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IMPERIAL

Consortium for Neonatal Neuroprotection Time Critical Trials:

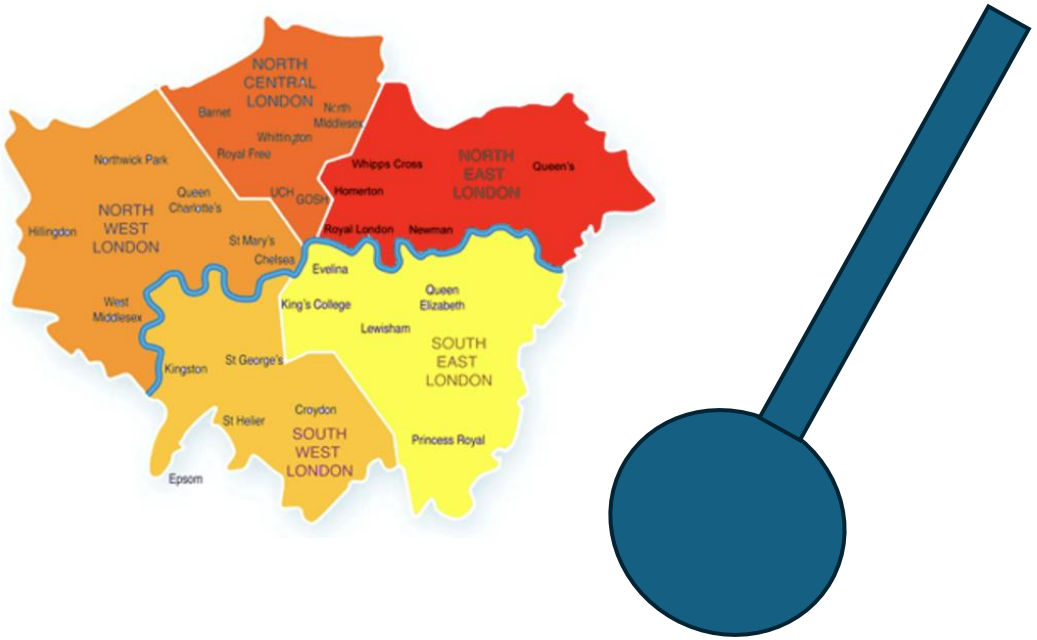
The CONNECTIONS COMET

Prof Sudhin Thayyil

Take home messages – “WHY” and “HOW”

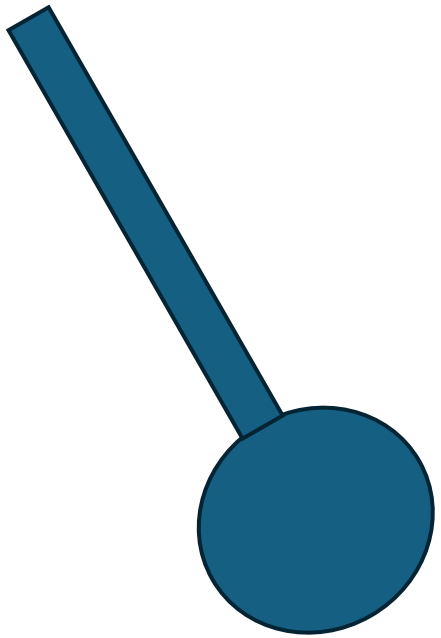
1) Standardised neurological assessment
2) eScreener
3) Video assessments
4) Consent

