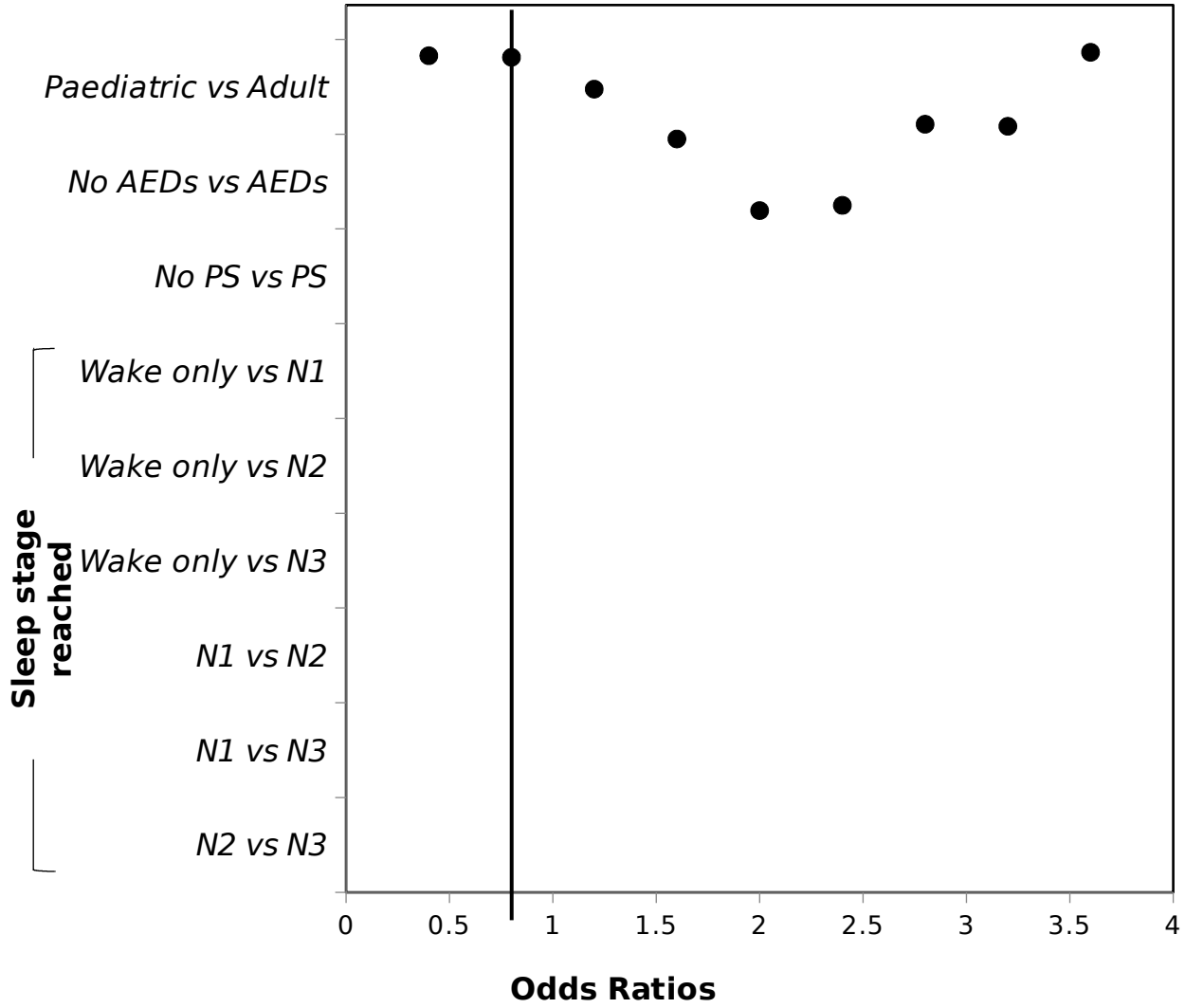
- Binary logistic regression modelling (stepwise and backwards elimination)
- Dependent variable “normal SDEEG” or “abnormal SDEEG”
- Alpha to enter and remove of 0.05

