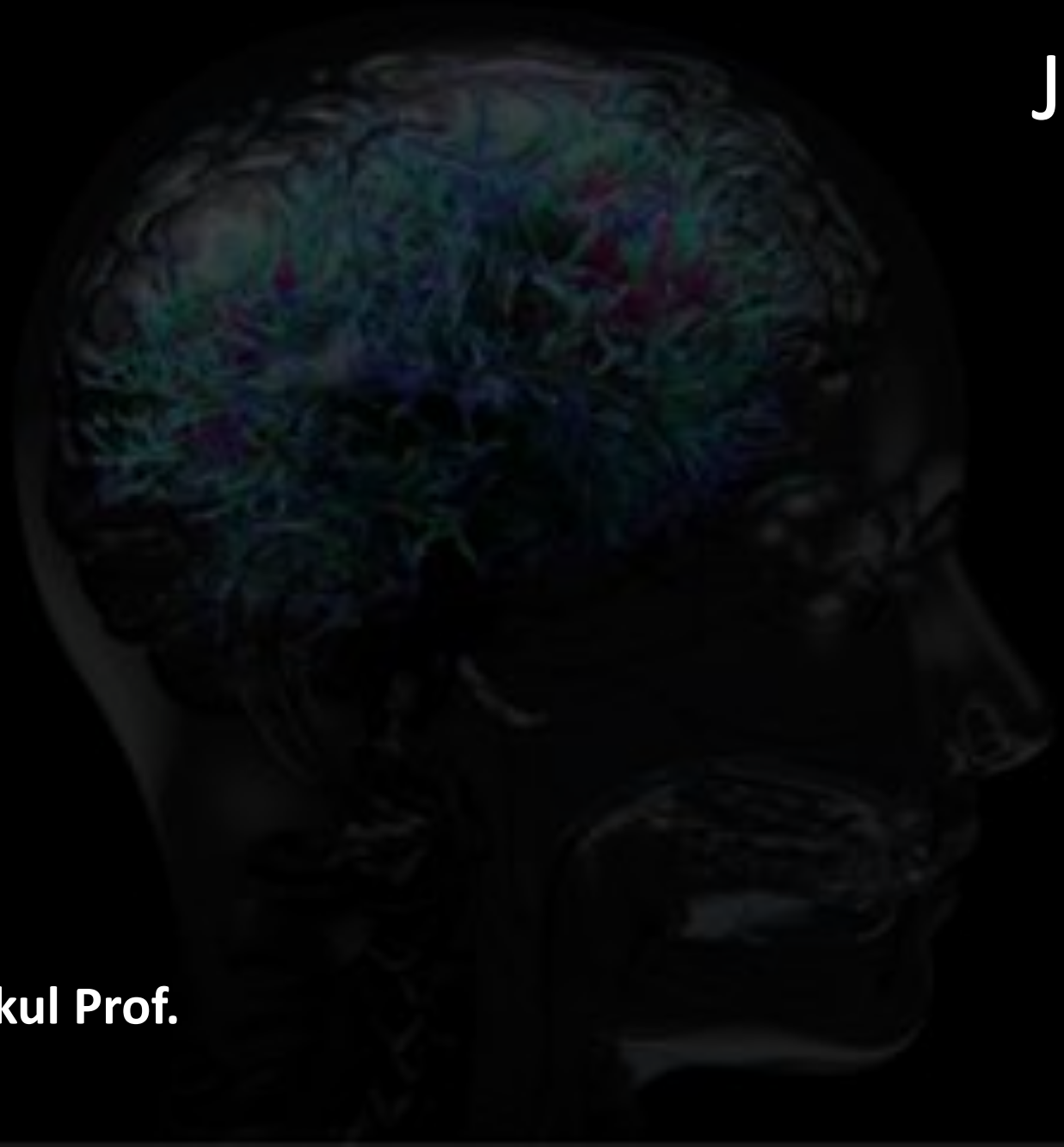

Journal club

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Monochromic light reduces emergence delirium in children undergoing adenotonsillectomy; a double-blind randomized observational study

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BMC Anesthesiology 2021

Introduction

- Emergence delirium (ED) is common in pediatric anesthesia
- Usually occurs within the first 30 min of recovery from anesthesia
- The incidence ranges between 10-80%

  -Depend on the scale used for assessment
- Most common

  -Younger children (3-7 years)