What doctors do vs what parents (nurses) prefer Swing in Pendulum



Cool before ‘Sudhin’ comes

What doctors do vs what parents (nurses) prefer Swing in Pendulum

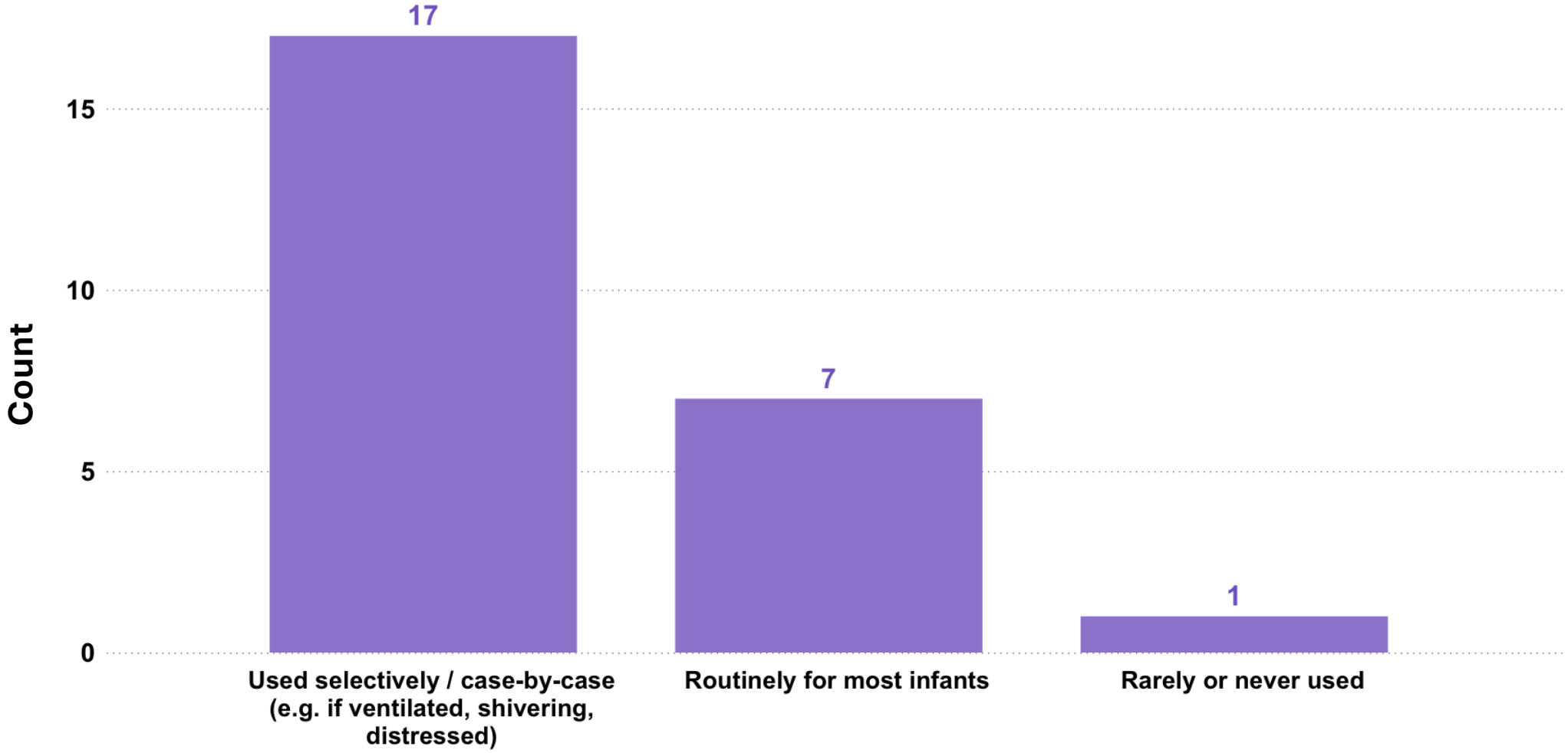


“Don’t worry, it is only mild – they are not going to cool your baby”

Sedation and Ventilation

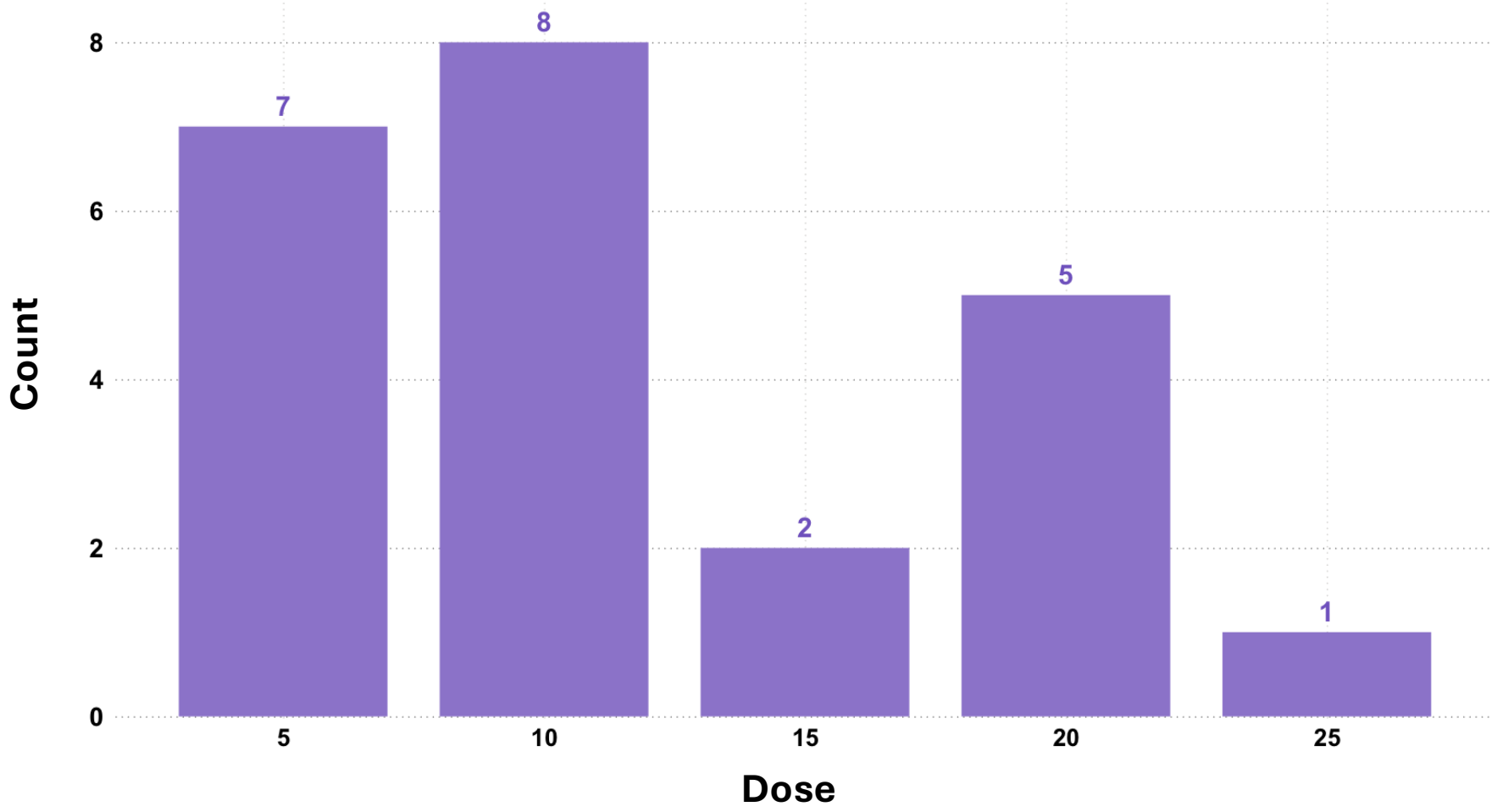
Qualtrics Survey Responses

Q1. If an infant with mild HIE is randomised to the cooling arm of the COMET trial at your unit, how would opioid sedation most likely be used?

