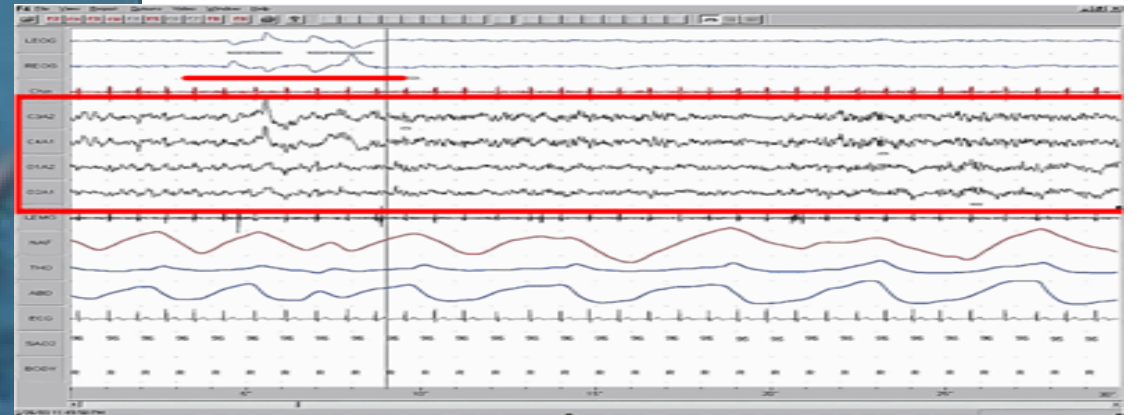


Melatonin, sleep and EEG



Drs Caroline Ross and Lesley Notghi
Joint ANS/BSCN audit meeting October
2014

MELATONIN

- What is it?
- What does it do?
- Personal experience treating patients
- Adverse effects
- Literature review
- Personal experience process in EEG recordings
- Preston and Birmingham Children's Hospital audits of sleep recordings

What is melatonin?

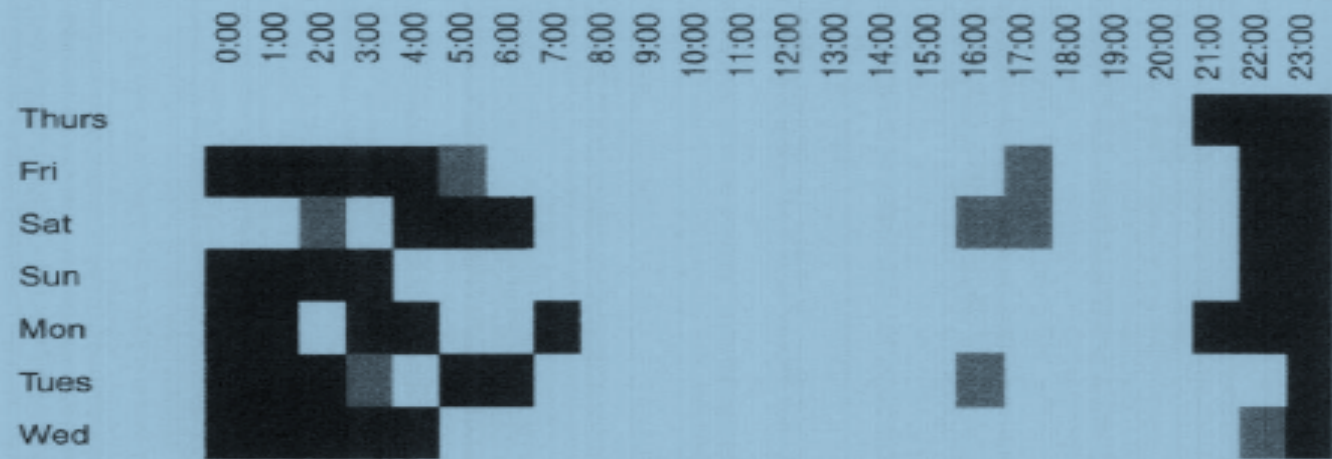
- MT, or N-acetyl-5-methoxytryptamine, is a small lipid and water-soluble indoleamine molecule which can easily cross membrane barriers.
- The circulating MT is produced by the pinealocytes in the pineal gland.
- Normally the pineal gland begins to produce MT in the evening and it is rapidly released into the blood stream.
- Light causes specialized retinal ganglion cells to send information to the suprachiasmatic nucleus of the hypothalamus (SCN).

- Light exposure tends to inhibit the pineal MT secretion while darkness promotes it.
- The SCN is a critically important small paired structure containing about 10000 scattered neurons with a circadian rhythm in vivo and in vitro.
- It gives rhythmicity to MT secretion, sleep, temperature, and cortisol, but it also has such widespread physiological circadian actions through MT that its main function appears to be the changing of the processes in the body from daytime to nighttime in a well coordinated manner.
- MT feeds back to the SCN and can advance or delay sleep onset

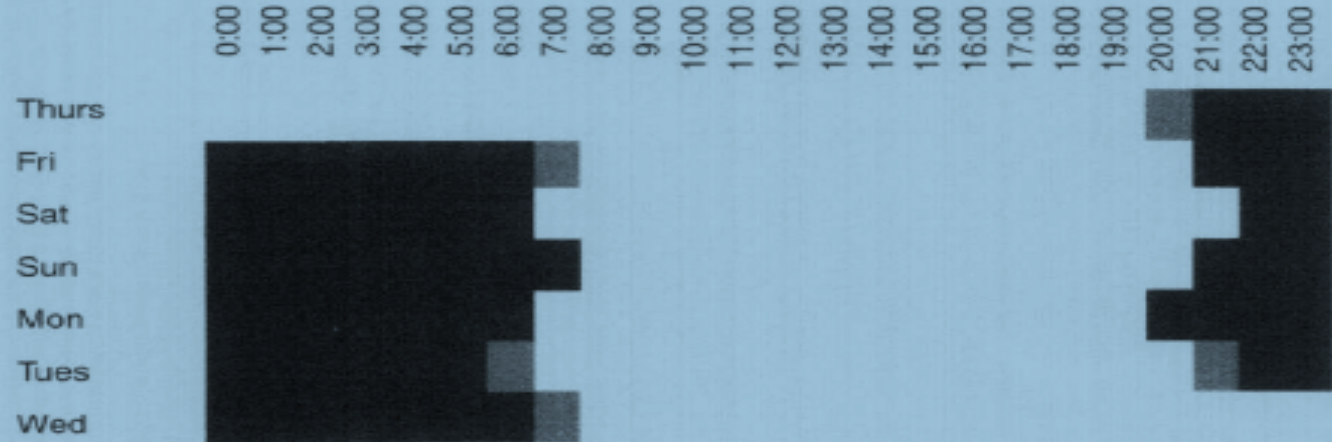
Non -sleep actions melatonin

- Decreased serum luteinizing hormone and increased prolactin- may inhibit hypothalamic-pituitary-gonadal axis and delay puberty if given long-term to prepubertal patients
- ?hypothermia
- Seizure control- most publications neutral or beneficial, one report (Sheldon 1998) reported increased seizures 4 of 6 children but this not replicated

- Mostly with reference to chronic therapy rather than single dose for procedures
- Initially in literature re visual impairment- particularly Jan and Espezel
- Paediatric neurology community in UK became aware after publication paper by Richard Appleton et al 1994 "The treatment of sleep disorders with melatonin" Dev Med and Child Neurology **36**: 97-107
- Prompted my interest as topic for dissertation and subsequent paper



Pretreatment, week 1



Melatonin 2.5 mg, week 2

Figure 1: *Patient 1, difficulty settling and frequent waking.*

Table III: Responses to melatonin treatment by type of sleep disturbance

<i>Sleep problem</i>	<i>Beneficial</i>	<i>Not beneficial</i>
Fragmented sleep	3	2
Difficulty settling	12	2
Low requirement	7	1
Awakening	11	4
Delayed-sleep phase	2	9

- Common: More than 1 in 100 people who take Melatonin
- Back pain
- Headaches
- Inflammation of the nose and throat
- Joint pain
- (From “NHS Choices” re melatonin 2 mg modified release tablets)

Adverse effects

Adverse Effects

- **Side-effects that you must do something about**
- If your child gets a fast heart rate (they may have a fluttering feeling in the chest or feel the heart beating fast), contact your doctor before giving the next evening's dose.
- If they seem unwell, take them to hospital.
- **Other side-effects you need to know about**
- Your child's temperature may fall a little after taking melatonin. This is a normal reaction to melatonin.
- (From Medicines for Children leaflet)

- “In clinical trials the rate of patients with adverse events per 100 patient weeks was higher for Placebo than Circadin (5.743placebo vs. 3.013 Circadin)”
- (From advert Circadin seen in “Prescriber”)

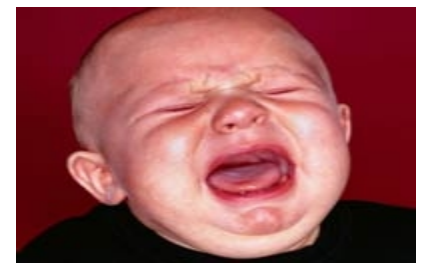
Melatonin as sleep inducer Rx

- 22 studies 1994-2003 of >5 children (7-100)
 - 6/22 double blind placebo controlled
- Sleep improvement:
- good response (>80%) in 16/22 studies
 - moderate -4 poor-2
 - Effect on sleep: mainly Phase Shift in 8/22
Efficiency -5 Induction - 6





Melatonin: -sleep induction for EEG



- Short-acting synthetic melatonin
- Sleep induction for adult EEG 1998 *Milstein*
- Birmingham series: Sleep EEG in children *Wassmer et al-* 2001,2002 4 papers
- Sleep induction for other procedures: audiology BAEPs; MRI; induction of anaesthesia *Schmidt, Johnson*

Melatonin -Sleep EEG in children

- *Wassmer* study (prospective)
- 163 children mean age 8y (1-16 y)
- 2-10mg melatonin. No prior SD (24% SD)
- EEG @ nap times-1100, 1400h
- Efficacy: sleep in 79%
- Sleep onset latency(SOL) 33min
- Epileptiform abnormalities cf SD
- Adverse effects - nil

Literature Review 2010

- *Gupta M*
- 7 DB trials
- 2 RCS + one prospective audit
- *Wassmer, Ashrafi, Wassmer*
- Quality:
'none of the studies were methodologically robust,
and all had their own limitations'...more RCB
studies needed

Melatonin vs Sleep deprivation

- *Wassmer* study 2 (included in 163 children)
- First 30 children with melatonin sleep EEG age/sex matched with 30 children SD only
- As useful as SD- sleep % & epil abnormalities same; but also
- Shorter sleep latency ; no advantage mel+SD
- Shorter duration sleep (38% spontaneous waking after 16-27 min)
- Behaviour better on EEG day

Sleep deprivation	Melatonin
54/68	56/68
36 +/- 5.8	23 +/- 1.2*
28/54	30/56
7/18	8/16

Patients who fell asleep

Time to sleep onset (minutes)
(95% Confidence Interval)

Seizure activity on sleep EEG

Seizure activity on sleep EEG,
but **normal standard EEG**

Studies since 2010

- *2012 Sander* (Hamburg) 50 children
(27 with epilepsy) age 1 – 18y :92 EEGs
- Compared SD only to SD +Mel –
- serial EEG same children
- Assessed EEG quality, abnormal findings, depth of sleep
- Mel does not alter quality of EEG in children with epilepsy, but does not increase success of obtaining recordings in SD children

Studies since 2010

- *2010 Eiserman*
- *70 – 84 EEGs*
- *Dose -6y 10mg*
- *>6y 20mg*
- *SOL 25m (15-45)*
- *Sleep duration 13m*
- *s/effects nil significant – 1 child tired after; 1 child with epil had seizure later in day*
- *Parental acceptability – good*
- *‘good technologist indispensable’*

Studies since 2010

- *2011 Eklof-Areskog*
- Melatonin as substitute for SD
- 273 mel, 191 SD age av 8y
- Dose 3mg 2-4y; 6 mg 5 -17y + 3mg
- 80%/ 78% sleep
- Ep activity 22%/19%
- Parent survey –preferred mel -best younger

Studies since 2010

- *2012 Gustafsson*
- *Diagnosis of epilepsy by means of SD or melatonin induced sleep EEG*
- *Retrospective*
- *115 SD 2007-8*
- *130 Mel 2010-11*
- *Age/sex matched*
- *Sleep: 60% SD 71% mel (NS)*
- *Epil activity no difference NS*
- *Mel some advantage for sleep obtained, n disadvantage, easier for parents!*

Studies since 2010

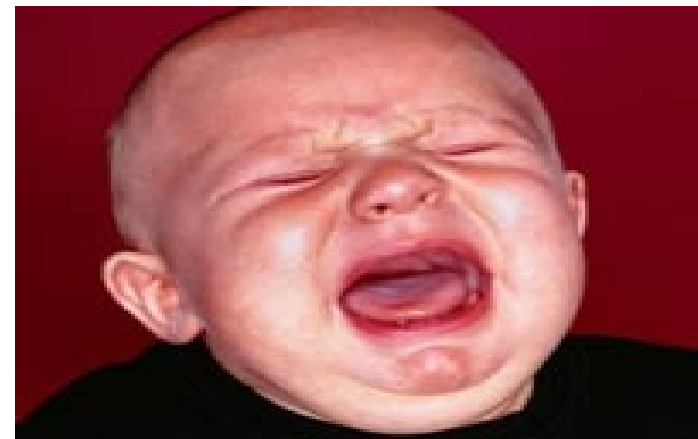
- *Gnidovec 2012*
- *30 infants /toddlers up to 3 y cf sleep dep*
- *Low dose 0.1mg/kg vs 1mg <1 y 2.5mg 1-3*
- *Matched to group of 15 given chloral hydrate*
- *No difference: sleep, SOL, sleep duration*
- *No s/e mel; chloral vomit x2*

Studies since 2010

- *Wilmshurst (SA,CT) on-going April- Aug 2014*
- *6m- 13y; required sleep EEG or failed standard*
- *to determine the safety and effectiveness of oral melatonin as natural inducer of sleep to acquire useful EEGs in South African children*
- *Dose : 3mg<15Kg> 6mg (+ additional if>1hr)*
- *Non-randomised, open label, retrospective*
- *(cf previous use of chloral hydrate:in 6m, n=22)*

Birmingham Children's Hospital Audits

2005: Pre-protocol change



- Standard EEG was attempted on 2-4 year olds
- Hard to get young children to cooperate with hyperventilation and photic stimulation
- Large amount of artefact
- All children 2 and under- sleep EEG (if possible to get them to sleep!)

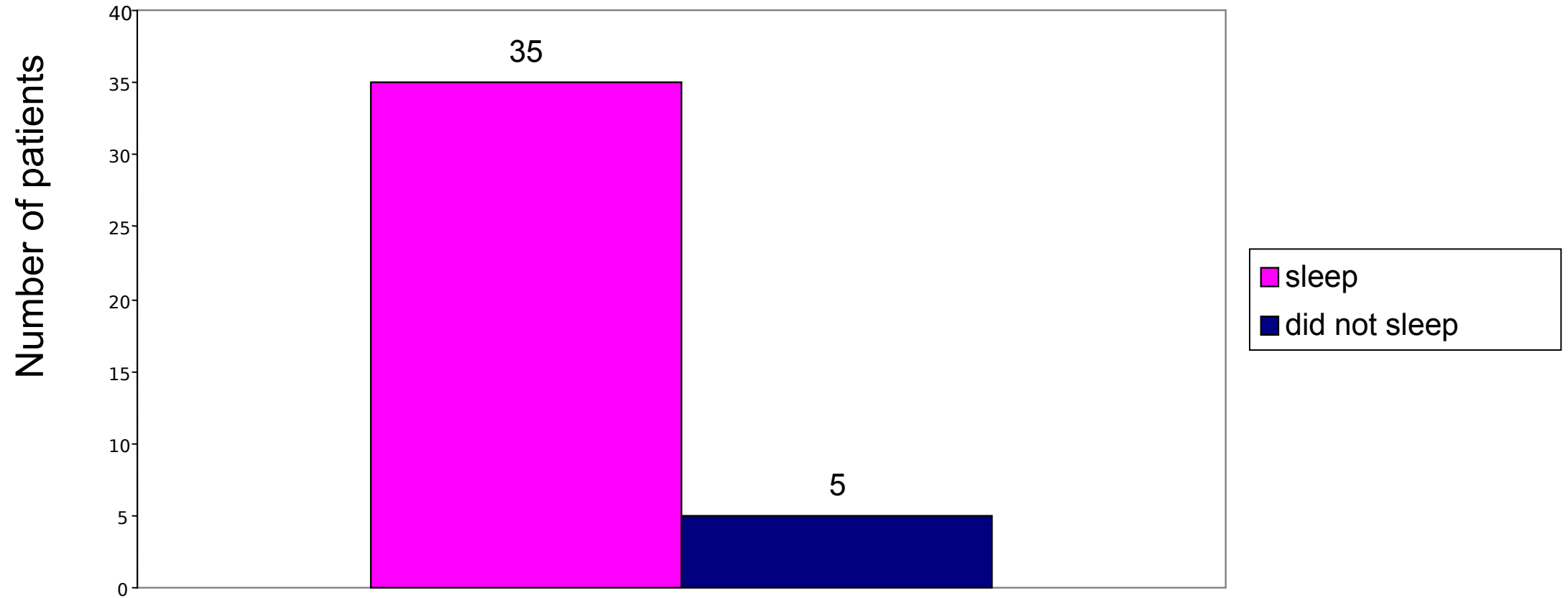
Questions Addressed

- Does using melatonin increase the likelihood of sleep in EEG in a young child 4y and under?
- Is a sleep EEG more sensitive than a standard EEG in children 4 and under?