  -Ophthalmology and Otorhinolaryngology procedures

Introduction

- Dissociative state in which the patient is confused from the surroundings and flailing
  - -Can be self-injurious
  - -Disruption to tubes, lines, and drains
  - -Upsetting for parents and staff
- Treatment is by administration of sedation
  - -Most common propofol, benzodiazepines, or dexmedetomidine
- Results in delayed discharge from PACU

Introduction

- **<u>The aim of this study</u>**

Determine if exposure to monochromatic blue light (MBL) in the immediate phase of recovery could reduce the overall incidence of emergence delirium in children following general inhalation anesthesia

METHODS

- Texas Children's Hospital, Houston, USA
- Between November 2017 and June 2020
- Ethics

  -Prospective, Double-Blinded and Randomized controlled study

  -Approved by the Ethical Committee at Baylor College of Medicine

  -The trial was register at www.clinicaltrials.gov

  -Informed consent from parents or legal guardians participating

METHODS

Patients: Children 2-6 years old undergoing adenotonsillectomy under GA

Intervention: Monochromic blue light (MBL)

Control : Sham blue light

Outcome

<u>Primary outcome</u>

-Compare the incidence of emergence delirium in MBL group and control group

METHODS

Inclusion criteria

- Children 2-6 years old
- Adenotonsillectomy under GA
- ASA 1,2 (3 when due to sleep apnea with no other co-morbidities)

METHODS

Exclusion criteria

- Premedication with midazolam and dexmedetomidine
- Patients received midazolam, dexmedetomidine, or ketamine intraoperative
- Patients taking stimulants for appetite or attention deficit hyperactive disorders

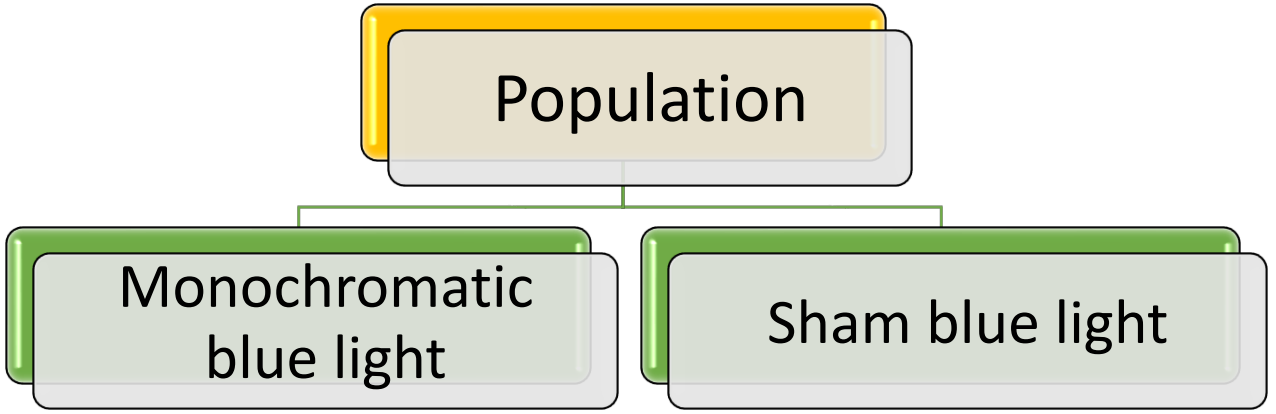
METHODS

Exclusion criteria

- Patients with known
  - -Ocular disorders
  - -Migraines, seizures
  - -Psychiatric or behavioral health conditions
  - -Developmental delay

- Patient unable to be transferred to PACU immediately following extubation

Randomization



- ✓ Random numbers in 1:1 ratio
- ✓ Sealed envelopes assigning patients to group A (MBL) and B (Sham)
- ✓ The envelope was opened immediately on arrival to the PACU
- ✓ The lightbox was set to A and B accordingly
- ✓ To reduce bias, all PACU nurses were kept blinded to the patient grouping

Anesthetic conduct

Anesthetic conduct

All patient underwent routine anesthetics with inhalation induction (sevoflurane 8% with nitrous oxide in oxygen 70%/30%)

The patients were intubated and received opioids at the discretion of the anesthesiologist

Propofol was given prior to intubation if deemed necessary by the anesthesiologist