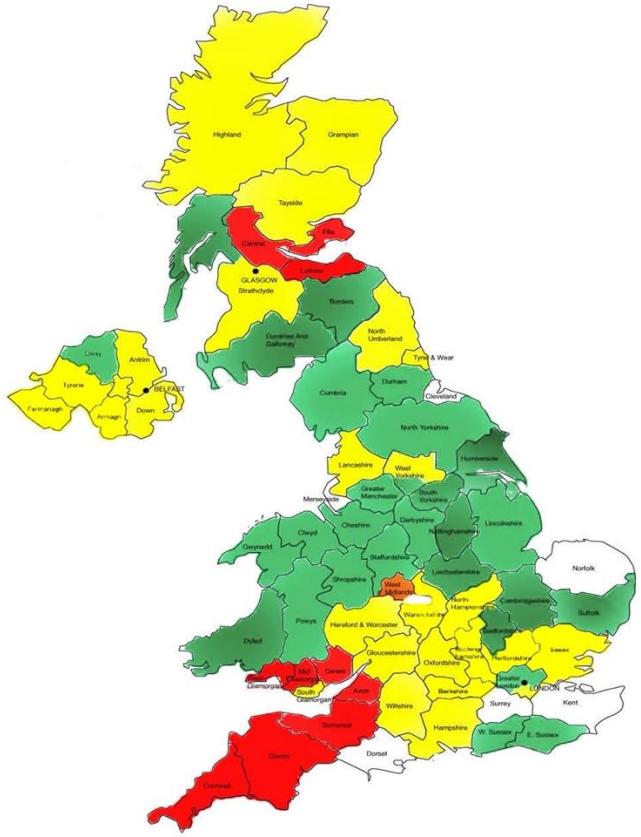


Qualtrics Survey Responses

Q2. What is the maximum dose of morphine that you would use during cooling in mild HIE? (assuming no PPHN) - Dose



Morphine and cooling



Increases hospital stay and ventilation

20 microgram/kg/h
15 microgram/kg/h
10 microgram/kg/h
5 microgram/kg/h
0 microgram/kg/h