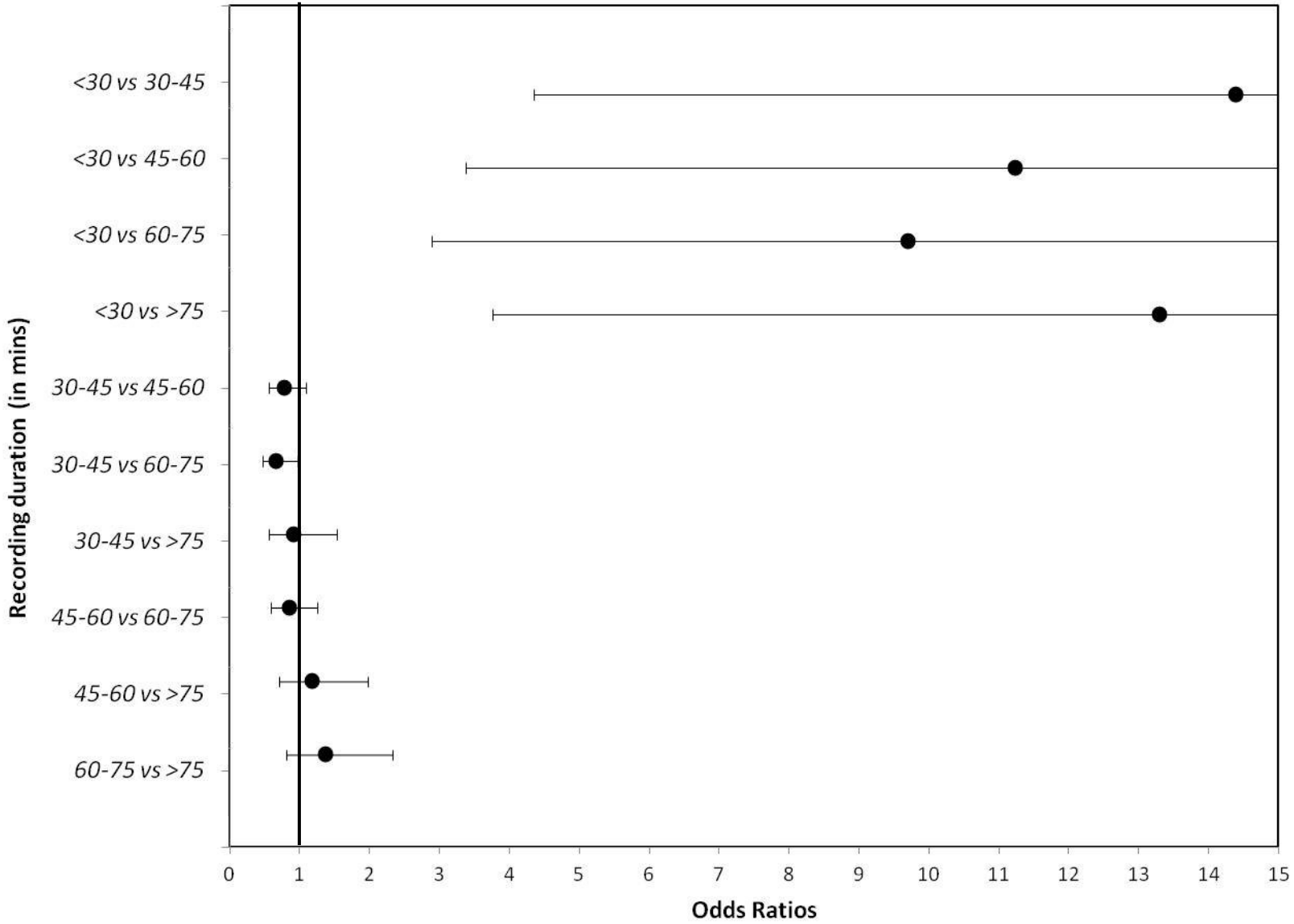
- Both stepwise and backwards elimination models identified the same variables