Midazolam, ketamine and dexmedetomidine were not administered

Maintenance with sevoflurane

Anesthetic conduct

Intravenous ondansetron and dexamethasone were administered to all patients

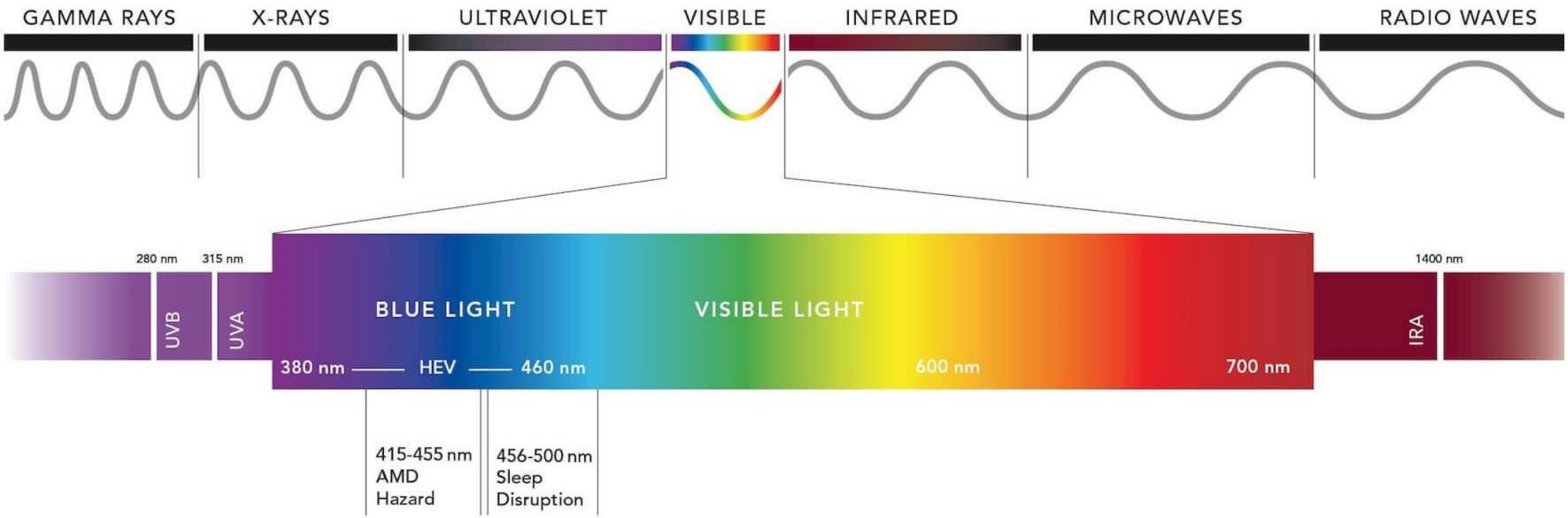
At the conclusion, the head of the bed was turned 90 degree to standard position and the patient extubated