} Potentially Toxic

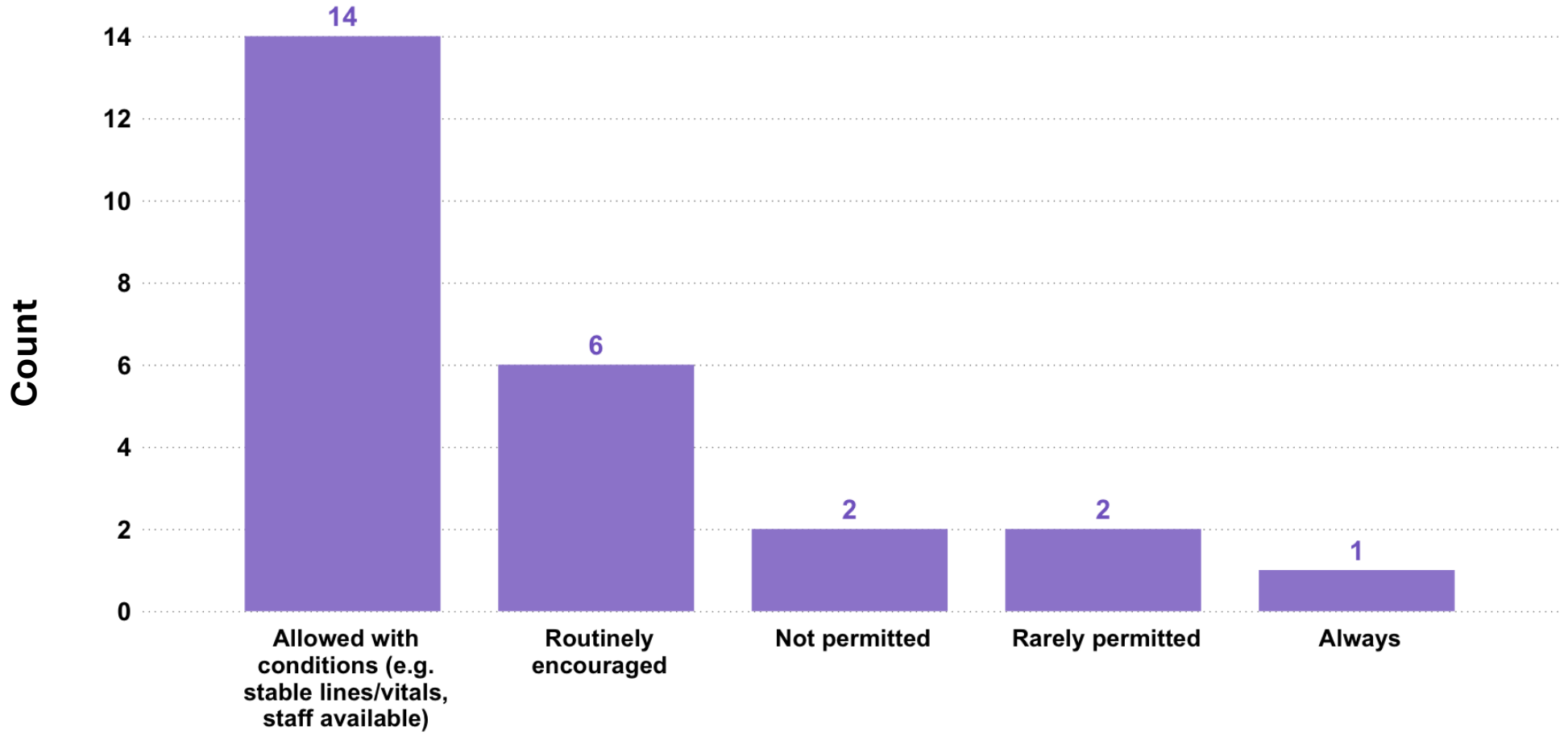
Montaldo et al Arch Dis Child 2019

Natarajan et al J Perinatology 2018

Liow, Montaldo et al Ther Hypo Temp Man 2019

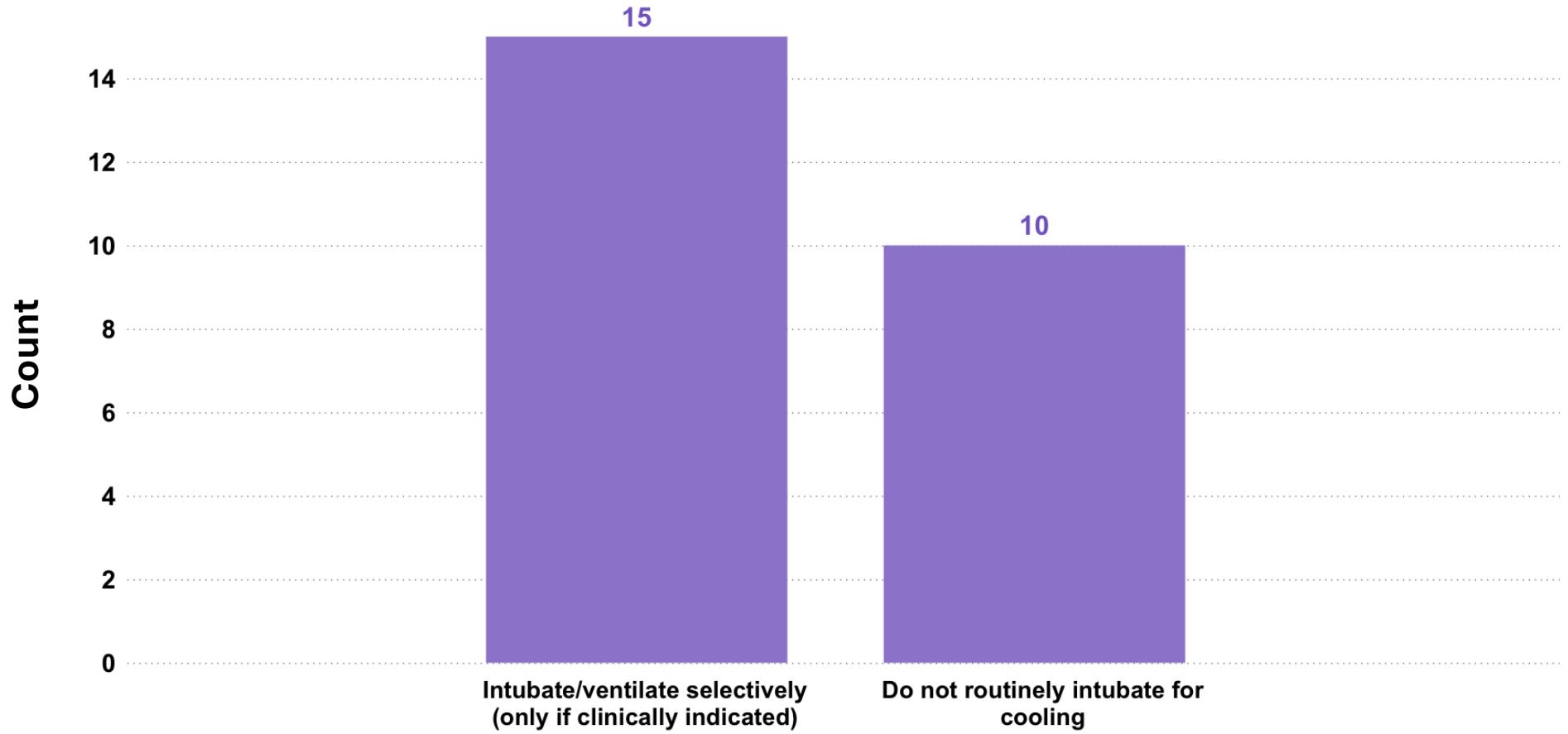
Qualtrics Survey Responses

Q3. At your site, what is the usual approach to parents cuddling during cooling in infants with mild HIE?



Qualtrics Survey Responses

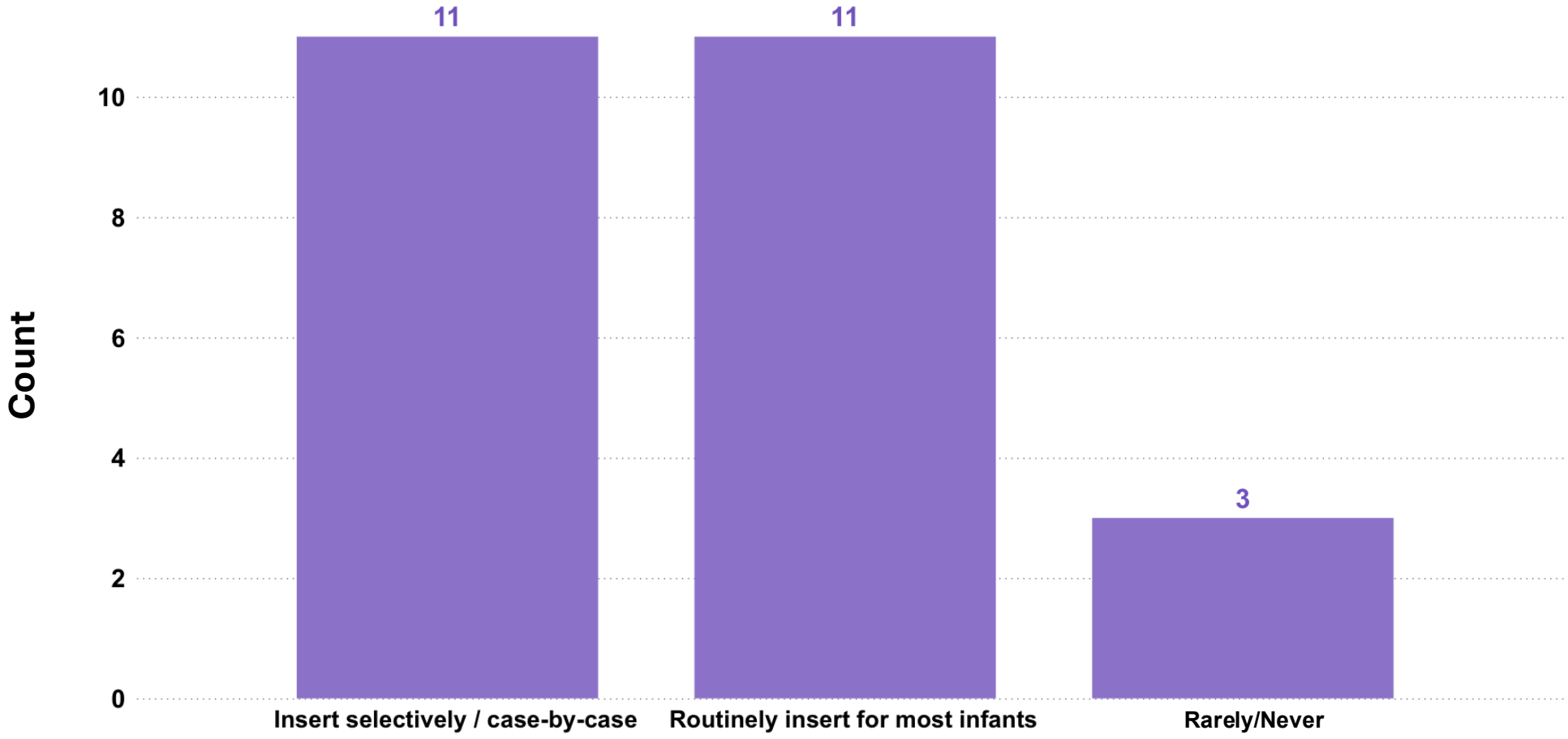
Q4. If an infant with mild HIE is randomised to the cooling arm of the COMET trial, how would your unit typically manage intubation and ventilation?