40 children 18m - 4 yrs,
consecutively referred for EEG

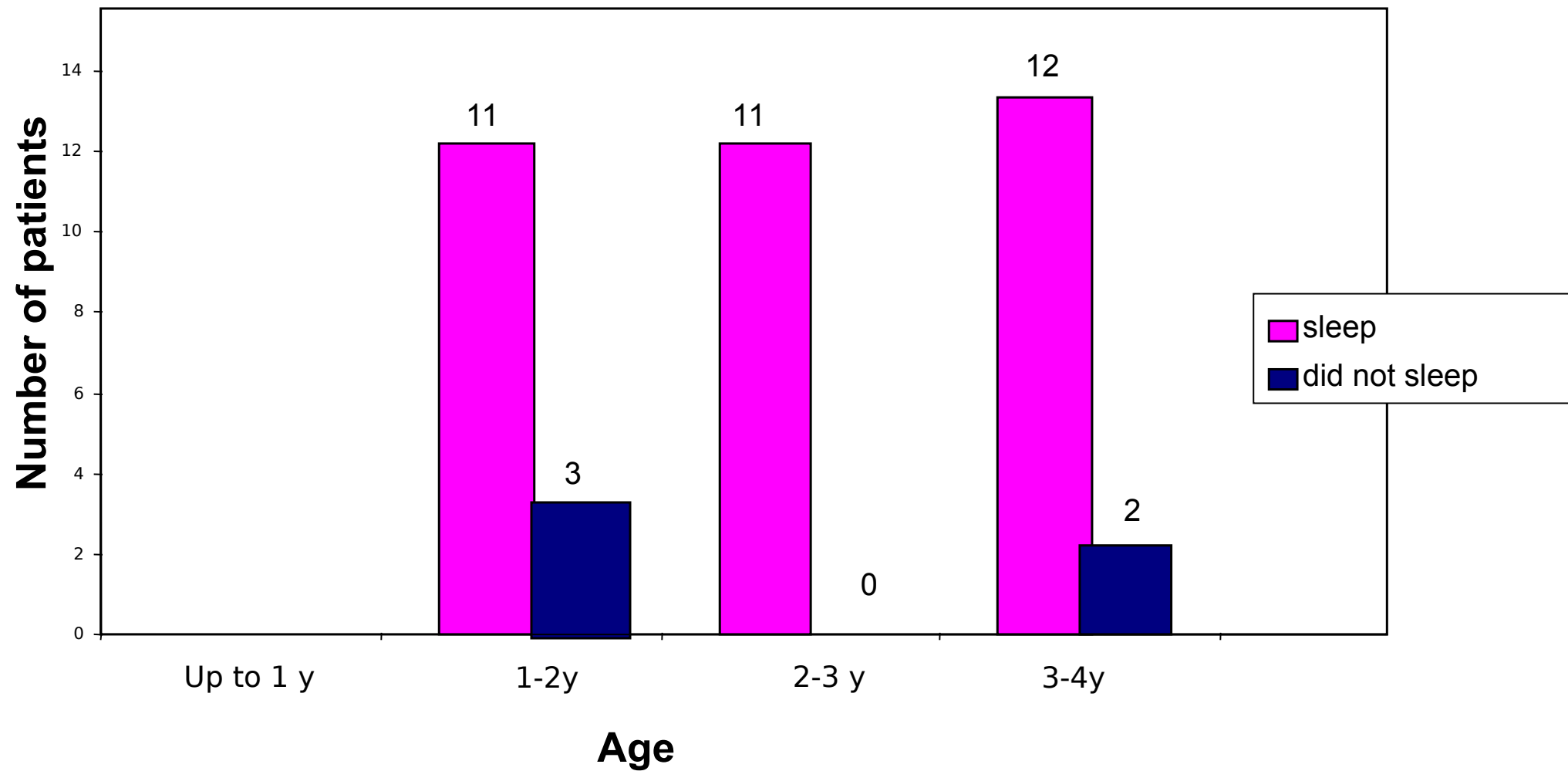


Number of patients that slept after melatonin administration



87.5% of patients that received melatonin went to sleep

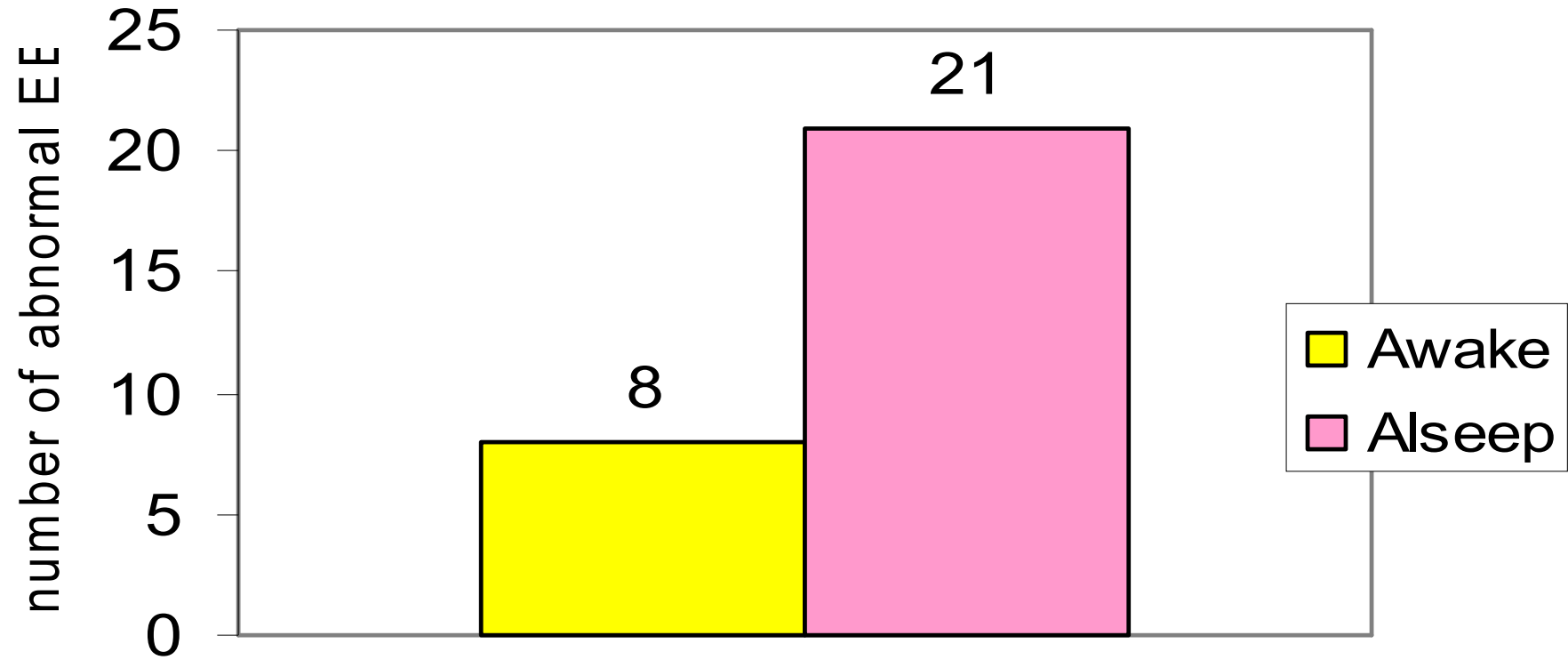
Ages of patients that did/did not sleep



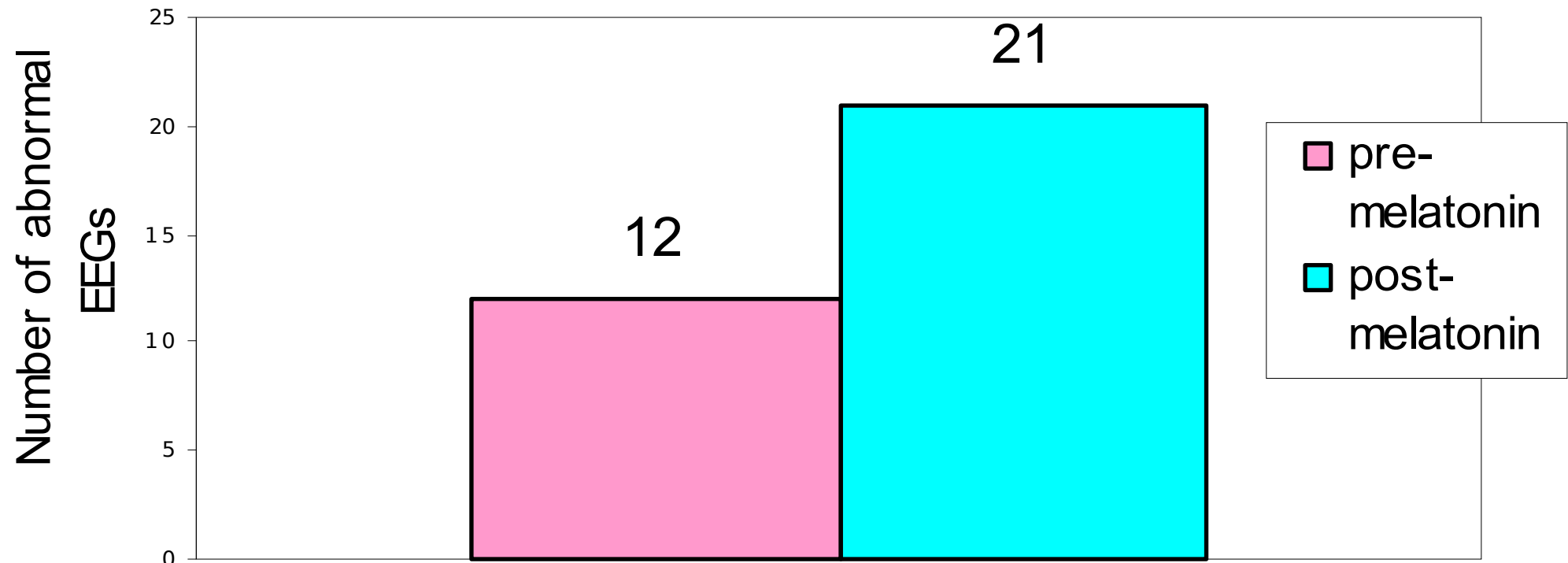
Results: EEG sensitivity

- 15 patients had a normal wake EEG and abnormal sleep EEG
- 1 patient had a seizure during sleep
- 3 patients had an increase in epileptiform activity during sleep- in 1 patient activity became continuous
- 1 patient was uncooperative and electrode application could only be achieved when the child was asleep

Number of abnormal EEGs when awake and asleep



Number of abnormal EEGs pre and post melatonin protocol change



Current Practice BCH

Under 2y : natural sleep

2 – 8 years : melatonin sleep

9 – 16 years: sleep deprivation (+ mel if need)

Full size bed (parent) Dark curtain. Sleep music.

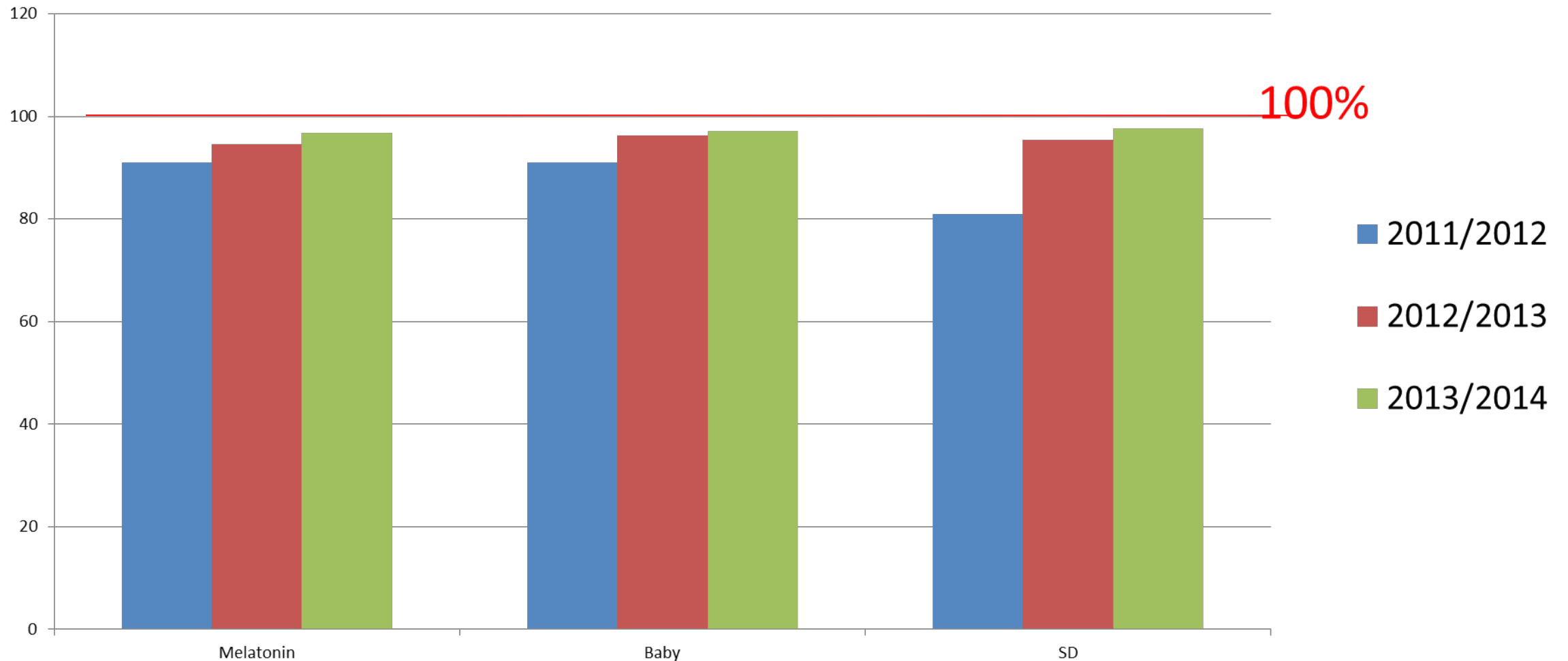
Mel Dose :12- 24 m: 3 mg

2 – 4 y : 6 mg

5y + : 9(occ.12mg)

Prescribed by Consultant Neurophysiologist in advance. Delivered by pharmacy to dept. Stored in Dept .(secure) Child weight for age estimated. Administered by recording physiologist/parent (eg PEG). Signed and witnessed, countersigned.Verbal consent. Taken whole or mixed with juice, by cup/syringe.,

EEG Sleep Achieved Rates- BCH 2011- 2014



EEG Sleep Achieved Rates -BCH

• Year		MELATONIN	BABY	SD
• 2011/2012	%	90.96(231)	91.03(266)	80.95(80)
• 2012/2013	%	94.57(244)	96.22 (236)	95.45(90)
• 2013/2014	%	96.8 (251)	97.13(239)	97.67(101)

Process/Protocols in use- my personal experience

- Coventry 2005- prescribed by paediatrician, administered on children's ward; EEG by single named tech required to have APLS certification
- Birmingham Children's 2005- prescribed by consultant clinical neurophysiologist, administered in department

- Royal Preston until 2009- not prescribed, in either of 2 departments, dosage by age and recorded in controlled drugs book by pharmacy-trained techs (checked by another tech)
- After 2009- outpatient prescription by consultant, only in main Neurophysiology dept, otherwise same protocol

RPH sleep audit

- Sleep EEG audit performed Preston by Angela Riley and Sarah Mayland to assess impact on service of change in protocol, with particular reference to success in recording sleep
- 2 time periods
- - 1 April to 30 September 2008 (24 paediatric, 83 adult)
- - 1 January to 30 June 2010 (25 paediatric, 67 adult)

Dose:

Up to 2 years 2.5mg

2-5 years 5mg

5-12 years 10mg

12years 10mg +5mg if necessary

Melatonin is administered in 2.5 mg capsules.

If necessary, Chloral Hydrate is given (in liquid form).

For children < 10 years dose = 30 mg/kg

>10 years dose =1500mg

.