All patients were extubated under deep general anesthesia

Immediately transferred to a stretcher and brought directly to PACU with oxygen

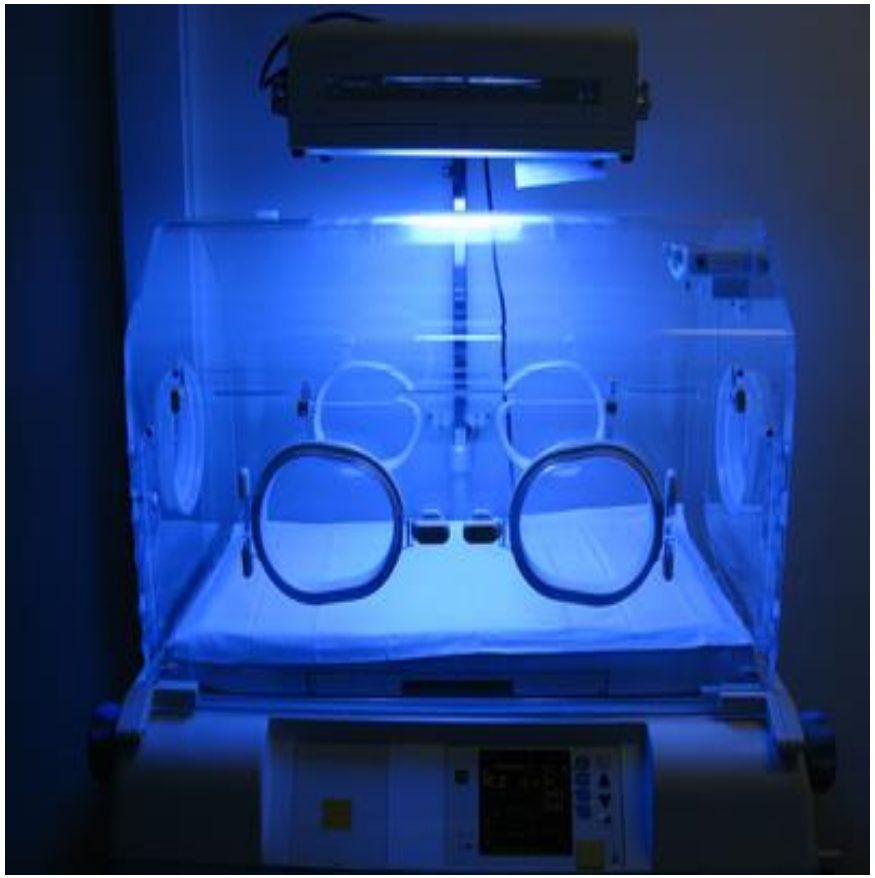
Study conduct

- The light box Draeger Phototherapy 4000 (Draeger Medical, Lübeck, Germany)
- Placed behind the head to the bed directly over the patient at 90 degrees and 12-18 inches above the face
- All patients were positioned supine for maximal exposure
- Patients were immediately randomized to a study group or placebo


GAMMA RAYS
X-RAYS
ULTRAVIOLET
VISIBLE
INFRARED
MICROWAVES
RADIO WAVES
280 nm
315 nm
UVB
UVA
BLUE LIGHT
VISIBLE LIGHT
380 nm
HEV
460 nm
600 nm
700 nm
1400 nm
IRA
415-455 nm
AMD
Hazard
456-500 nm
Sleep
Disruption

Study conduct

- The light was started within 1 min of entry to the PACU
- Sham blue light (control) that was not monochromatic but contained all wavelengths within the visible spectrum (appear blue due to an outer coating on the bulb)
- To maintain blinding, both the Sham and experimental bulbs were within the same light box



Patient assessment

- PAED scores were taken on entry to the PACU (baseline) and at 10, 20, and 30 min
- Assess by pediatrics PACU nursing staff
- The exposure to the light was also for 30 min
- If the patient was awake and appropriate or ED (study outcome is now definitely known) → not recorded PAED scores
- If the patient to have ED, they notified anesthesiologist to provide pharmacologic treatment

PAED scale

Table 2 PAED scale (from Bajwa and colleagues,[4] with permission. ©2010 Blackwell Publishing Ltd). Score is sum of all values

Behaviour	Not at all	Just a little	Quite a bit	Very much	Extremely
Makes eye contact with caregiver	4	3	2	1	0
Actions are purposeful	4	3	2	1	0
Aware of surroundings	4	3	2	1	0
Restless	0	1	2	3	4
Inconsolable	0	1	2	3	4

A score of >12

-100% sensitivity and 94.5% specificity for the diagnosis of ED

Statistical Analysis

- Means and standard deviations (SD)
- Student's t-test for continuous variables (e.g., age, PAED score)
- Chi-square test for categorical variables (e.g., % female, ASA category)
- Statistical analysis

  -Stata/MP 15.1 for Windows

  -All p-values <0.05 were considered statistically significant

Statistical Analysis

- Sample size was done using an incidence of 40% of ED in similar patient population[1]
- We assume an absolute reduction of 25% in incidence of emergence delirium to be clinically significant
- To detect difference at 80% power with a two-sided alpha of 0.05

  -Require N = 98 participants

Makkar JK, Bhatia N, Bala I, Dwivedi D, Singh PM. A comparison of single dose dexmedetomidine with propofol for the prevention of emer- gence delirium after desflurane anaesthesia in children. Anaesthesia. 2016;71:50–7.