Umbilical Lines and Feeding

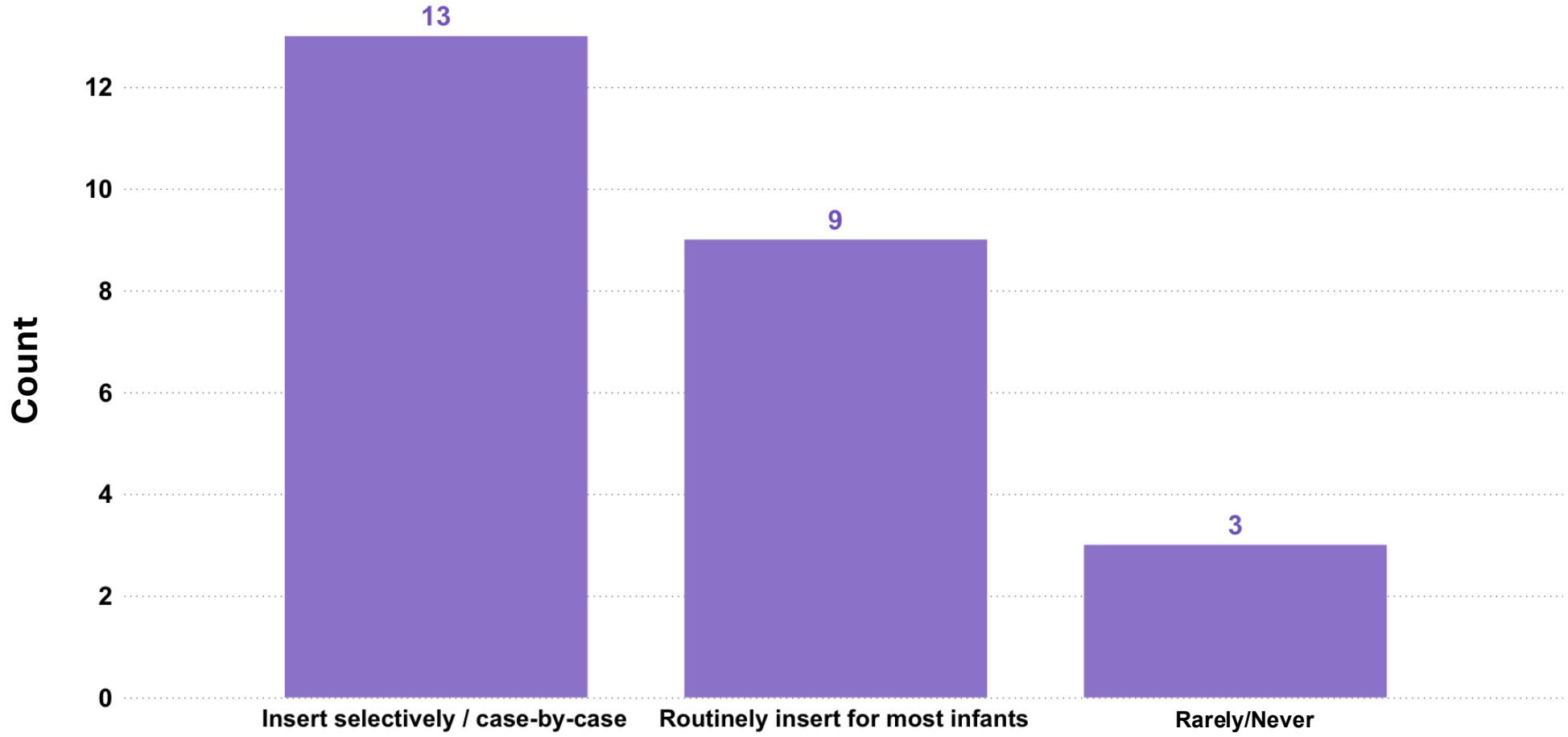
Qualtrics Survey Responses

Q5a. If an infant with mild HIE is randomised to the cooling arm of the COMET trial, what is your unit's usual approach to inserting umbilical lines? - Umbilical venous catheter (UVC) for infusions