Melatonin dosage protocol

Adult Sleep EEG before and after change in protocol

		Sleep		No sleep		Total	
		Before	After	Before	After	Before	After
Sleep deprived only		61	54	13	12	74	66
Sleep deprived plus medication	Melatonin	5		1		6	
Medication only	Melatonin	2		1	1	3	1
No sleep deprivation or medication							
Total		68	54	15	13	83	67

Number of adult patients given medication or sleep deprived only

	Before	After
Given medication	9 (7/9 slept 78%)	1 (0/1 slept 0%)
Sleep deprived only	74 (61/74 slept 82%)	66 (54/66 slept 82%)

Paediatric Sleep EEG before and after change in protocol

		Sleep		No sleep		Total	
		Before	After	Before	After	Before	After
Sleep deprived only		3	11	2	2	5	13
Sleep deprived plus medication	Melatonin	6				6	
Medication only	Melatonin	10	9	1	2	11	11
	Melatonin and chloral	1	1			1	1
No sleep deprivation or medication		1				1	
Total		21	21	3	4	24	25

Number of paediatric patients given medication or sleep deprived only

	Before	After
Given medication	18 / 24 (17/18 slept 94%)	12/12 (10/12 slept 83%)
Sleep deprived only	5 / 24 (3/5 slept 60%)	13 / 13 (11/13 slept 85%)

Conclusions Preston audit

- The number of children receiving medication in the department has decreased from 75% to 48%, all of whom now have a prescription.
- Number of adults given melatonin reduced from 11% to 1%.
- No significant difference sleep before and after groups (paediatric 87.5% vs, 84%, adults 82% vs 81%)
- Quality of service maintained.

Current Practice BCH

Under 2y : natural sleep

2 – 8 years : melatonin sleep

9 – 16 years: sleep deprivation (+ mel if need)

Full size bed (parent) Dark curtain. Sleep music.

Mel Dose :12- 24 m: 3 mg

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Prescribed by Consultant Neurophysiologist in advance. Delivered by pharmacy to dept. Stored in Dept .(secure) Child weight for age estimated. Administered by recording physiologist/parent (eg PEG). Signed and witnessed, countersigned. Verbal consent. Taken whole or mixed with juice, by cup/syringe.,

Inducing sleep for Paediatric EEG: a national service evaluation

Reasons for project

- Sleep EEGs adds information to help diagnose and classify seizures as well as identifying epileptic syndromes.
- Natural sleep can be achieved but often sleep induction is required:
 - **Sleep deprivation**
 - Administering **Melatonin**
- **Survey** and **audit** of how paediatric sleep EEGs are performed in UK:
 - To determine differences of Sleep deprivation and Melatonin in:

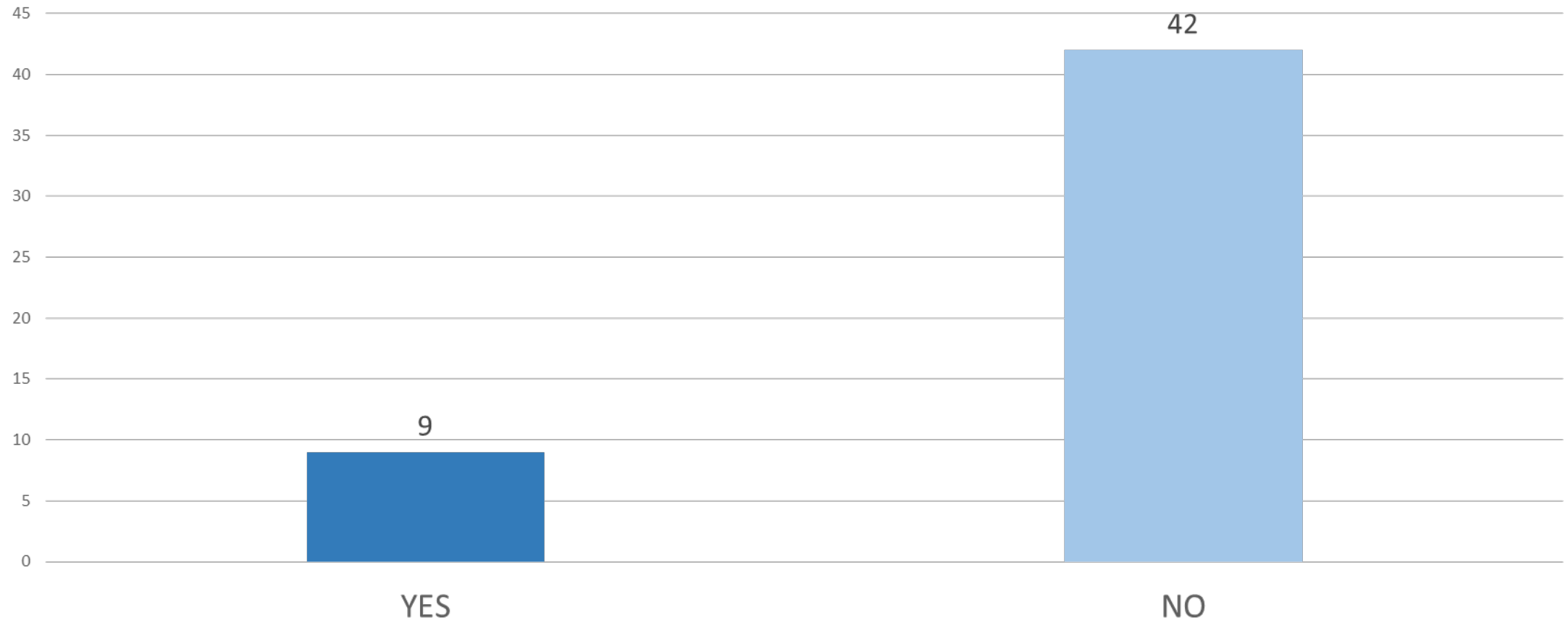
Methods

- Participation: 51 clinical neurophysiology departments in the UK
- **Survey:**
 - Form A I: completed by all departments
 - Form A II: completed only if Melatonin is used
- **Audit:**
 - Form B : details of the sleep EEG done on every patient between Nov-Dec'13

Findings

Form A I

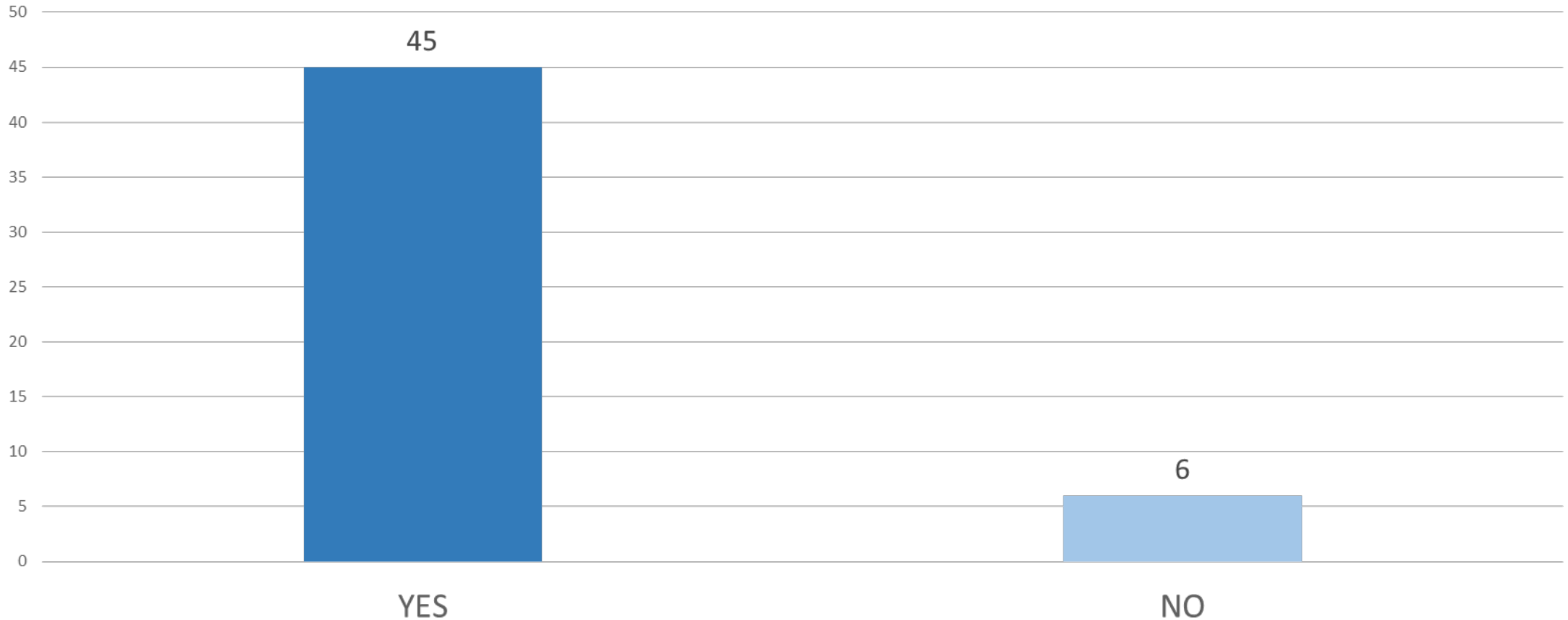
1. Do you use published guidelines for recording paediatric sleep EEG?



2. References (n=9)

- 3/9
Melatonin as a sleep inductor for EEG recordings in children.
Wassmer E et al. Clinical Neurophysiology 2001, 112 (4), 683
Melatonin versus chloral hydrate for recording sleep EEG. Ashrafi MR et al. European Journal of Paediatric Neurology, 2010, 14 (3), 235
- 2/9
Neonatal and Paediatric Clinical Neurophysiology (Pressler, Binnie, Cooper & Robinson)
- Others:
Variety of other papers, NICE guidelines on epilepsy and drug formularies

3. Do you use a local protocol for recording paediatric sleep EEG?



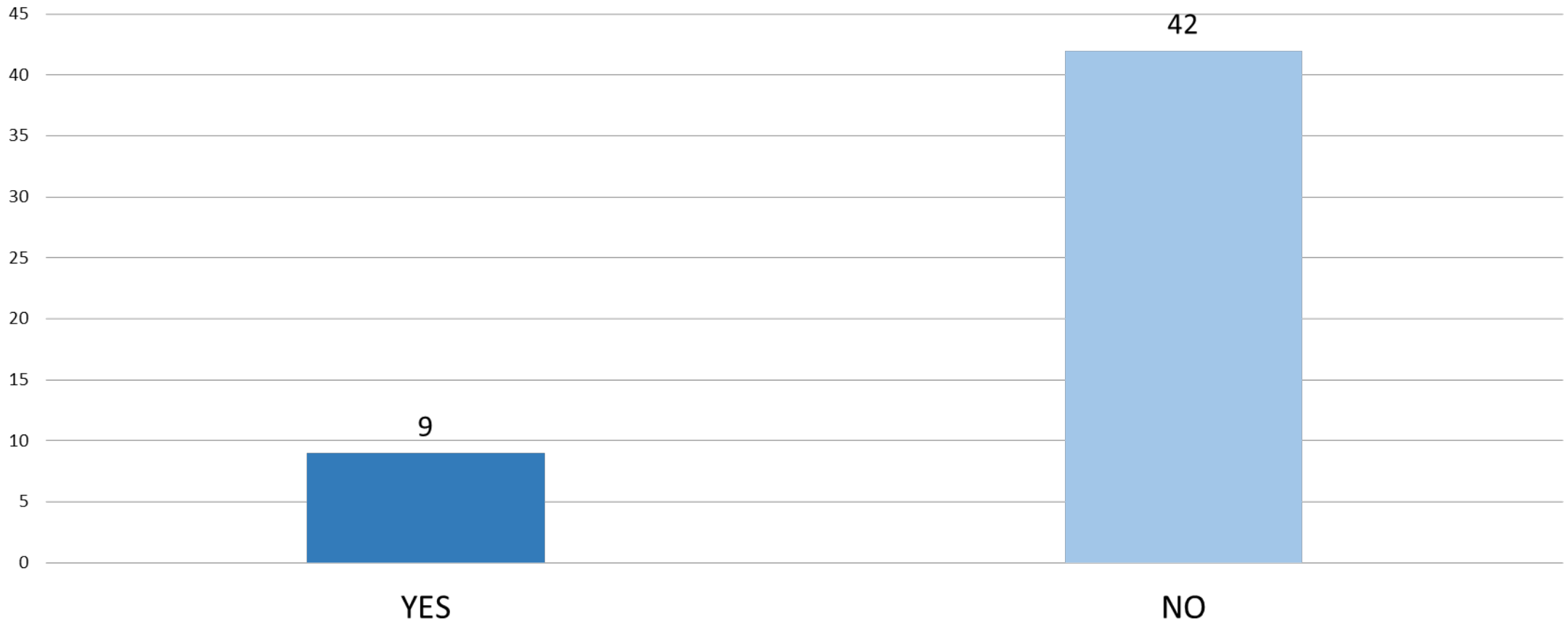
4. Protocols (n=38)

- Great variability
 - From ½ A4 to 27 A4 pages
 - How to record a sleep EEG
 - Adult and children, children
 - Patient preparation
 - Obtain consent and information to parents
 - Use of equipment
 - How to perform activation procedures (HV & PS recommended in most protocols)
 - Minimum length of sleep recording: 20 to 60 minutes (most 20-30 minutes)
 - Mandatory paediatric basic life support facilities

4. Protocols (n=38)

- Type of sleep study
 - Some protocols for natural sleep, sleep deprived, sleep using sedative drugs
- Melatonin guidelines → significant variability (reflected in the results of survey)
 - Who prescribes it
 - Who administers it
 - First dose: many $\leq 5y$ 3 mgr/ $\geq 6y$ 6mgr
 - Repeat doses, maximum dose (increased in autistic spectrum disorder)
 - When should it be given
 - Where is it stocked (pharmacy, department, paediatric ward)
 - Which preparation should be prescribed
 - Basic life support facilities
 - How long should child be in department/hospital after waking up

5. Have you performed a local or regional audit on this topic?



6. Summary and main recommendations (n=9)

Audit Themes:

1. Which type of sedation is more successful in producing a sleep EEG in children with various degrees of cooperation
2. Usefulness of sleep EEG in clarifying or making diagnosis and management
3. Procedures, consent and contraindications

6. Summary and main recommendations (n=9)

Recommendations:

1. Melatonin:

- very successful in inducing sleep (particularly in cooperative children),
- greater efficacy if used in combination with chloral hydrate in uncooperative children
- should be used when routine EEG does not show abnormalities
- preferred to chloral hydrate
- consider larger doses of melatonin in some cases
- not considered to be needed in one department; natural and sleep deprived EEGs successfully induced sleep

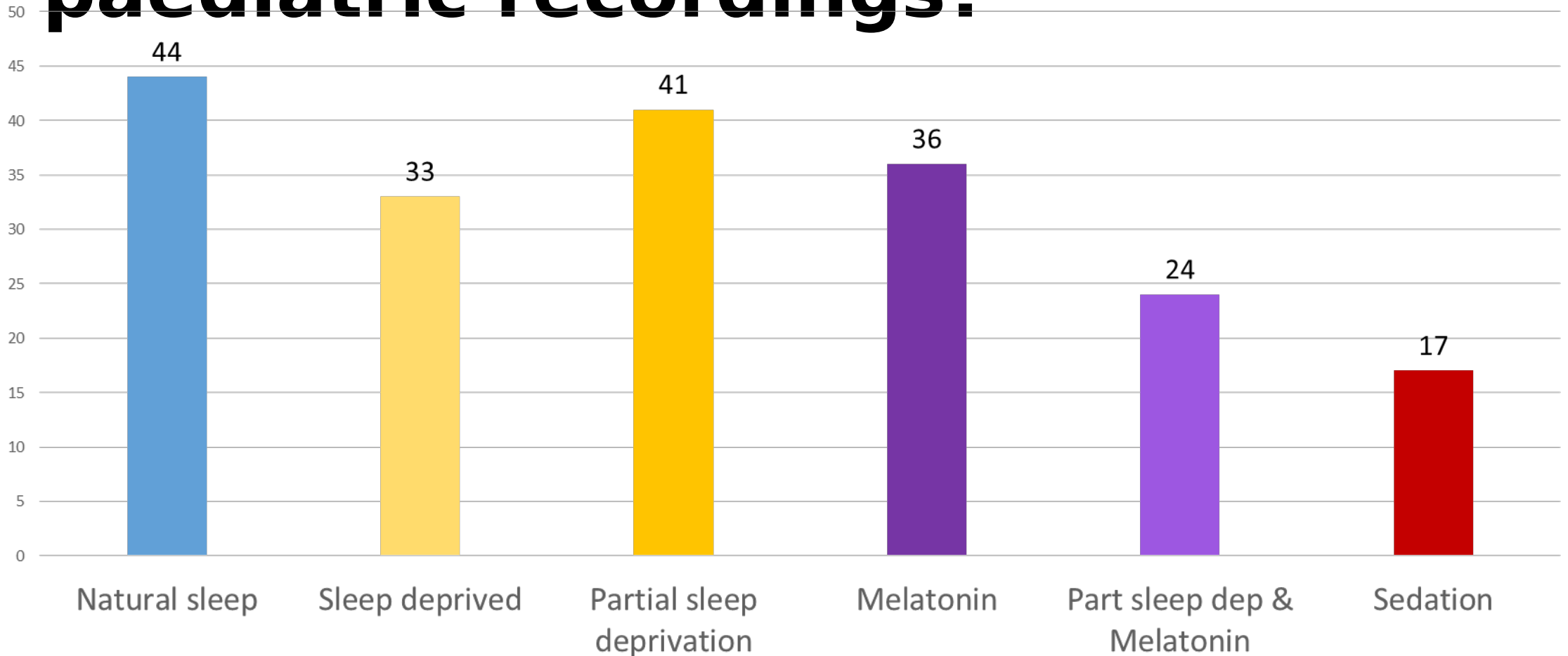
2. Longer appointments and more flexibility with appointment times increases the chances of obtaining a sleep EEG