Results

Texas Children's Hospital
November 2017 – June 2020

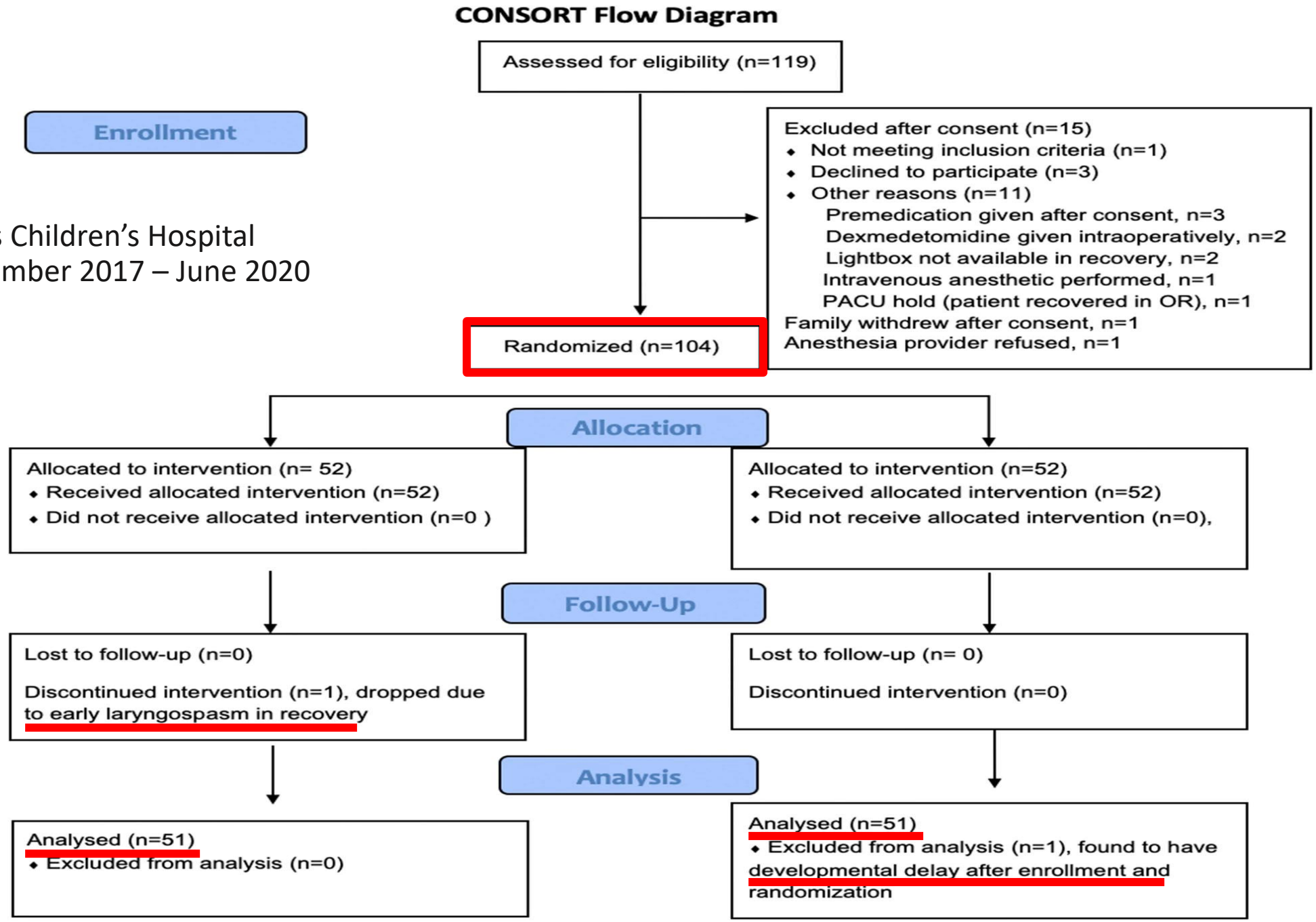


Table 1 Patient demographics for children undergoing adenotonsillectomy by study group. ASA = American Society of Anesthesiologists

Variables	Control Group (sham); $N = 51$	Study Group (Monochromatic Blue light); $N = 51$	Absolute Standardized Differences
Age (Mean, SD)	4.2 (1.4)	4.7 (1.3)	0.40
% Female (n, %)	24 (47.1%)	24 (47.1%)	0.00
Weight (kg) (Mean, SD)	20.3 (7.2)	21.8 (7.0)	0.21
ASA physical class (n, %)			
1	0 (0%)	4 (7.8%)	
2	40 (78.4%)	36 (70.6%)	0.42
3	11 (21.6%)	11 (21.6%)	
Baseline (time = 0) Pediatric Anesthesia Emergence Delirium Scale Score (Mean, SD)	12.0 (0)	11.9 (0.7)	0.20