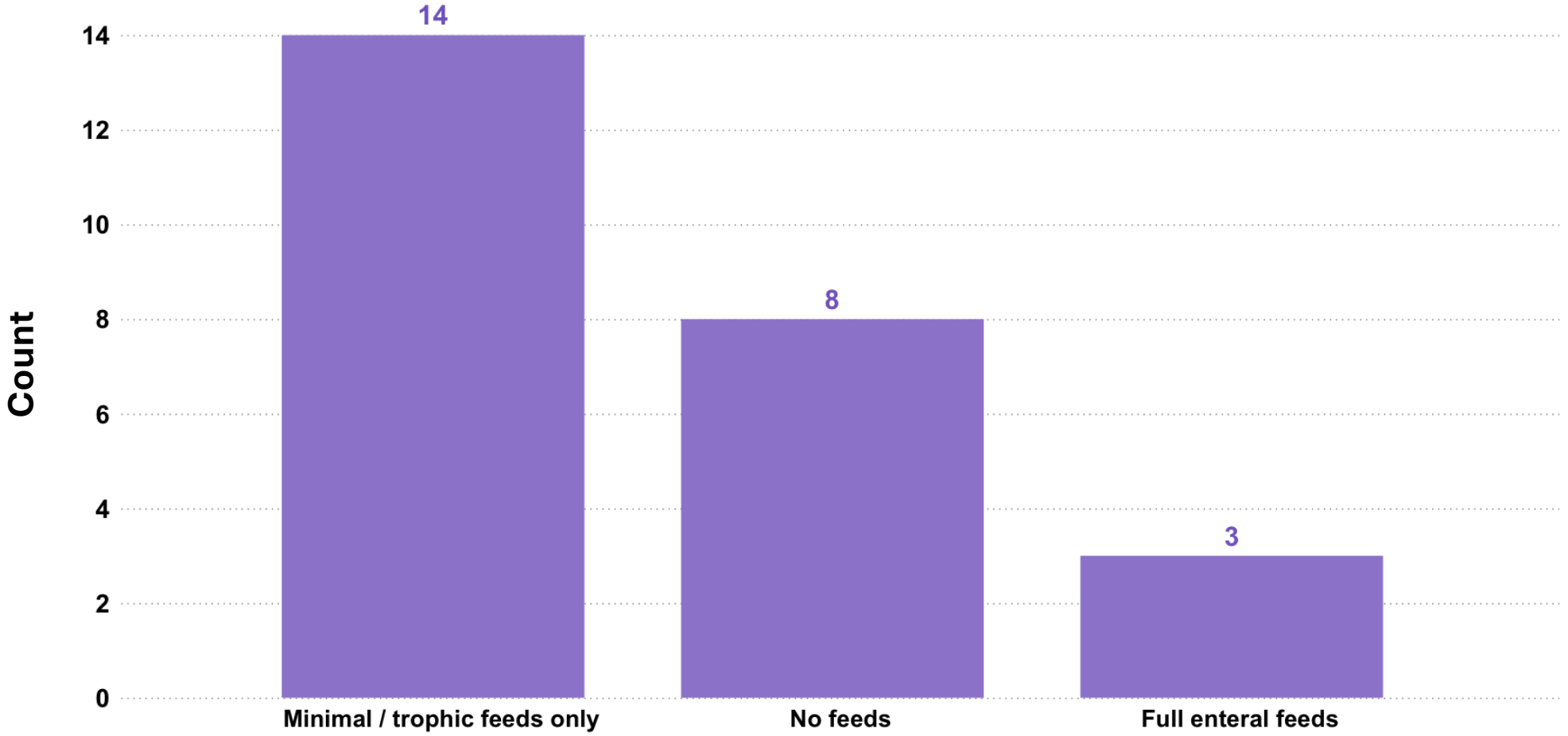
Qualtrics Survey Responses

Q5b. If an infant with mild HIE is randomised to the cooling arm of the COMET trial, what is your unit's usual approach to inserting umbilical lines? - Umbilical arterial catheter (UAC) for blood sampling



Qualtrics Survey Responses

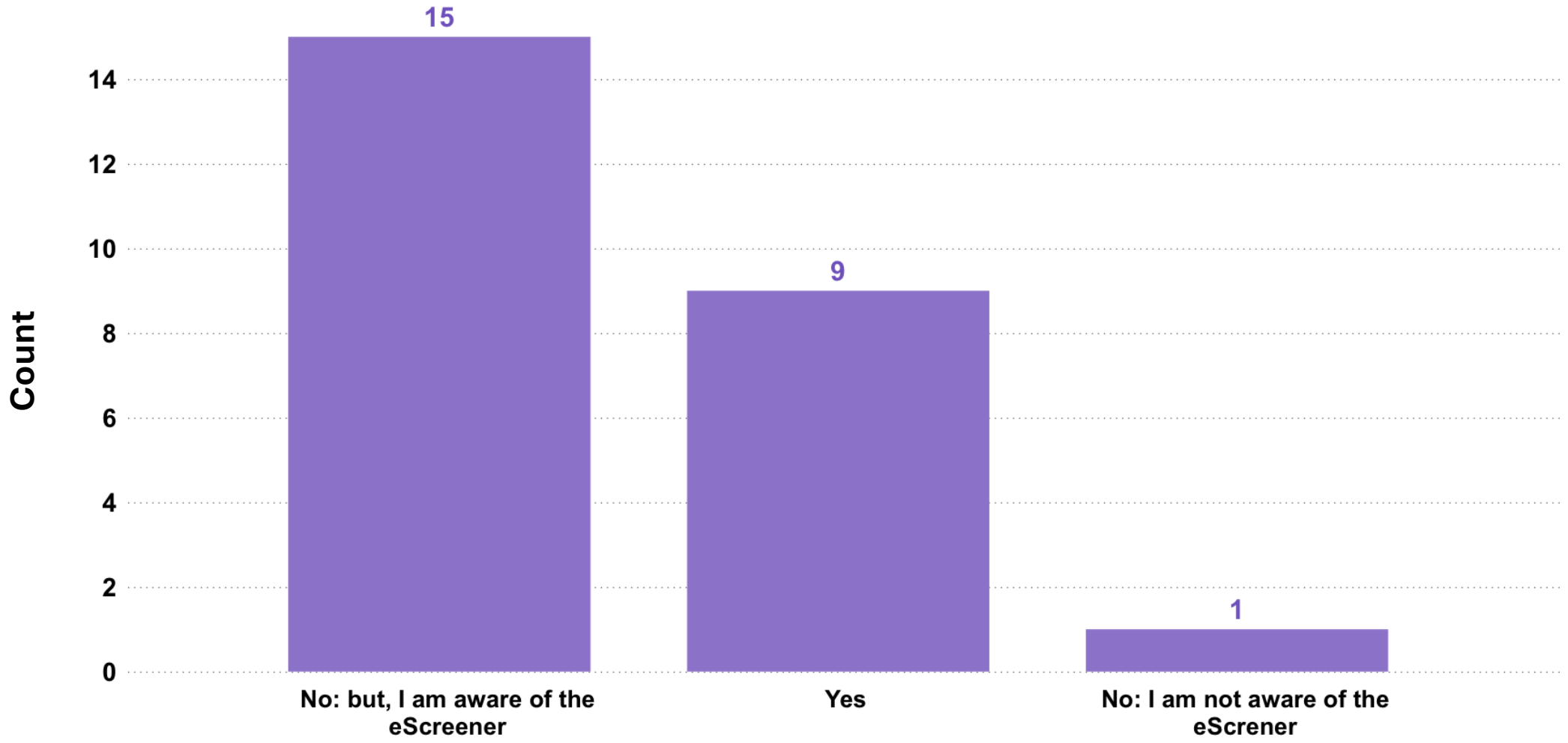
Q6. If an infant with mild HIE is randomised to the cooling arm of the COMET trial, what is your unit's usual approach to feeding during cooling?