6. Summary and main recommendations (n=9)

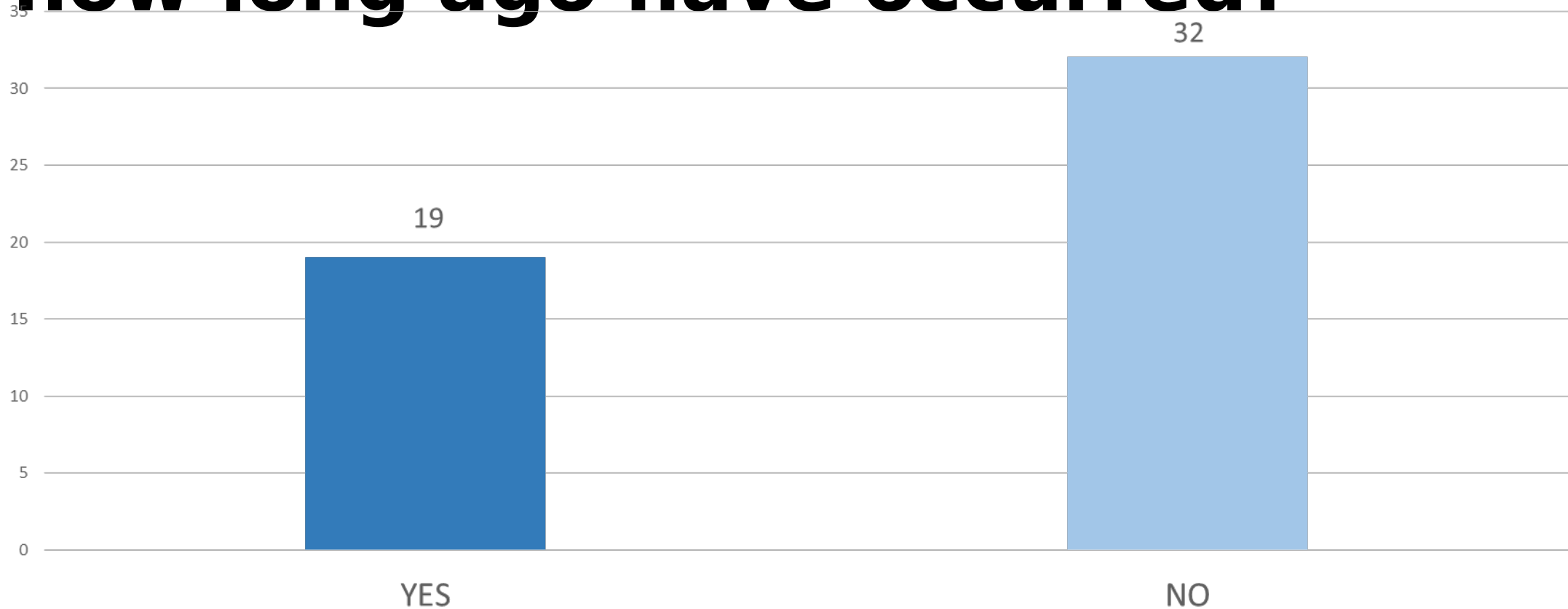
Recommendations:

3. Sleep EEG is more useful than routine EEG and increases the yield of abnormalities (regardless of the method used)
4. Need to agree on sleep EEG protocols

7. Which of the following methods do you use to induce sleep in paediatric recordings?



8. Can you remember any adverse events that occurred during paediatric sleep EEG regardless of how long ago have occurred?



9. Adverse events and changes in clinical practice (n=19)

- 4/19

- Crash call after child became unwell following sedation with chloral hydrate
→ Subsequently sleep EEGs performed on paediatric ward and eventually sedation changed to melatonin
- Syringe used to administer melatonin left in waiting room and found by another patient → melatonin given in recording room and syringes disposed of by physiologist
- Midazolam prescribed instead of melatonin → new protocol for sedation with melatonin
- 1 child remained asleep for 12 hours after melatonin → no changes in clinical practice

9. Adverse events and changes in clinical practice (n=19)

- 14/19: Seizures

“Seizures have occurred, although it is not considered to be an adverse event”

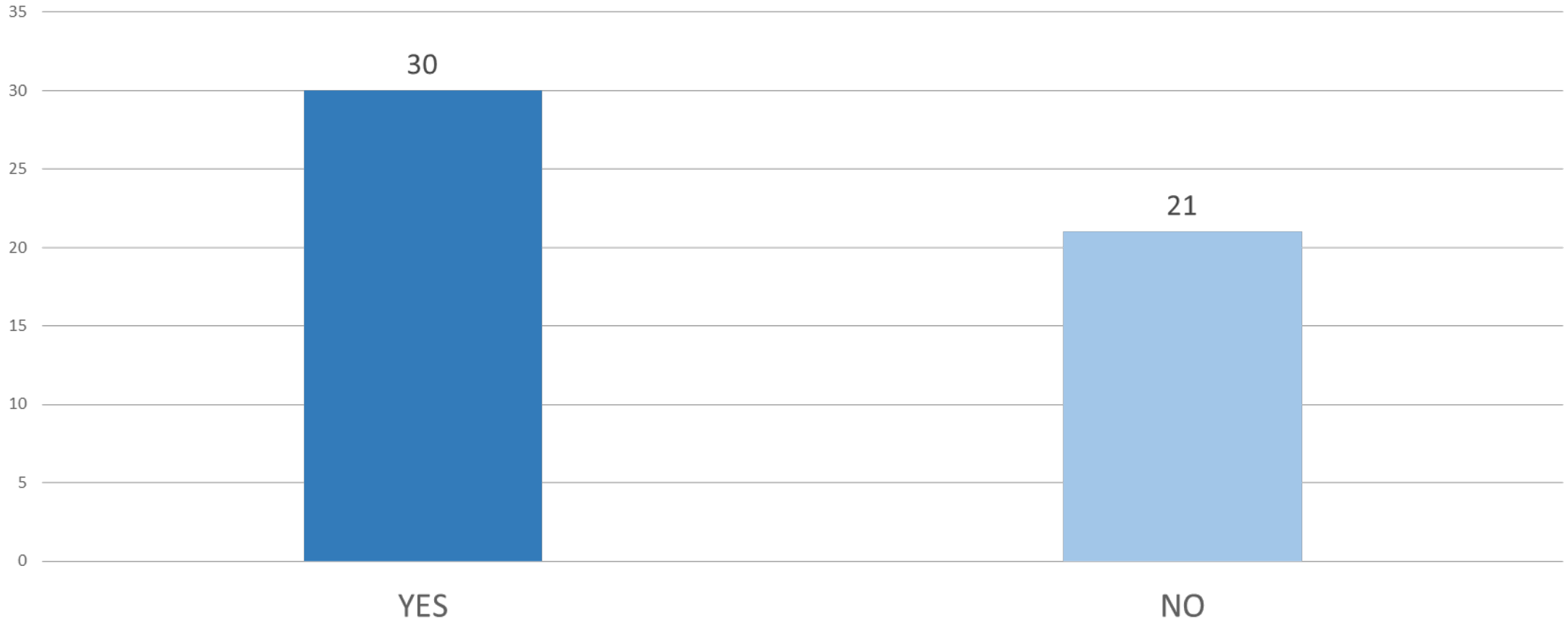
“5 patients in 33 years have had a seizure during sleep deprived EEG”

4/14: Change in clinical practice

- Guideline/protocol to act on seizures in the department and a paediatric resus kit
- Encourage use of routine recording with natural sleep rather than sleep deprivation
- Referrals scrutinised more carefully and if possible JME no sleep deprivation performed

10/14: No change in clinical practice

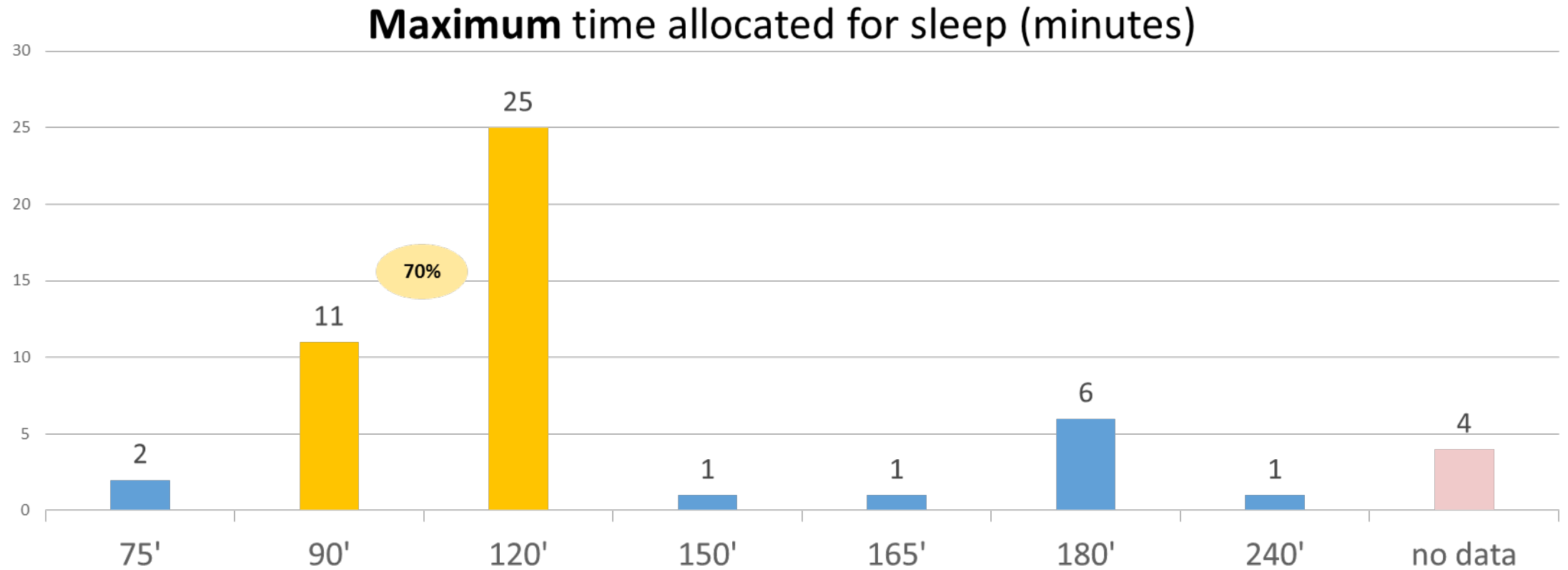
10. Do you have specific provision for sleep EEG different to routine EEG?



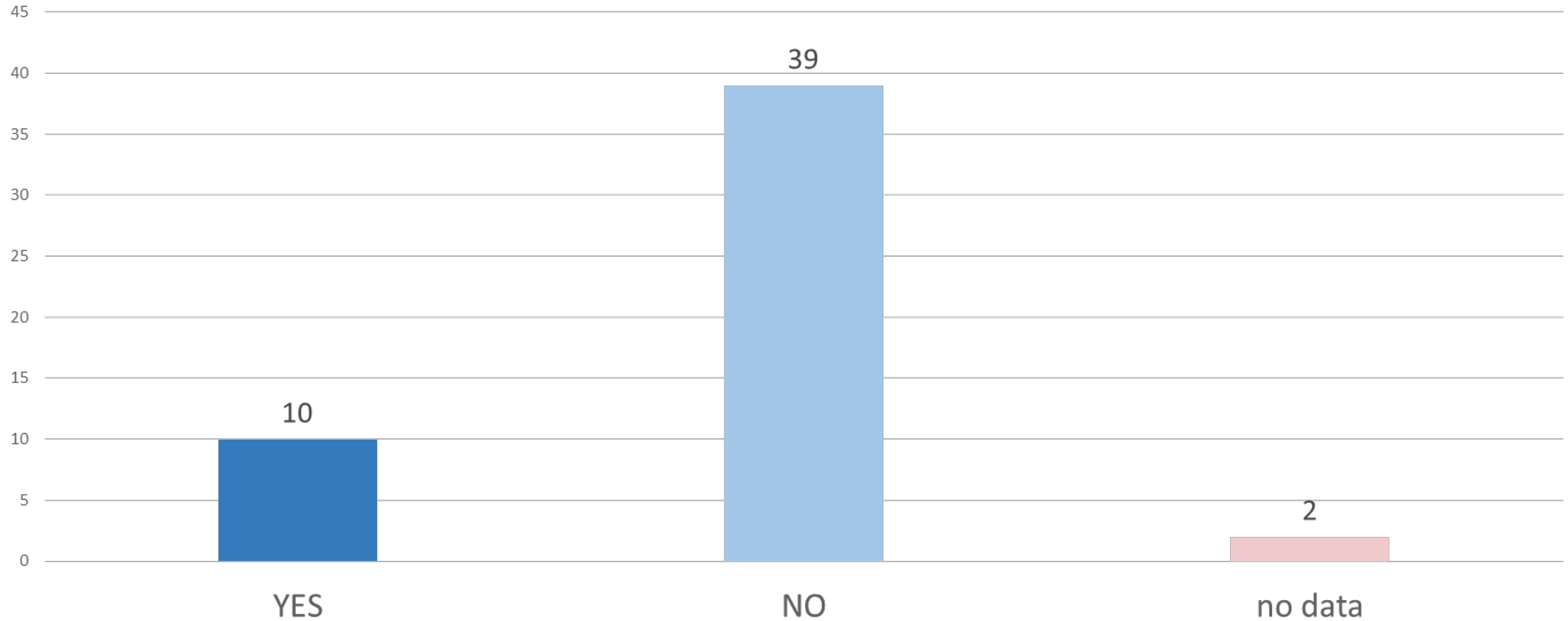
11. Type of provision made (n=27)

- **Room**
 - Quiet, dark, away from noisy parts of department
 - Bed, blanket, pillow, cot sides
 - Single separate adjacent room for EEG machine and physiologist
- **Longer time allocated for study**
- **EEG performed at special times/days, end of clinic**
- **Signs/lights indicating a sleep EEG is being recorded**
- Play specialists, paediatric nurses to check drugs
- Consultant in department if melatonin given
- Order of activation changed

12. What is the allocated appointment duration for a sleep EEG?



13. Have you considered routine use of Melatonin but run into operational issues?



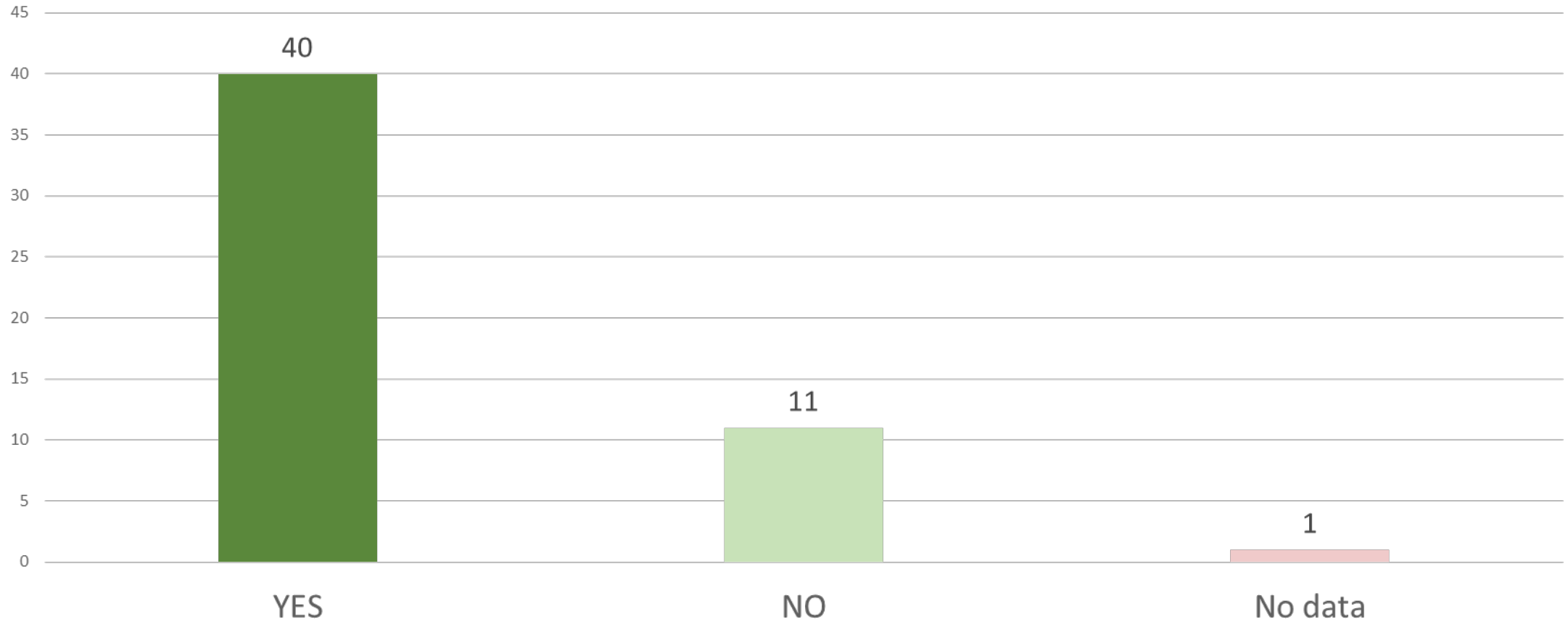
14. Melatonin operational issues (n=9)