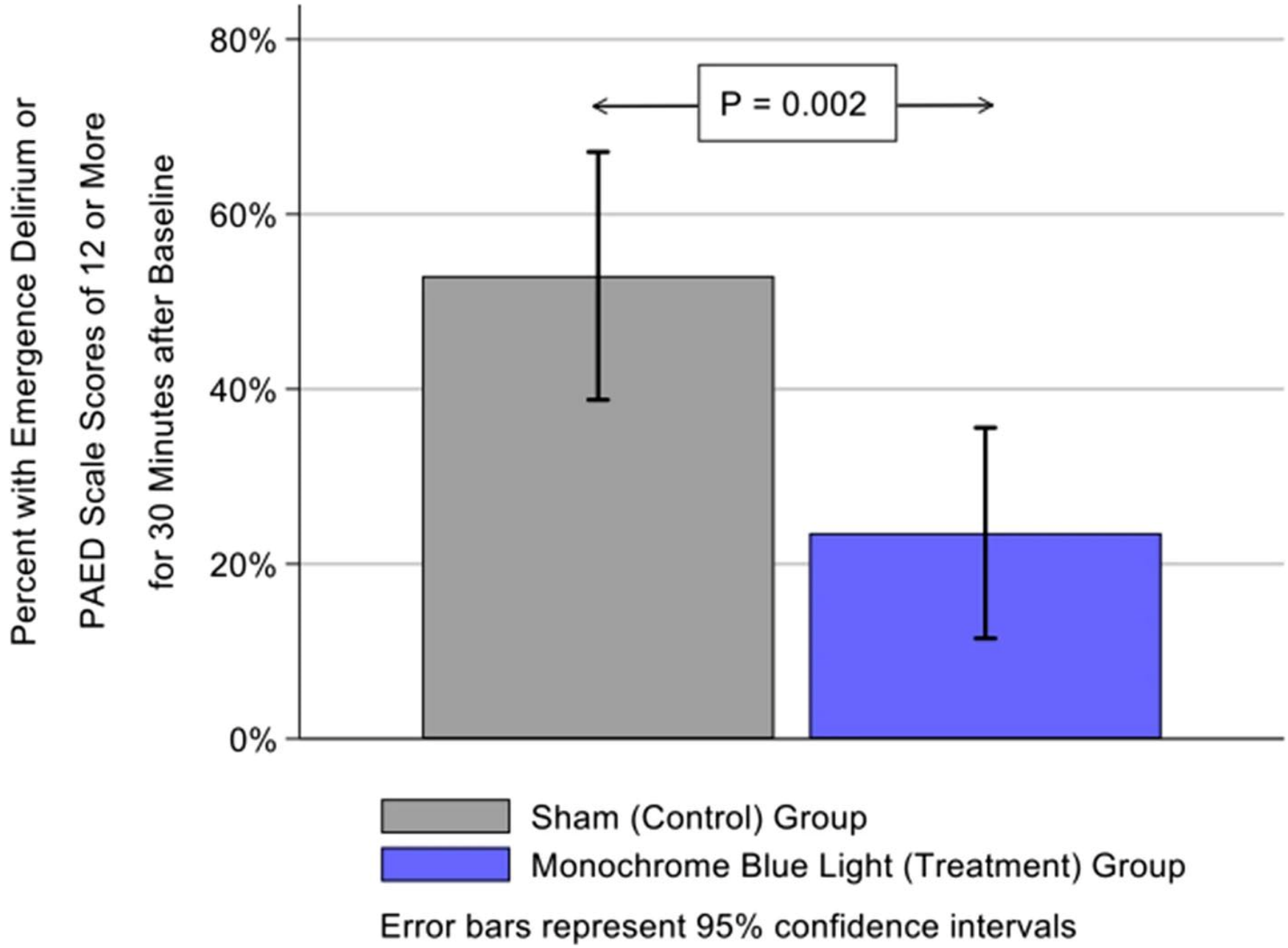
No difference identified in demographic data between groups

Table 2 Patient assessment of emergence delirium. PAED = Pediatric Anesthesia Emergence Delirium