E Screen

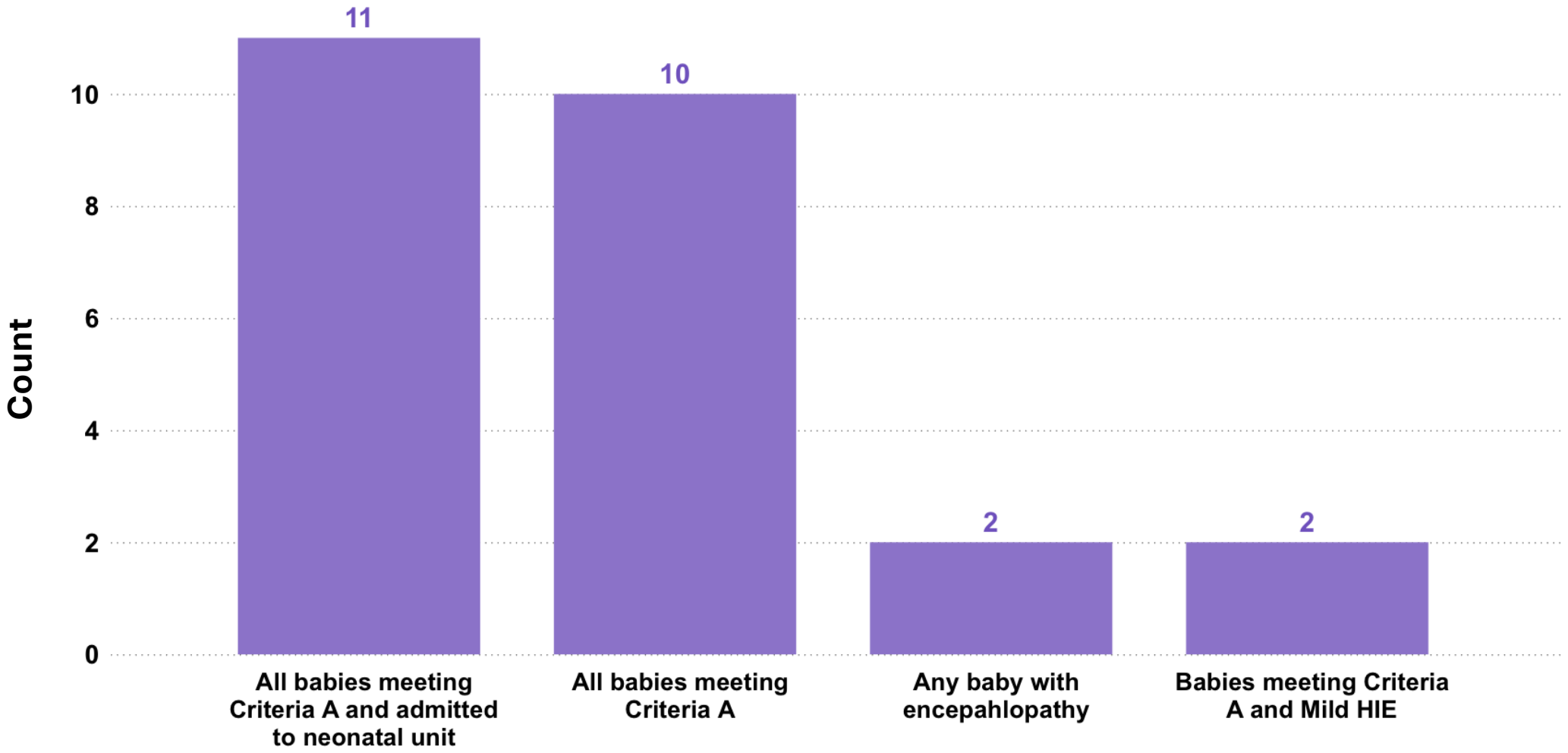
Qualtrics Survey Responses

Q7. Have you used the COMET eScreener for neurological assessment?