- Safety of administering Melatonin in EEG departments
 - Melatonin has to be given in wards
 - Resus facilities need to be in place in EEG departments
- Prescription of Melatonin
 - Difficulty in obtaining prescriptions from Paediatricians
- Supply of Melatonin
 - Difficulty in obtaining Melatonin from either hospital pharmacy or other hospitals or community pharmacies
 - The prescribed doses are not always supplied directly to patients

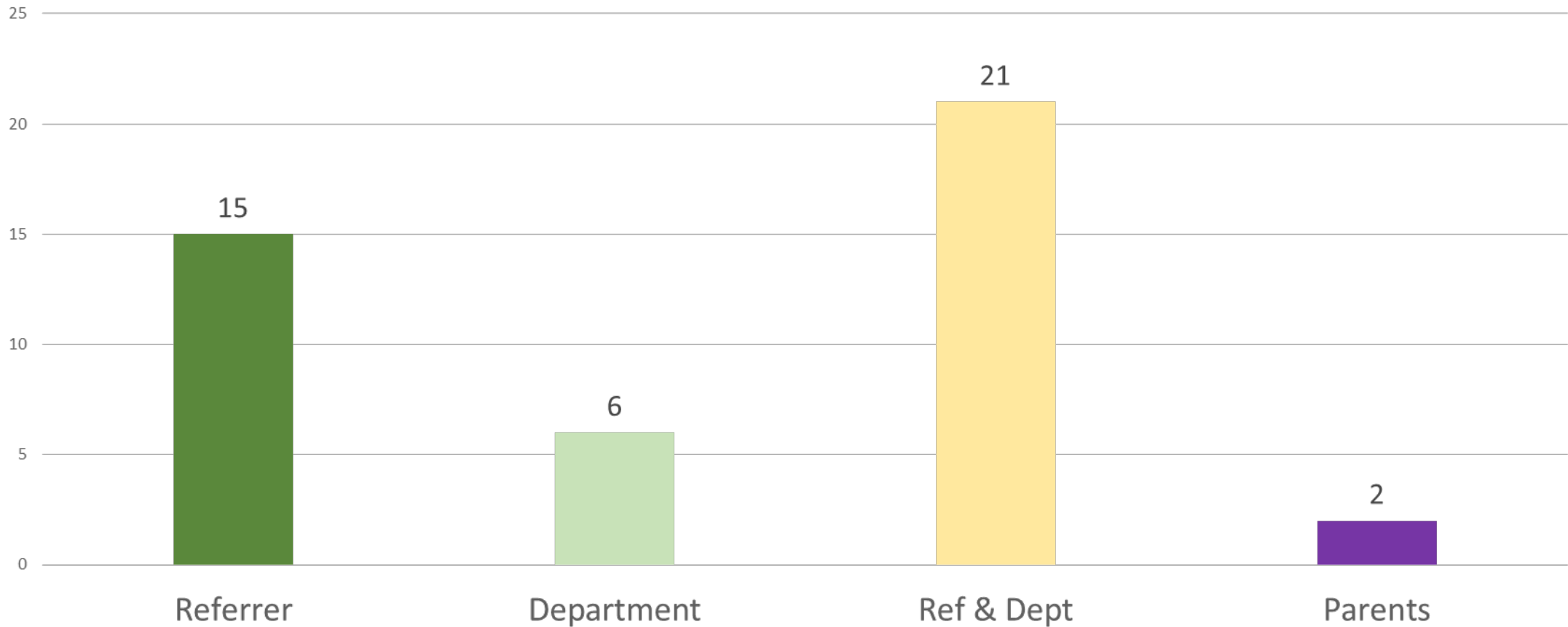
Findings

Form A II

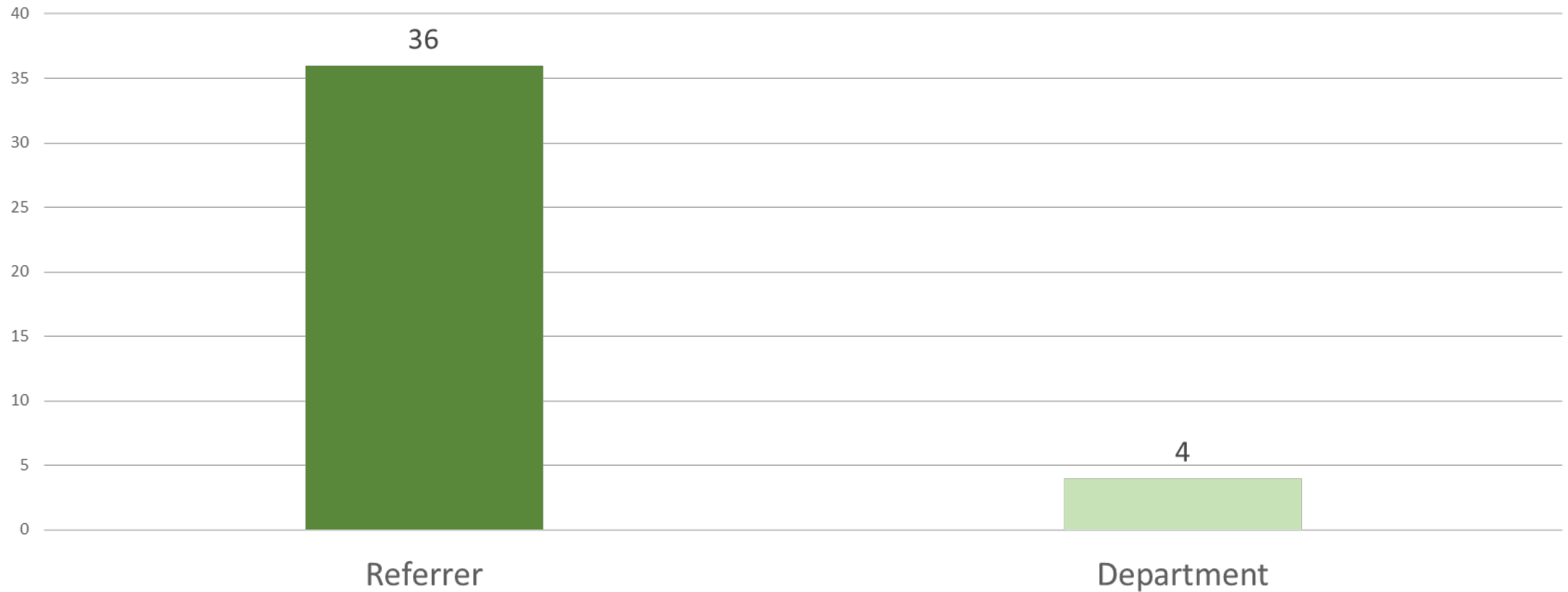
Departments using Melatonin: 40/51



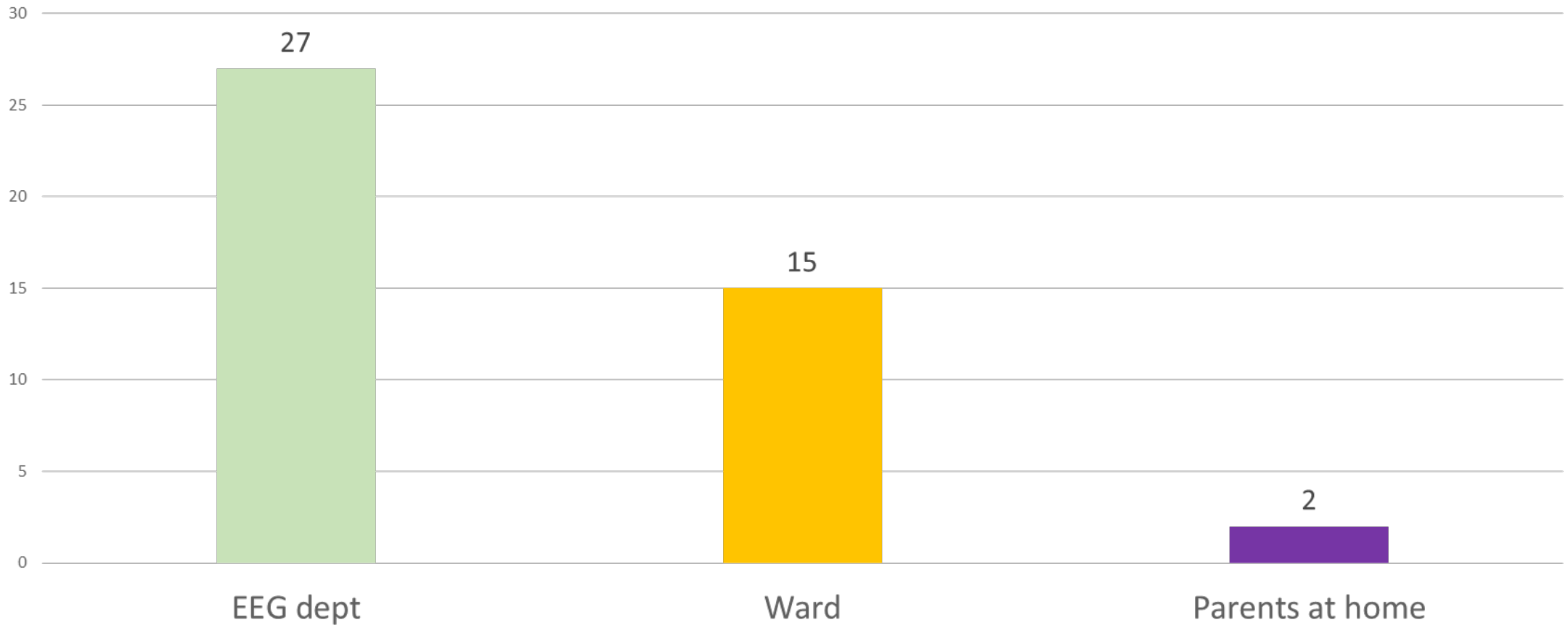
1. Who makes decision to use Melatonin for sleep EEG?



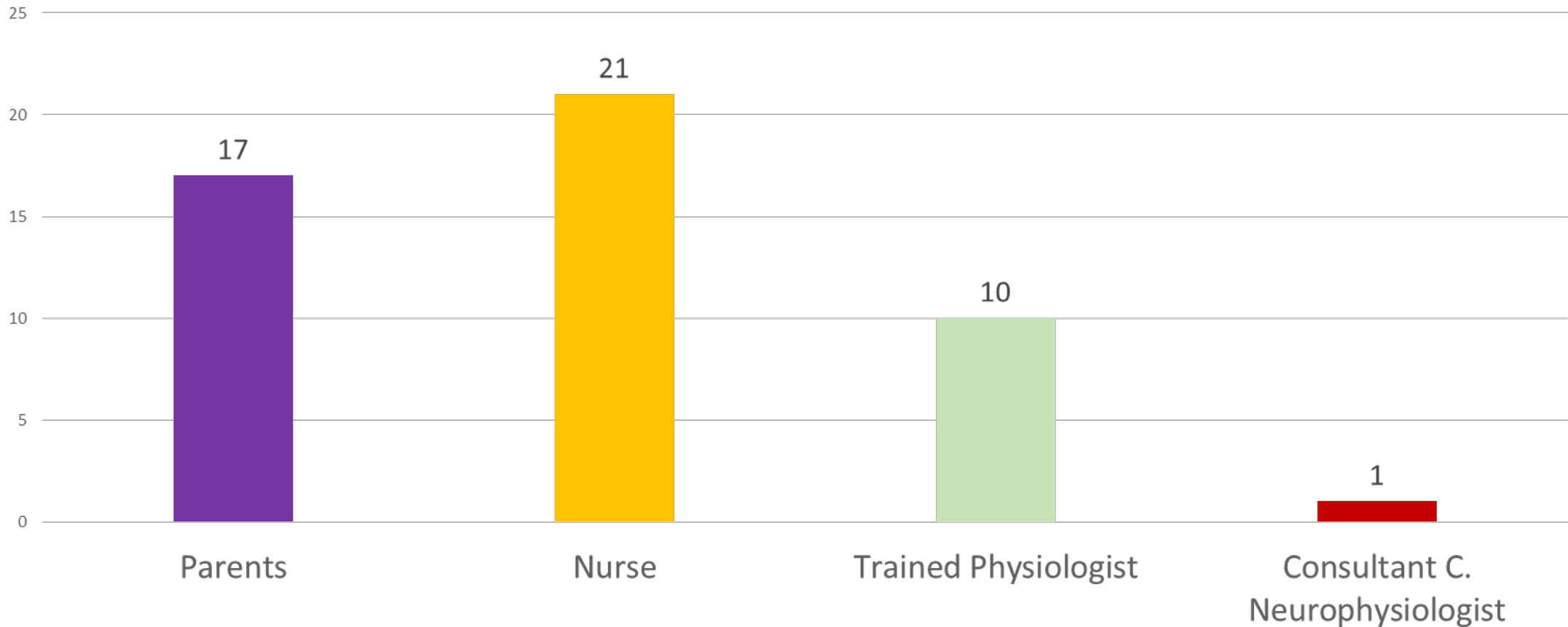
2. Who prescribes Melatonin for sleep EEG?



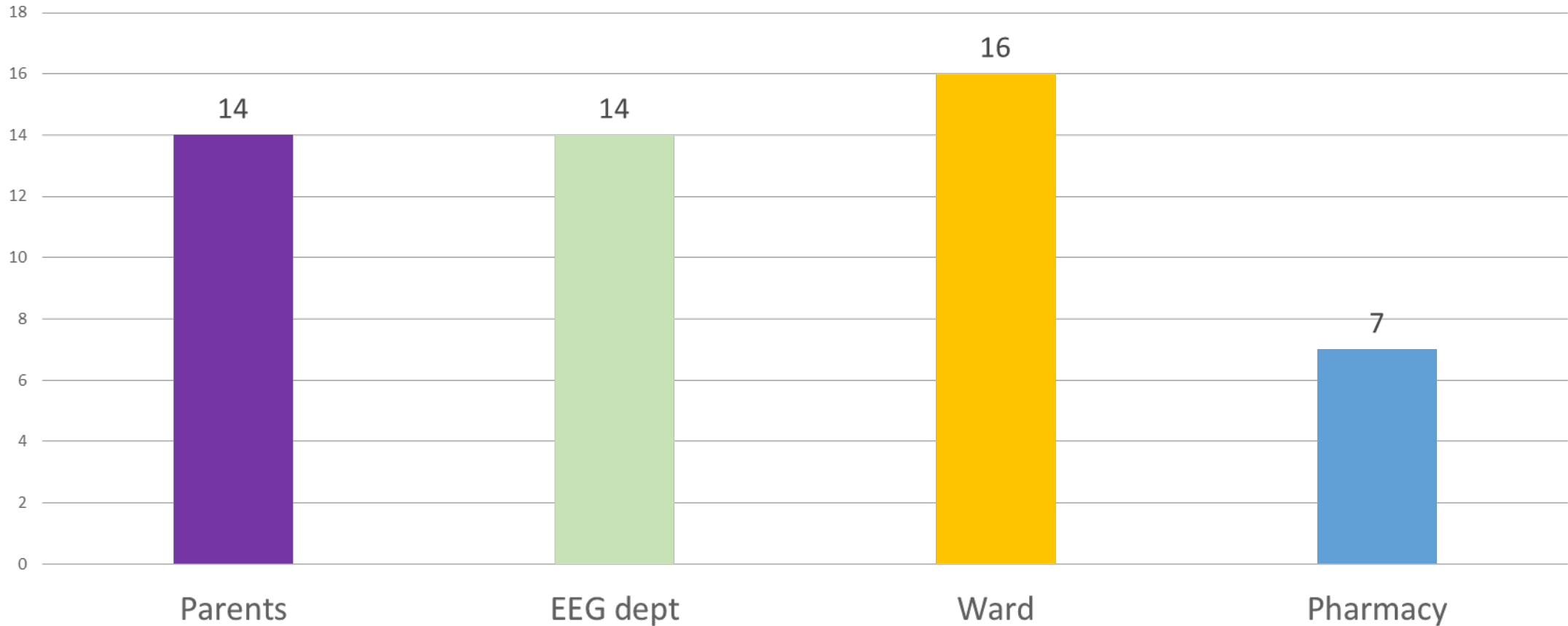
3. Where is Melatonin administered?