Variable	P-value
Patient age	**0.002**
Patient gender	*>0.05*
Use of AEDs	**0.021**
Sleep stage reached	**<0.001**
Total or partial sleep-dep	*>0.05*
Recording duration	**<0.001**
Time of day of recording	*>0.05*
Use of sedatives	*>0.05*
HV	*>0.05*

Goodness-of-Fit Tests

Test	DF	Chi-Square	P-Value
Hosmer-Lemeshow	8	14.03	0.081




<30 vs 30-45
<30 vs 45-60
<30 vs 60-75
<30 vs >75
30-45 vs 45-60
30-45 vs 60-75
30-45 vs >75
45-60 vs 60-75
45-60 vs >75
60-75 vs >75
Recording duration (in mins)
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
Odds Ratios

Subgroup analysis

- Adult patients
- Partial sleep deprivation group

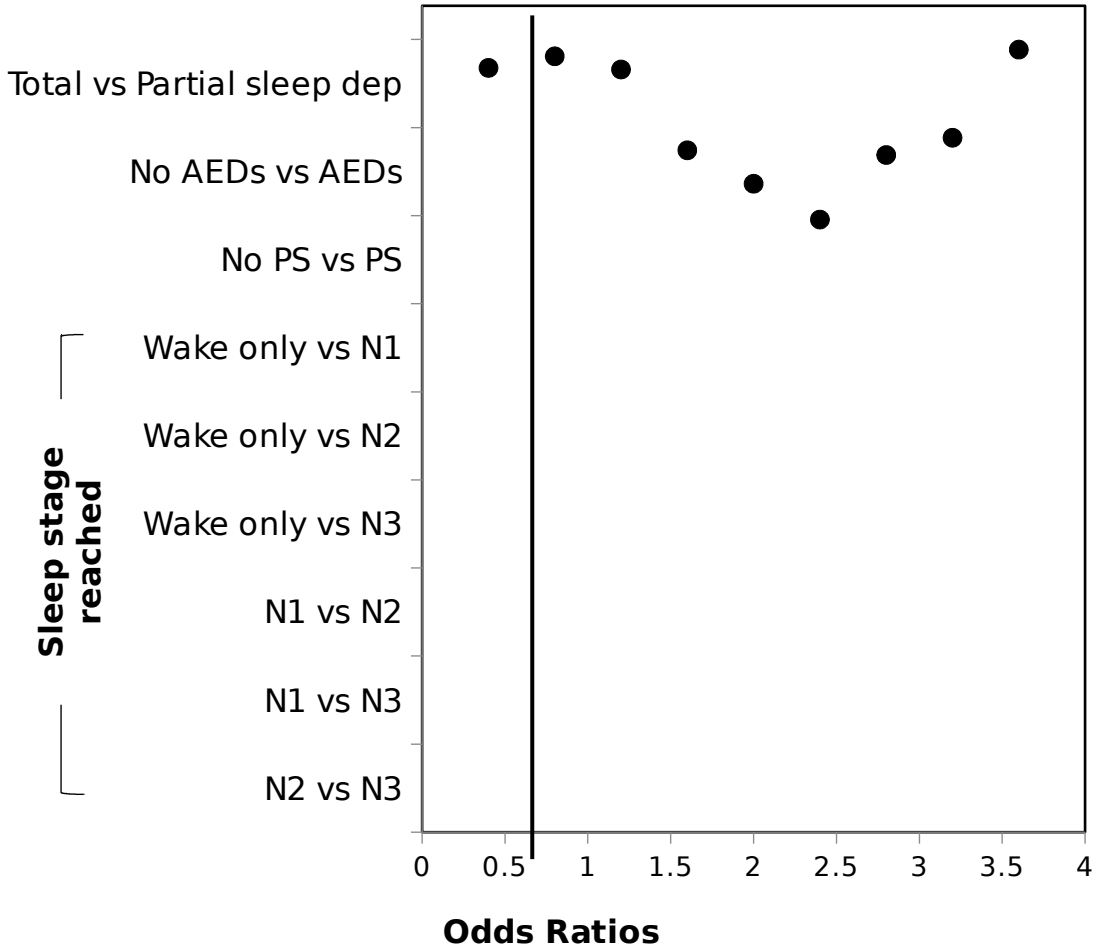
Subgroup analysis: *Adult patients*

Variable	P-value
Patient gender	*>0.05*
Use of AEDs	**0.023**
Sleep stage reached	**0.039**
Total or partial sleep-dep	**0.016**
Time of day of recording	*>0.05*
HV	*>0.05*
PS	**0.004**

NB: "Recording duration" variable not included due to low sample size in some groups

Goodness-of-Fit Tests

Test	DF	Chi-Square	P-Value
Hosmer-Lemeshow	8	4.37	0.822



Study limitations

Limitations

- Heterogenous patient group including patients with and without epilepsy, including epilepsy type e.g. JME
- Classification of epileptiform abnormalities may vary across different participating centres
- Didn’t assess effect of different types of AED
- In assessing seizures in relation to sleep-derivation EEG, we cannot say seizures were “provoked” as we have no knowledge of normal seizure frequency. Also don’t know what happened after patient’s left the department

Summary of main findings

Findings

- Concern exists regarding seizure provocation with SDEEG
- Examples of change in practice resulting from this
- Patients are informed of “risk” (pre-test information sheet)
- Variable use of consent procedures

- Seizure occurrence in a typical referral population is similar to a comparable non sleep-deprived population
- 0.2% of study population had seizures preventing immediate return home following the SDEEG

Findings

- Detection of epileptiform abnormalities in 38.6% of a heterogenous patient group without reported abnormality on routine EEG

- Variables related with detection of epileptiform abnormalities include:
  - Recording of sleep (all sleep stages)