Variables	Sham Group (control); *N* = 51	Monochromatic Blue Light Group (treatment) *N* = 51	*P*-value
Outcomes			
Patient had Emergence Delirium (n, %)	17 (33.3%)	3 (5.9%)	0.001
Patient had Emergence Delirium or a PAED Scale Score of 12 or more for 30 min after Baseline (n, %)	27 (52.9%)	12 (23.5%)	0.002
PAED Scale Score over time (after Baseline)			
Time = 10 min (Mean, SD)	*n* = 50; 12.8 (2.8)	*n* = 47; 12.5 (2.0)	0.592
Time = 20 min (Mean, SD)	*n* = 40; 12.9 (4.4)	*n* = 38; 11.6 (4.5)	0.185
Time = 30 min (Mean, SD)	*n* = 25; 10.9 (5.2)	*n* = 27; 6.6 (5.9)	0.007
PAED score recorded at all 3 periods (n, %)	25 (49.0%)	27 (52.9%)	0.692
Percent change from baseline PAED score to last recorded PAED score (Mean, SD)	-1.7% (46.5)	-26.8% (49.6)	0.012

Table 3 Multivariable Logistic Regression Model Identifying Factors Involved In Experiencing Emergence Delirium. ASA = American Society of Anesthesiologists

Variable	Relative Risk Rat	95% Confidence Interval	*P*-value
Study Group (Baseline Category = Control Group)	0.18	(0.06, 0.54)	0.001
Age (per year)	0.88	(061, 1.26)	0.470
Weight (per kg)	1.02	(0.96, 1.09)	0.554
Female Sex (Baseline Category = Male)	1.45	(0.83, 2.56)	0.186
ASA Category			
1 or 3	1		-
2	0.70	(0.29, 1.68)	0.447


Percent with Emergence Delirium or
PAED Scale Scores of 12 or More
for 30 Minutes after Baseline
80%
60%
40%
20%
0%
P = 0.002
Sham (Control) Group
Monochrome Blue Light (Treatment) Group
Error bars represent 95% confidence intervals

Discussion

Emergence delirium

- Outcome : exposure to MBL in the immediate recovery phase reduces the incidence of ED

- The incidence of ED in the control group was similar to the reported incidence in children undergoing adenotonsillectomy

- In the MBL group, the incidence was significantly less than in the Sham group (5.9% VS 33.3%)

Discussion

PAED score

- PAED score ≥ 12 at the time periods of 10, 20, and 30 min
- 23.5% of MBL had this outcome versus 52.9% of the Sham group (p=0.002)
- Difference in the PAED scores were most pronounced after the 20-min mark of the study

- Theorize that this is due the time of emergence in patients for which deep extubation is performed