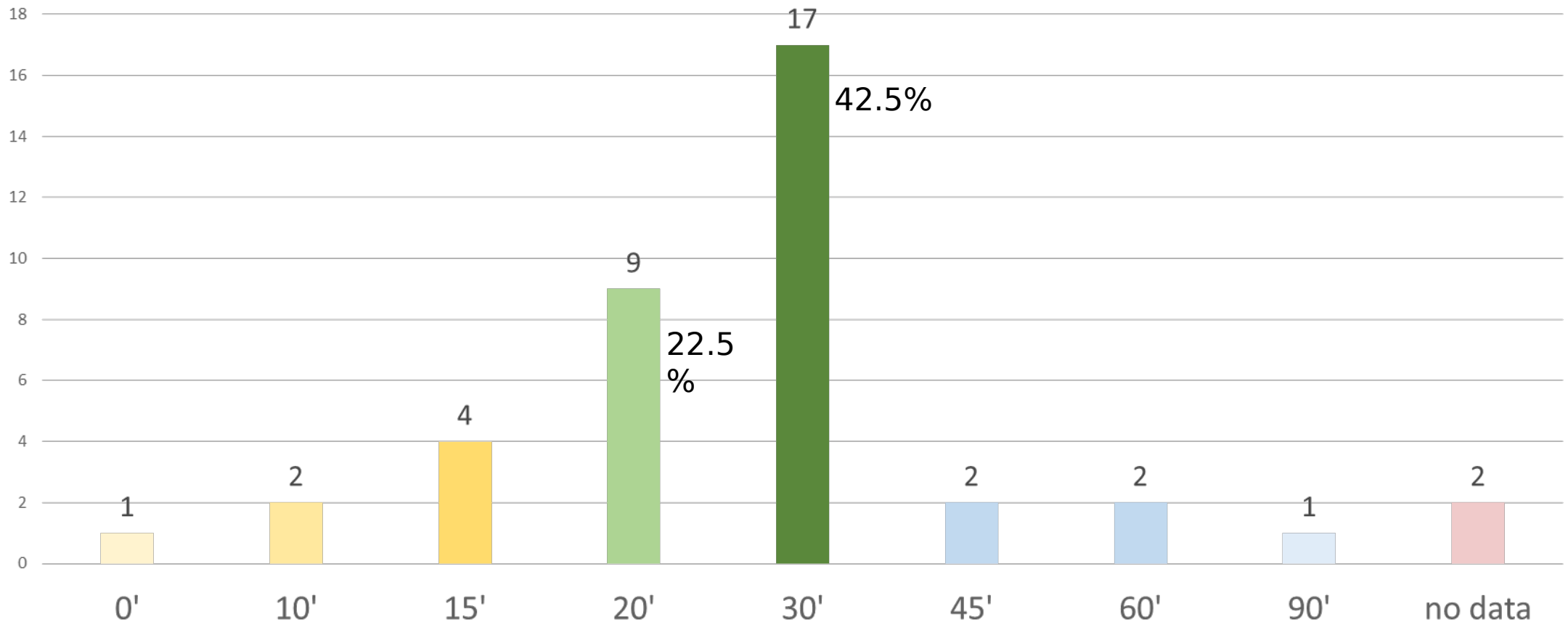
4. Who administers the Melatonin?



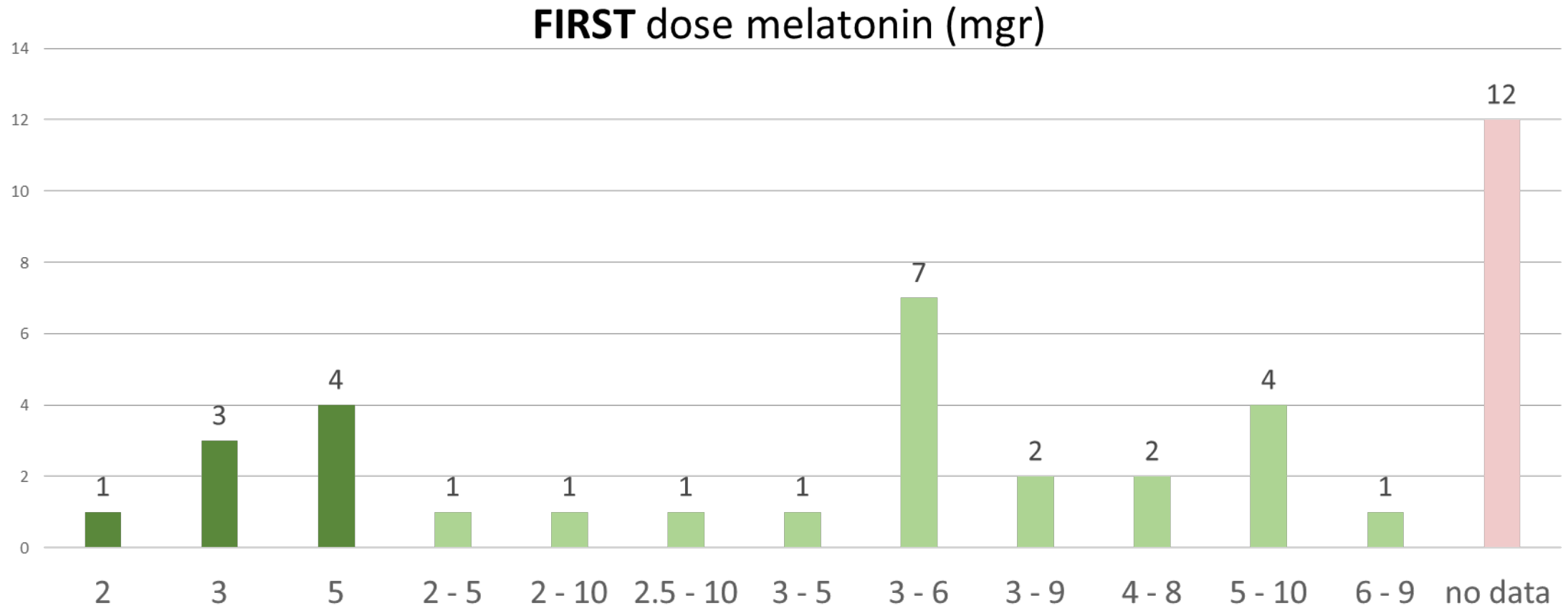
5. Where is Melatonin stored prior to appointment?



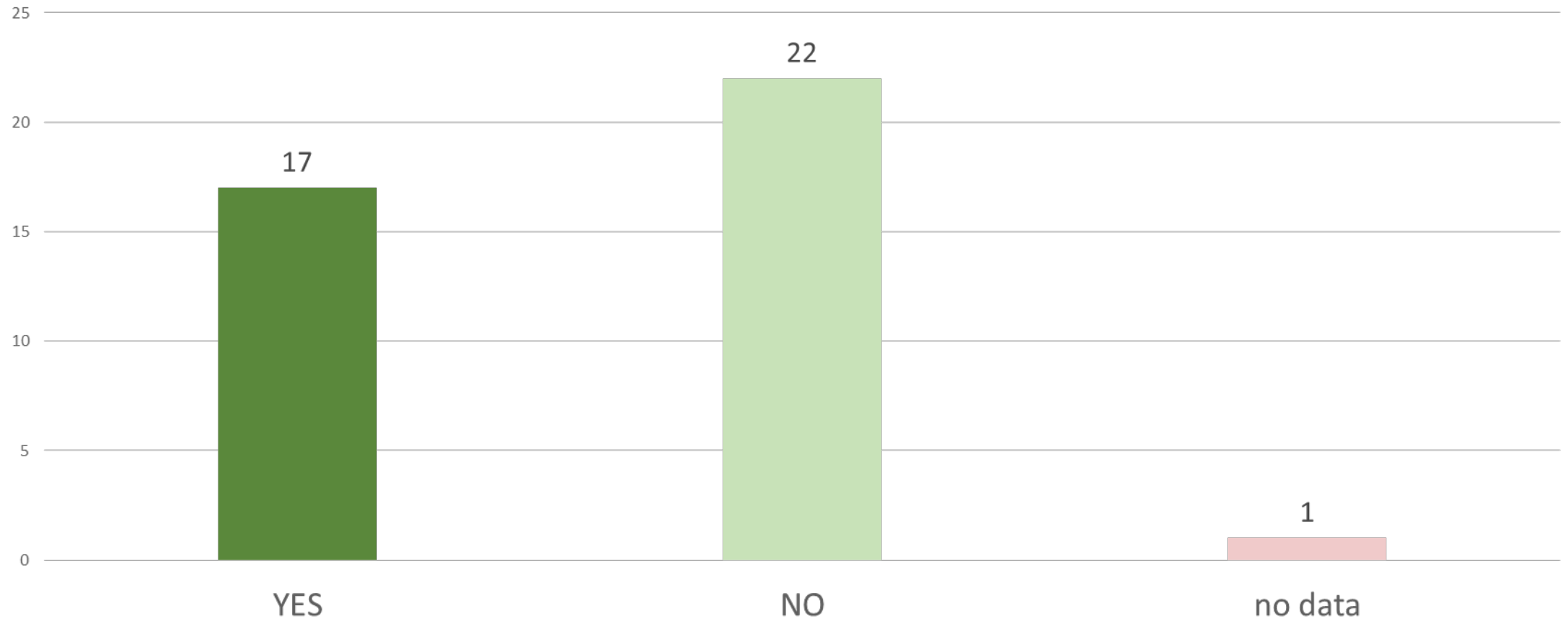
6. How long prior to the recording Melatonin is given? (minutes)



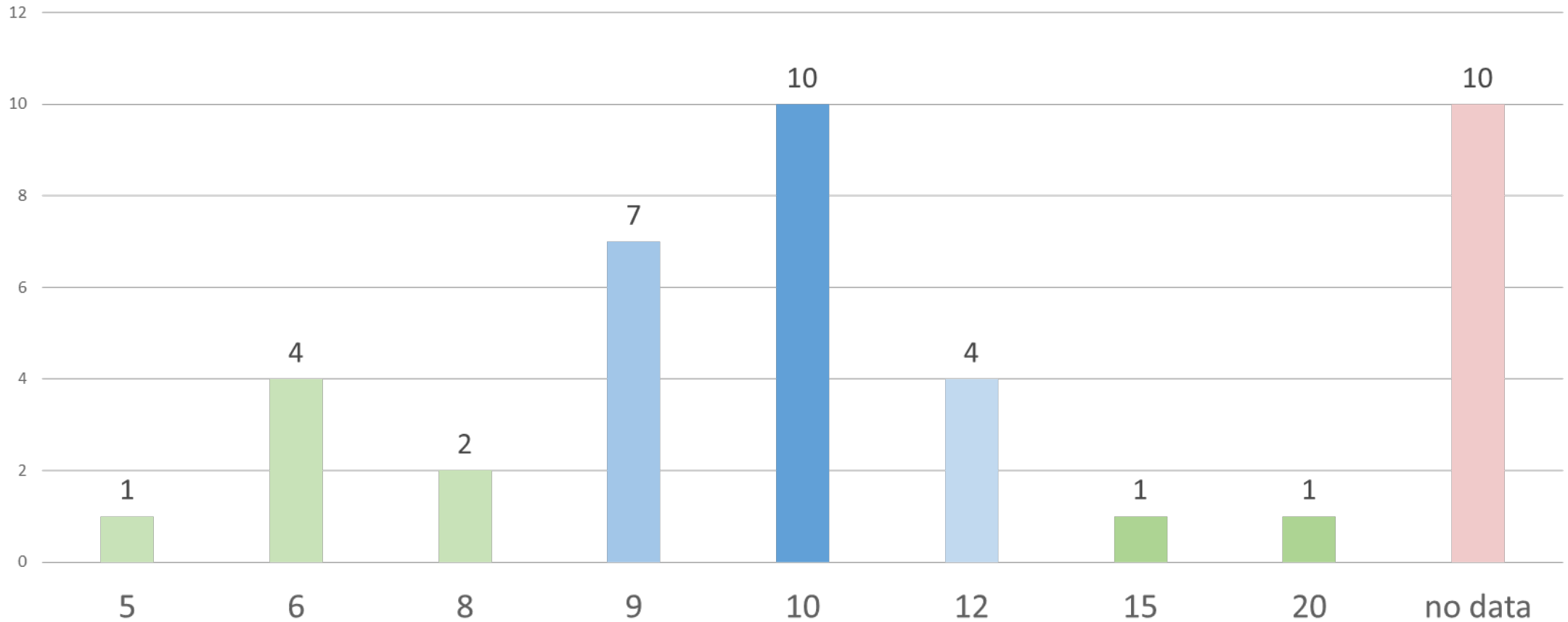
7. What dosage of Melatonin is given in the first instance?



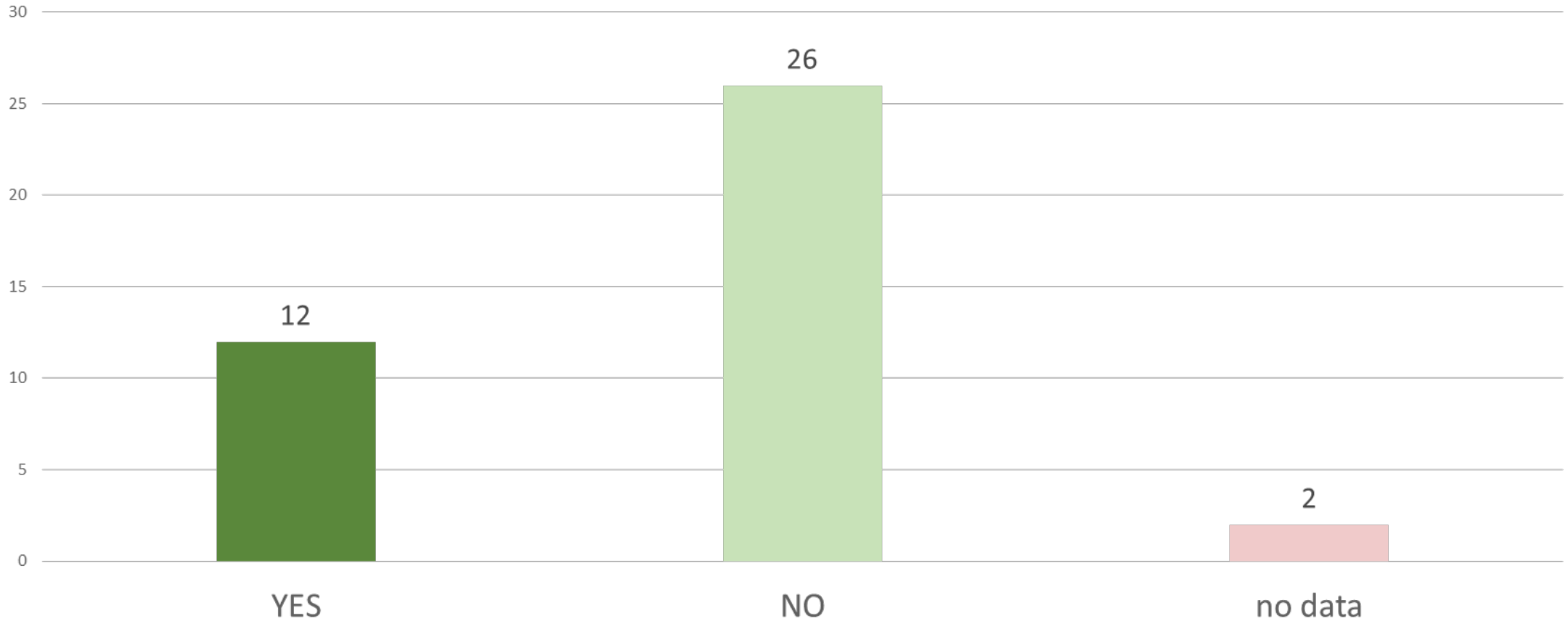
8. Is there an opportunity to give further dose if unsuccessful?