  - Younger age (paediatric > adult age groups)
  - Recording duration > 30 minutes
  - Performance of photic stimulation
  - Total overnight sleep-deprivation (adult patients only)

Findings

- Use of AEDs at time of SDEEG did not appear to reduce detection of epileptiform abnormalities

- Higher rate of detection of epileptiform abnormalities in paediatric patients when sedative medication used in addition to sleep-deprivation, although not quite reaching statistical significance

Recommendations

Recommendations:
Statement for patient information leaflets

"Sleep-deprivation EEG is generally associated with a low added risk of having an epileptic seizure.

If you have a history of seizures occurring after sleep-deprivation and are concerned please contact_____"

Recommendations:
Practice guidelines

- Duration of EEG recording should be sufficient to allow recording of N3 sleep and as an absolute minimum should be 30 minutes*
- Use of total overnight sleep-deprivation in Adult patients
- Use of partial overnight sleep-deprivation in Paediatric patients
- Routine performance of photic stimulation in SDEEG
- Avoid stopping/with-holding anti-epileptic medication prior to SDEEG

**recommendation altered following discussion at national meeting*

Recommendations:
Practice options

- Performance of hyperventilation prior to sleep
- Use of sedative medication in addition to partial sleep-deprivation in paediatric patients
- Protocol for partial overnight sleep-deprivation
  - Aim to reduce normal sleep duration by 4 hours*
  - This can be achieved by either asking the patient to wake 4 hours earlier than normal *or* go to bed 2 hours later and wake 2 hours earlier than normal*

**recommendations based on commonest current UK practice rather than evidence-based recommendation*

Recommendations

Practice Guidelines

- Duration of EEG recording should be sufficient to allow recording of N3 sleep and as an absolute minimum should be 30 minutes
- Use of total overnight sleep-deprivation in Adult patients
- Use of partial overnight sleep-deprivation in Paediatric patients
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- Avoid stopping/with-holding anti-epileptic medication prior to SDEEG

Practice Options

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