Discussion

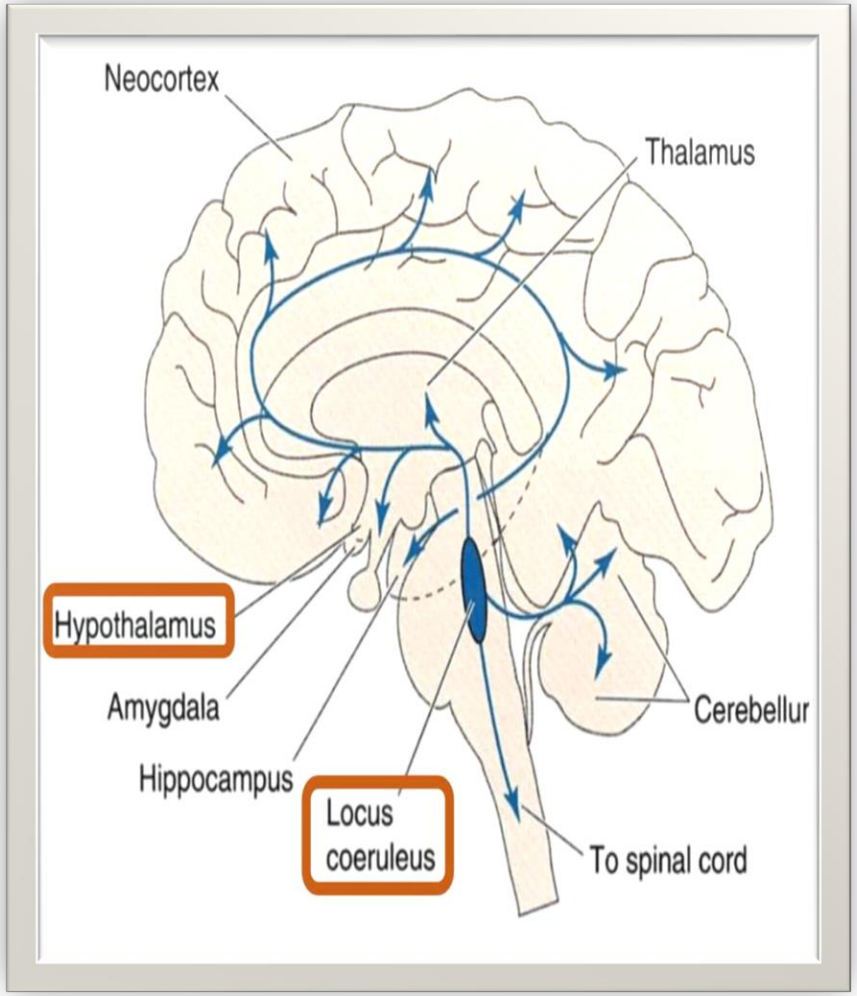
Monochromatic blue light

- Stimulate wakefulness and alertness
- Reduce reaction times and enhance cognition
- Functional MRI studies during MBL exposures

-Correlate with increase hippocampus, thalamic and amygdala activity

-Increase activity in frontal gyrus and bilateral area of the brainstem

-Activation of locus coeruleus



Discussion

Monochromatic blue light

- Martin et al.;

  -During emergence there is delta frequency slowing and frontally dominant alpha activity

- Increase frontal connectivity was observed in patients with ED immediately after termination of the sevoflurane

- EEG analysis during exposure to MBL of 460 nm

  -Reduced power density of delta and increase alpha waves

Martin JC, Liley DT, Harvey AS, Kuhlmann L, Sleigh JW, Davidson AJ. Alter- ations in the functional connectivity of frontal lobe networks preceding emergence delirium in children. Anesthesiology. 2014;121:740–52.

Limitations

"While a robust, double blind study design and rigorous statistic methods are study strengths, the study does have limitations"

- The assessment of ED/PAED scale is a subjective clinical determination
- Reduce Hawthorne effect

-Use a sham blue light with all PACU nurses completing the assessments remained blinded

Limitations

- Do not control for intraoperative IV acetaminophen administration
  - -Only 2 patients received intraoperative acetaminophen (15 mg/kg)
  - -1 ED and 1 did not
- Do not control for intraoperative opioid
  - -Most patients received opioids at the time of intubation
  - -The mean time from last opioid to extubation was 32.2 min (MBL group) and 24.5 min (sham group)
- Do not record EEG activity during emergence from anesthesia

Conclusion

- MBL significantly reduce the incidence of emergence delirium in children following sevoflurane anesthesia
- MBL was associated with reduced emergence delirium as lower mean PAED scores
- Exposure to MBL during the early emergence phase may be a potentially non-pharmacologic intervention that reduces ED in children

Critical Appraisal : RCT

Does this study address a clear question?

1. Were the following clearly stated:	Yes	Can't tell	No
• Patients	✓		
• Intervention	✓		
• Comparison Intervention	✓		
• Outcome(s)	✓		

Critical Appraisal : RCT

- Are the results of this single trial valid?

	Yes	Can't tell	No
2. Was the assignment of patients to treatments randomised?	✓		
3. Was the randomisation list concealed? Can you tell?	✓		
4. Were all subjects who entered the trial accounted for at it's conclusion?			✓
5. Were they analysed in the groups to which they were randomised, i.e. intention-to-treat analysis	✓		

Critical Appraisal : RCT

- Are the results of this single trial valid?

6. Were subjects and clinicians 'blind' to which treatment was being received, i.e. could they tell?	Yes	Can't tell	No ✓
7. Aside from the experimental treatment, were the groups treated equally?	✓		
8. Were the groups similar at the start of the trial?	✓		

Critical Appraisal : RCT

- What were the results?

9. How large was the treatment effect? Consider • How were the results expressed (RRR, NNT, etc).	✓
10. How precise were the results? Were the results presented with confidence intervals?	✓

Critical Appraisal : RCT

- Can I apply these valid, important results to my patients?

11. Do these results apply to my patient?	Yes	Can't tell	No
• Is my patient so different from those in the trial that the results don't apply?			✓
• How great would the benefit of therapy be for my particular patient?	✓		
12. Are my patient's values and preferences satisfied by the intervention offered?			
• Do I have a clear assessment of my patient's values and preferences?	✓		
• Are they met by this regimen and its potential consequences?	✓		