9. What is the **MAXIMUM** dose given? (mgr)



10. Do you encounter problems with the process of acquiring melatonin?



Problems acquiring Melatonin

- Supply of Melatonin by pharmacy
 - Not stocked in hospital pharmacy
 - Pharmacy reluctant to stock liquid preparations
 - Liquid or capsules often not in stock
 - Not available in other hospitals or community pharmacies
- Communication difficulties
 - Difficulty in finding prescriber (neurologist)
 - Melatonin needs to be prescribed in advance; if not great delays in supply
 - Difficulty in obtaining prescriptions for children from other hospitals

Summary (I)

- Guidelines/protocols for recording sleep EEGs
 - There are few (and partial) guidelines and no clear consensus
 - Very few departments follow published guidelines for recording paediatric sleep EEGs
 - Protocols for recording paediatric sleep EEGs are very variable
 - Time allocated for sleep EEG very variable (most common between 90-120')
- Safety of sleep EEG
 - Adverse effects are extremely rare and not serious
 - Seizures happen very occasionally and tend to occur only/mostly with sleep deprived EEGs (None reported with melatonin)
 - Melatonin is safe and used successfully in many departments

Summary (II)

- Melatonin
 - Significant difficulties in obtaining and prescribing Melatonin in many Trusts
 - High variability in administration of Melatonin
 - Very large range of doses used
 - Variable largest high dose
 - Great disparity amongst Trusts regarding safety issues during administration of melatonin
 - Melatonin is not a licensed drug for sleep EEGs; however, it is recommended by NICE to record sleep EEGs in children and young people
- Few audits performed in this subject

Inducing sleep for Paediatric EEG: A National Service Evaluation

Results of the UK Audit

Aims:

To compare use of sleep deprivation and melatonin in children in terms of:

- 1. Effectiveness and efficiency in inducing sleep**
- 2. Diagnostic yield**

Method:

Form B was completed prospectively for each consecutive paediatric patient attending for SLEEP EEG between **1st November and 31st December 2013**

1. What is the age of the patient?	
2. What is the gender of the patient?	M / F
3. What was the referral diagnosis?	Epilepsy Other (Please state)
4. Did the patient have previous standard EEG?	Yes / No
5. If Yes: was the previous EEG	Normal Abnormal Unrecordable / Uninterpretable
5. Did the patient have a previous failed sleep EEG? (Where child did not sleep)	No (no previous failed EEG) Yes - failed sleep EEG without melatonin Yes - failed sleep EEG with melatonin
6. Does the patient have an underlying neuro-behavioural condition? e.g. Autism, ADHD, Learning disability	Yes / No
7. What was the time of the appointment? (24 hour clock)	
8. What type of sleep study was undertaken?	Natural sleep Melatonin Sleep deprived (complete/partial) Sleep deprivation and melatonin Sedation
9. Did a seizure or any other adverse event occur?	No Yes - Seizure Yes - Other adverse event (please state)
9. Was sleep attained? If No answer questions 10 and 11 only If Yes go to question 11 and complete questionnaire	Yes / No
10. Did the record produce unequivocal epileptiform (i.e. sharp waves/spikes with or without slow waves) EEG activity NOT seen in the previous record?	Yes / No / No previous record
11. How long was the recording in total? (minutes)	
12. How far into the recording was sleep attained (please give latency to Stage 2 sleep in minutes)	
13. How long was sleep recorded for? (minutes)	
14. Did sleep produce unequivocal epileptiform (i.e. sharp waves/spikes with or without slow waves) EEG activity NOT seen in the resting record (either current or previous)?	Yes / No
15. Did sleep exacerbate epileptiform activity previously seen in the resting record?	Yes / No

Results

34 patient records excluded (data incomplete or an adult record)

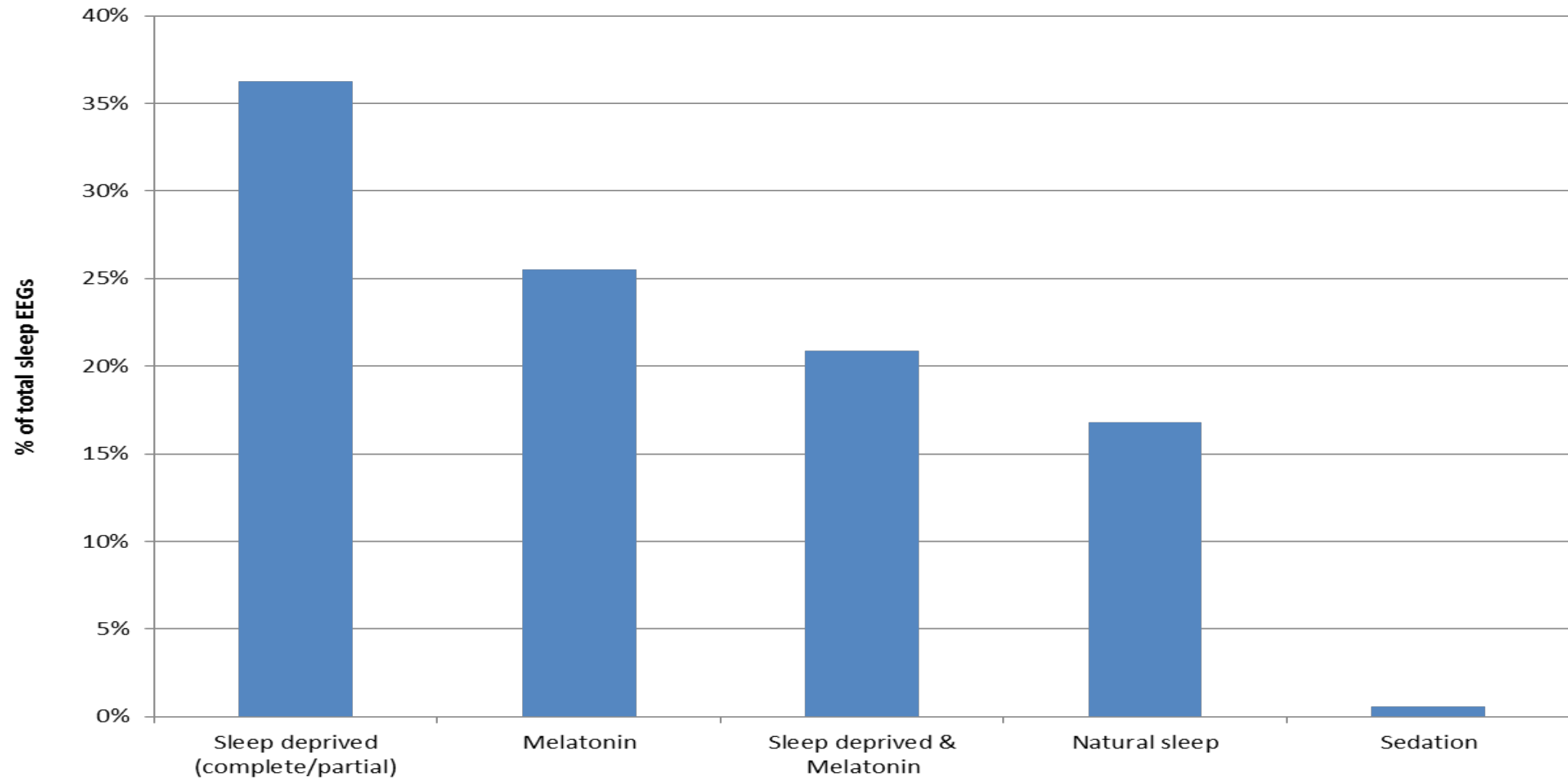
Total of 711 patient records from 51 Neurophysiology Centres.

1. What is the age of the patient?	0-18 years
2. What is the gender of the patient?	Male = 55% Female = 45%
3. What was the referral diagnosis ?	>98% Epilepsy
4. Neuro-behavioural condition?	25%

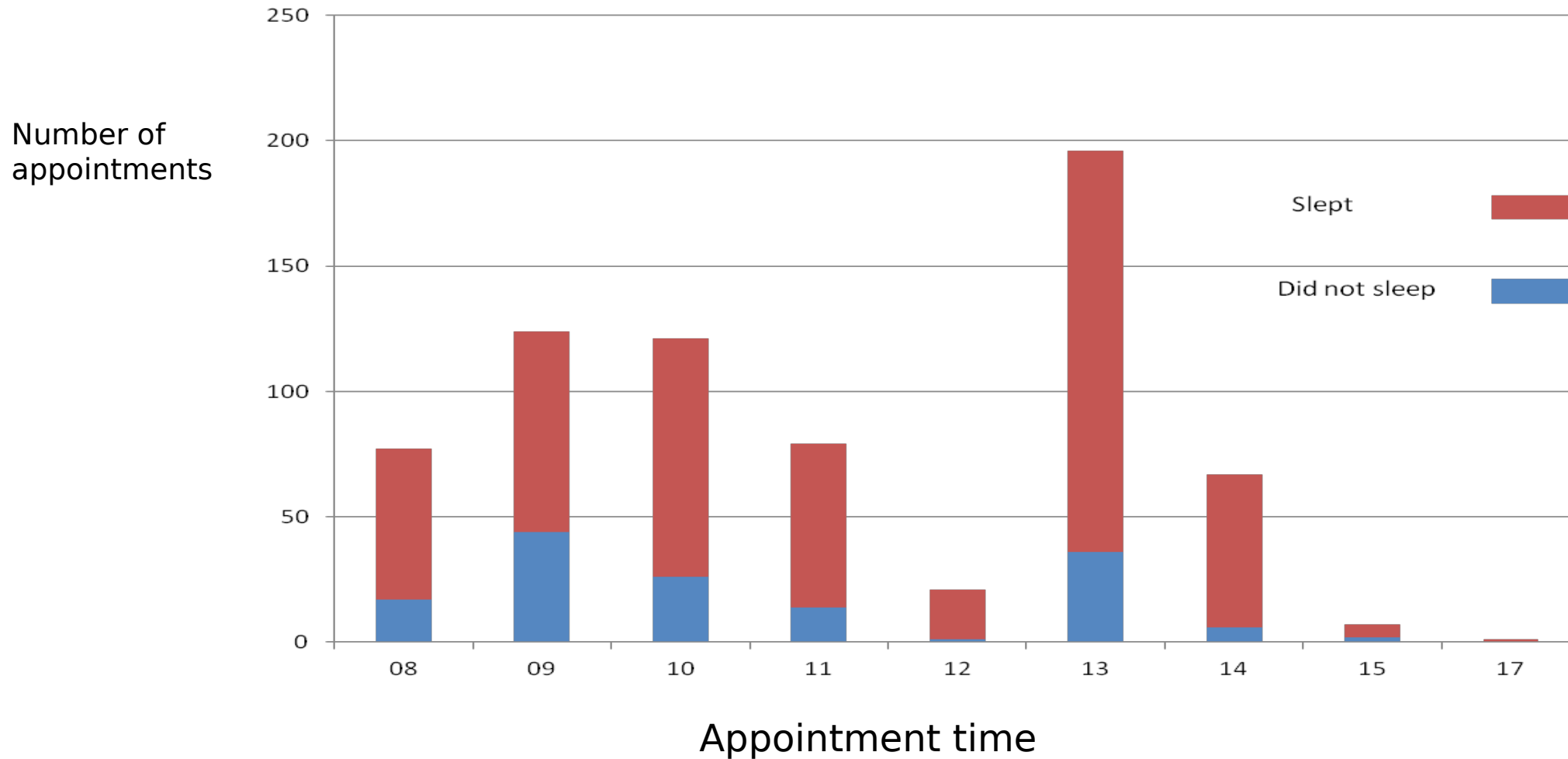
Did the patient have a previous standard EEG?

- 60% had standard EEG**
- 44% of these were abnormal (190/427)**
- Nature of abnormality was not asked for**

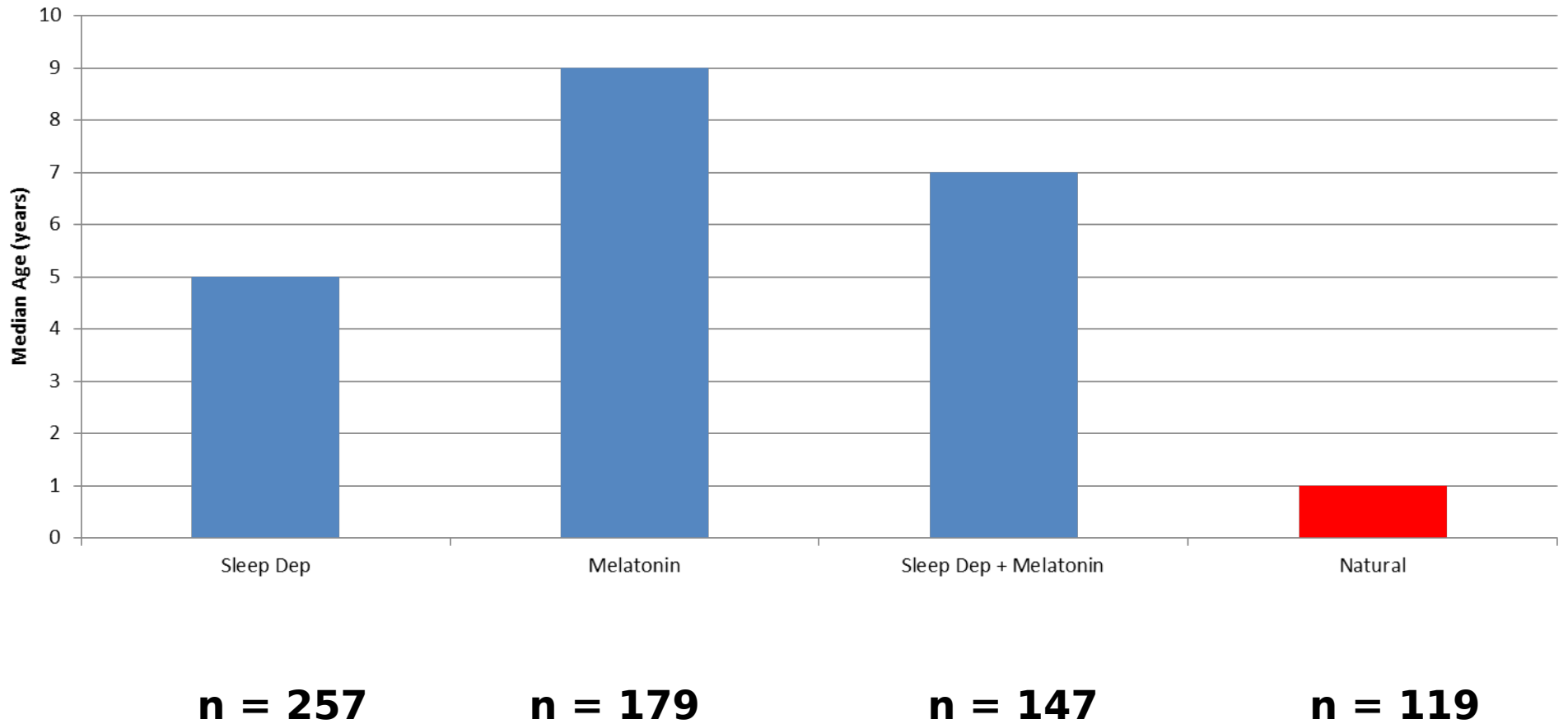
Type of sleep study undertaken



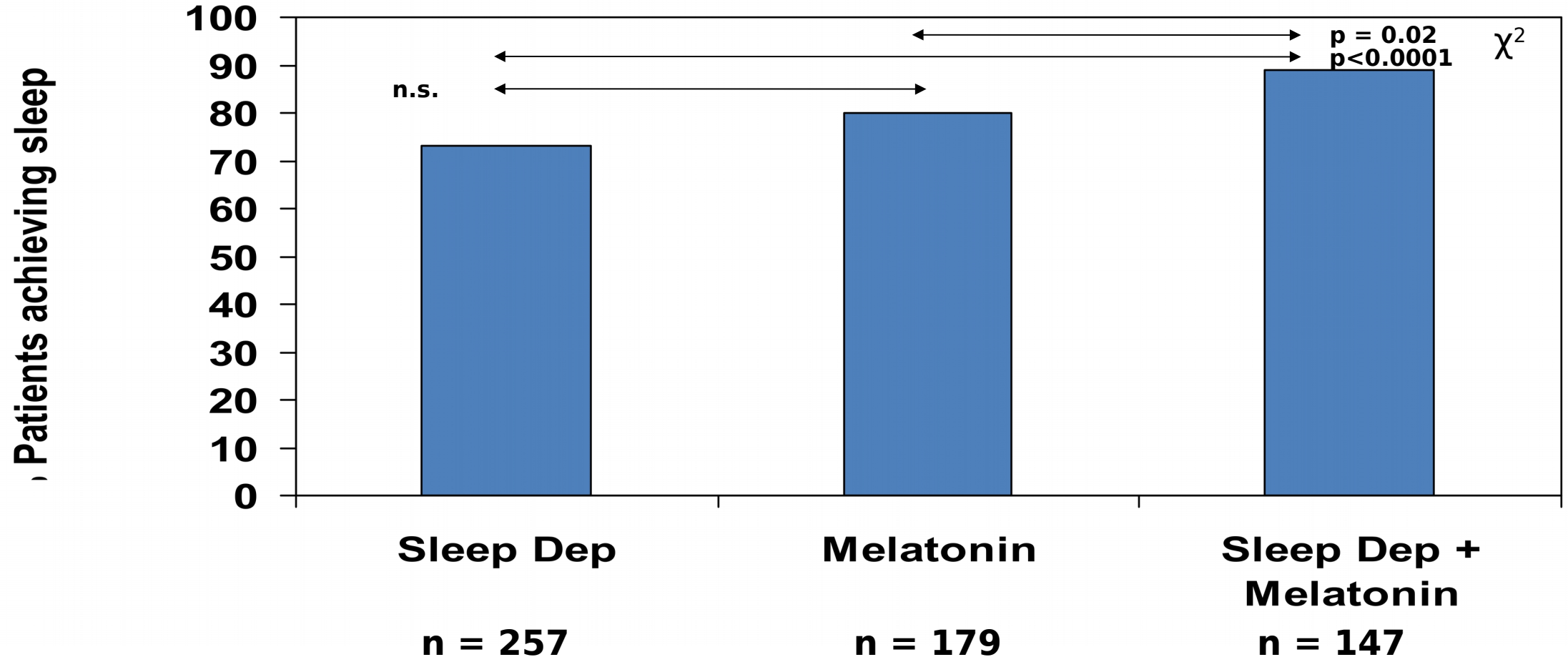
Appointment time and whether sleep was attained:



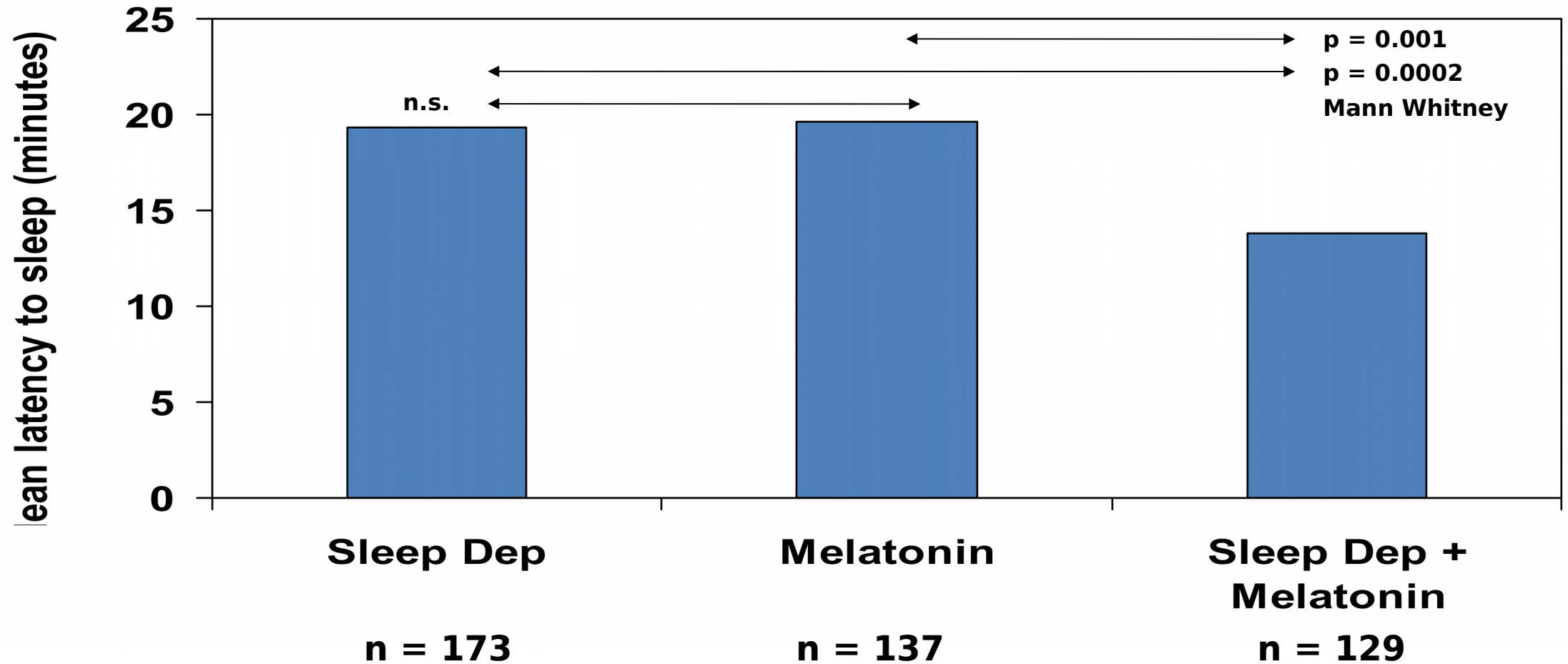
Patient Age



79% (563/711) of patients slept



Latency to sleep



- **Length of total recording:**
0-180 minutes
Mean = 49 minutes
- **Length of sleep recorded:**
3-105 minutes
Mean = 24 minutes

Comparison of sleep methods and diagnostic yield

**10. Did the record produce unequivocal epileptiform (i.e. sharp waves/spikes with or without slow waves) EEG activity NOT seen in the previous record?
(only answered if sleep was NOT attained)**

**Yes / No / No
previous record**

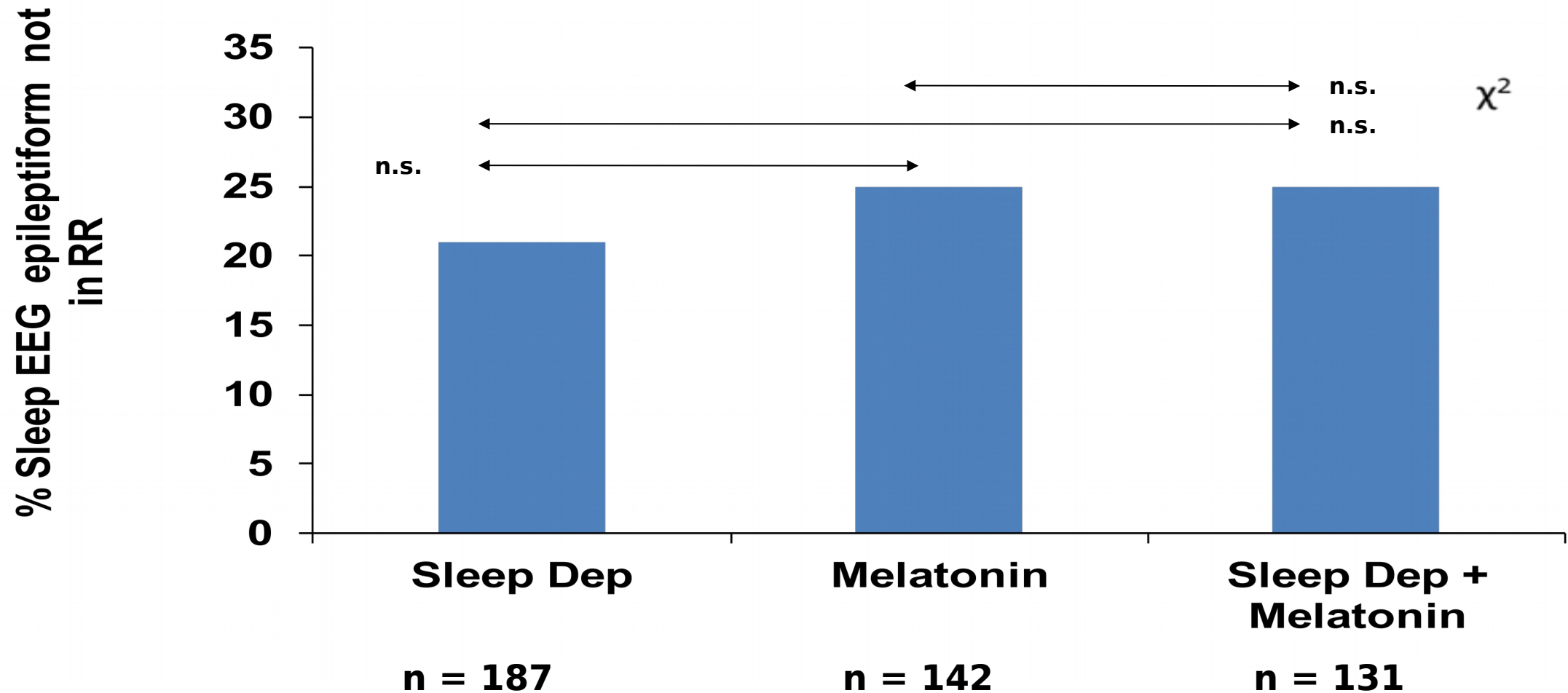
15% (16/105) of patients that did not sleep showed unequivocal epileptiform EEG activity not seen in the previous record.

Low numbers limits comparison between tests

14. Did sleep produce unequivocal epileptiform (i.e. sharp waves/spikes with or without slow waves) EEG activity NOT seen in the resting record (either current or previous)?

Yes / No

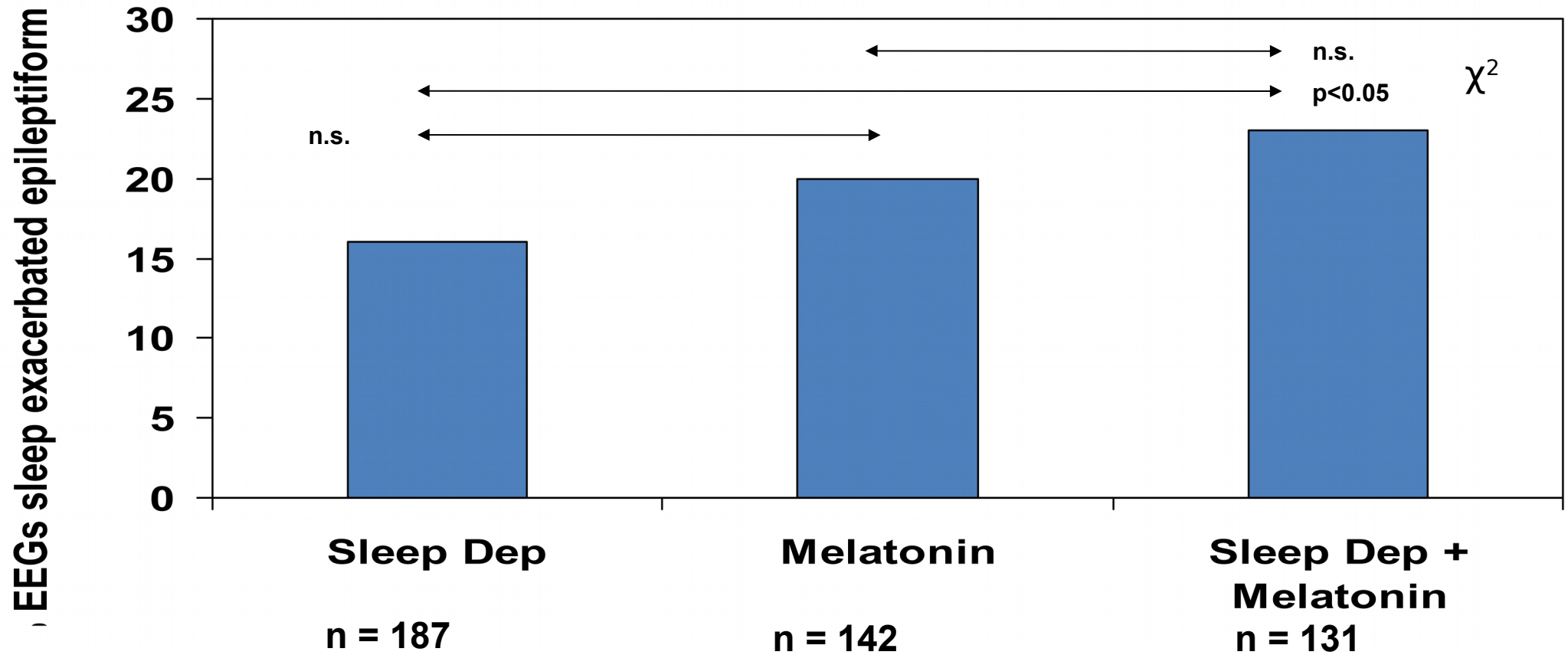
20% of the sleep patients - 115/563 produced epileptiform activity in sleep



15. Did sleep exacerbate epileptiform activity previously seen in the resting record?

Yes / No

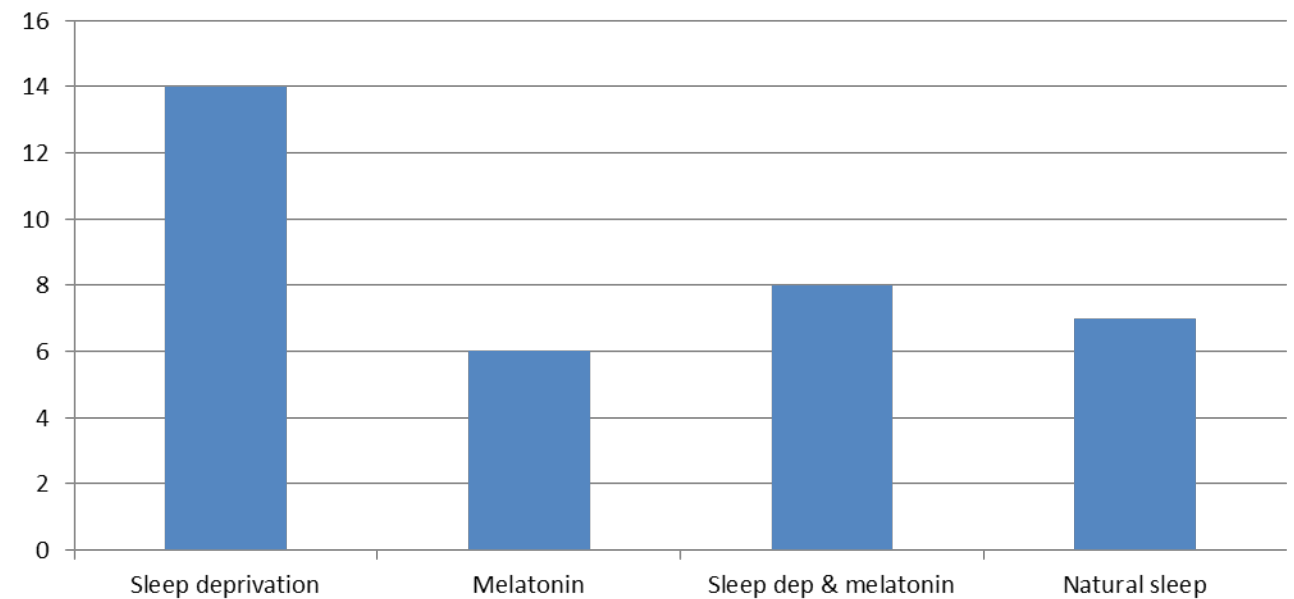
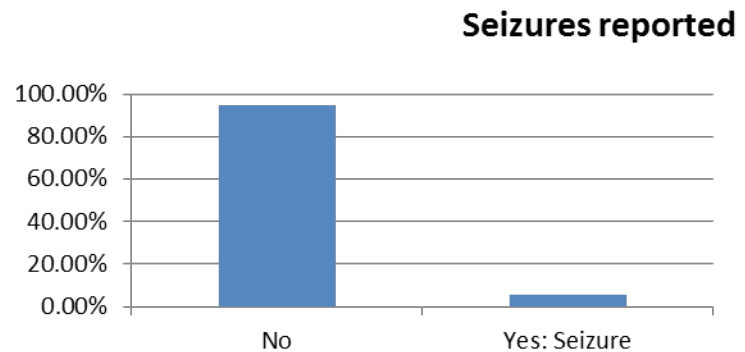
There was reported 22% exacerbation of epileptiform activity in sleep.



9. Did a seizure or other adverse event occur?

Yes / No

37/678 (5%) reported a seizure



Fisher - n.s

Summary: effectiveness and efficiency of sleep induction

- **High percentage achieve sleep (79%)**
- **Sleep deprivation with melatonin more effective in inducing sleep than either method alone**
- **Sleep deprivation with melatonin shortest mean latency to sleep**

Summary: Diagnostic yield

Sleep effectively improved diagnostic yield

- **5% seizures were reported**
- **Where no sleep, EEG yield increased by 15%**
- **Unequivocal epileptiform activity not seen in resting record 20%**
- **Exacerbation of epileptiform activity seen in resting record 22%**

No major difference in diagnostic yield between different methods

Suggested guidelines:

Standard 1: Patients (parent/guardians) should receive clear information about the sleep test by post.

Guideline: Also liaise with parents/guardians by telephone.

Suggested guidelines:

Standard 2: There should be provision of sleep friendly premises appropriate to the age of the child/parents needs

- Chair available for parents to hold child comfortably (or chair/bed for sleep)

Guideline: Sensory soothing lighting or audio equipment to aid sleep process

Suggested guidelines:

Standard 3: A minimum of 90 minutes should be available for the appointment

Suggested guidelines:

Standard 4: If melatonin is to be given it should be available at the time of the appointment, stored safely.

Guideline:

- Stored in lockable cupboard in department
- Parents may bring the melatonin with them
- Nursing staff may bring melatonin to the department

Suggested guidelines:

Standard 5: Melatonin should be given in the department

Guideline:

- Melatonin given by trained Clinical Physiologist
- The parent/guardian give their child melatonin
- Trained nursing staff may give the melatonin

Suggested guidelines:

Standard 6: Melatonin is prescribed by the referring Paediatrician or by the Consultant Neurophysiologist at the request of the referring doctor.

Suggested guidelines:

Standard 7: Melatonin to be given at the start of the appointment. Up to 6mg may be given as first dose up to 5 years. Up to 12mg may be given in older children.

The following doses are recommended:

Age	12-24m	Dose	3mg
	2-4y	6mg	
	5y+	9mg (occ 12mg)	

Guideline: A second dose may be given after 45 minutes if the first is unsuccessful.

Suggested guidelines:

Standard 8 : Protocols for dealing with seizures must be in place.

Suggested guidelines:

Standard 9: Should be aware of BNF guidance when melatonin is to be used to induce sleep.

Contraindications:

For patients younger than 18y.

: Hepatic impairment, galactosaemia and autoimmune disease

Precautions :

:Glucose-galactose malabsorption, lactose intolerance and renal impairment.

Comments/Discussion