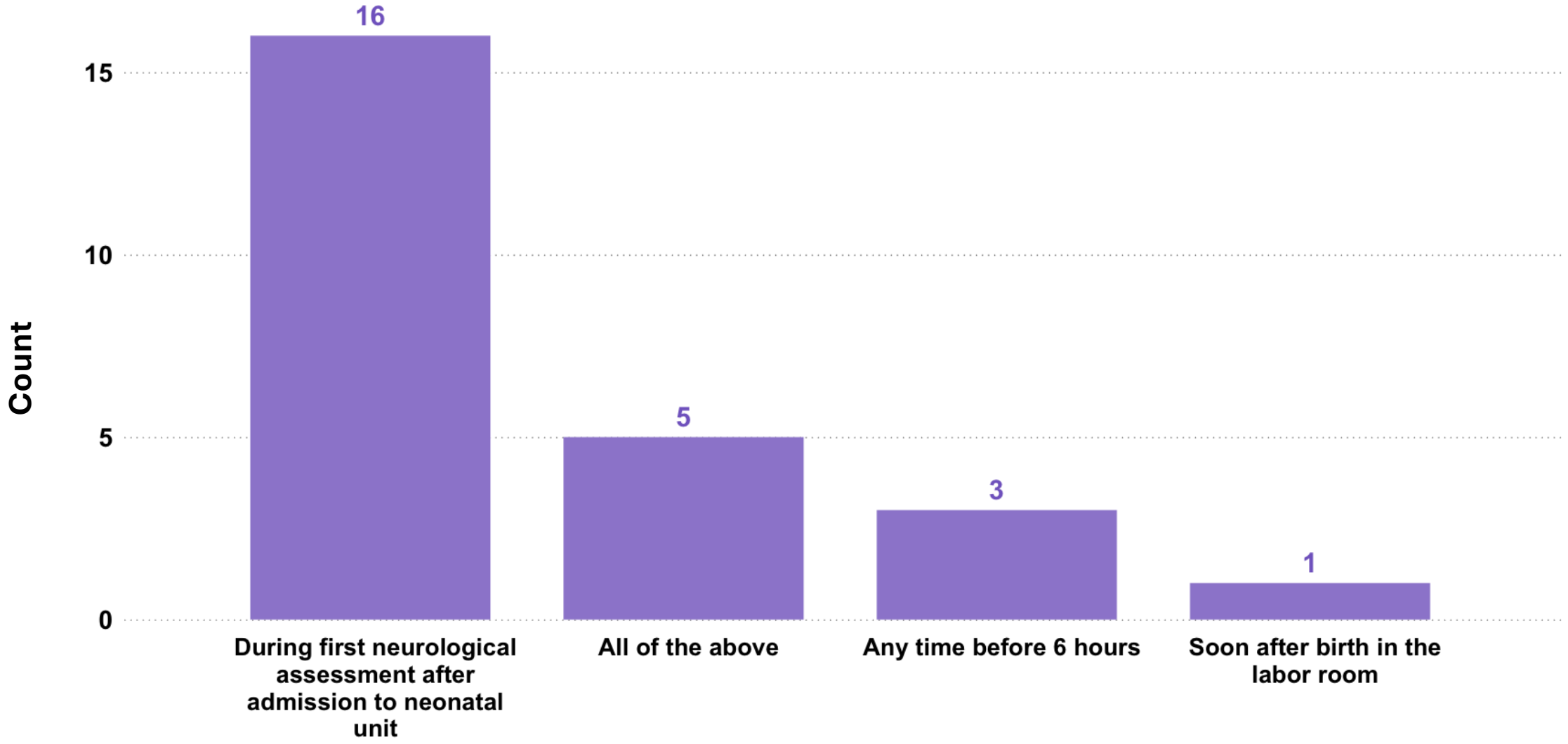
Qualtrics Survey Responses

Q8. Which babies should be assessed using eScreener as per protocol?



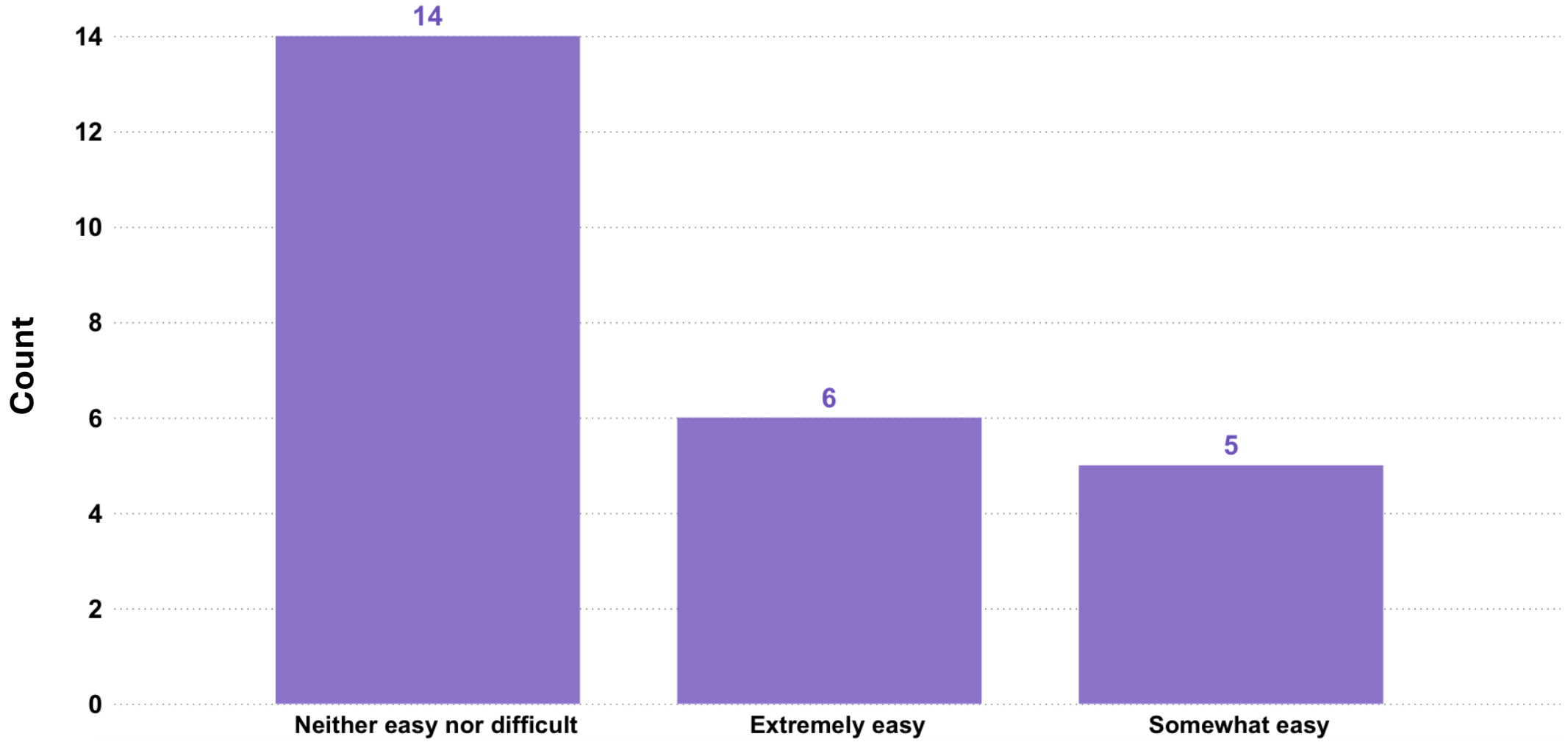
Qualtrics Survey Responses

Q9. When would you use the eScreener?



Qualtrics Survey Responses

Q10. How do you find the use of eScreener within your workflow?

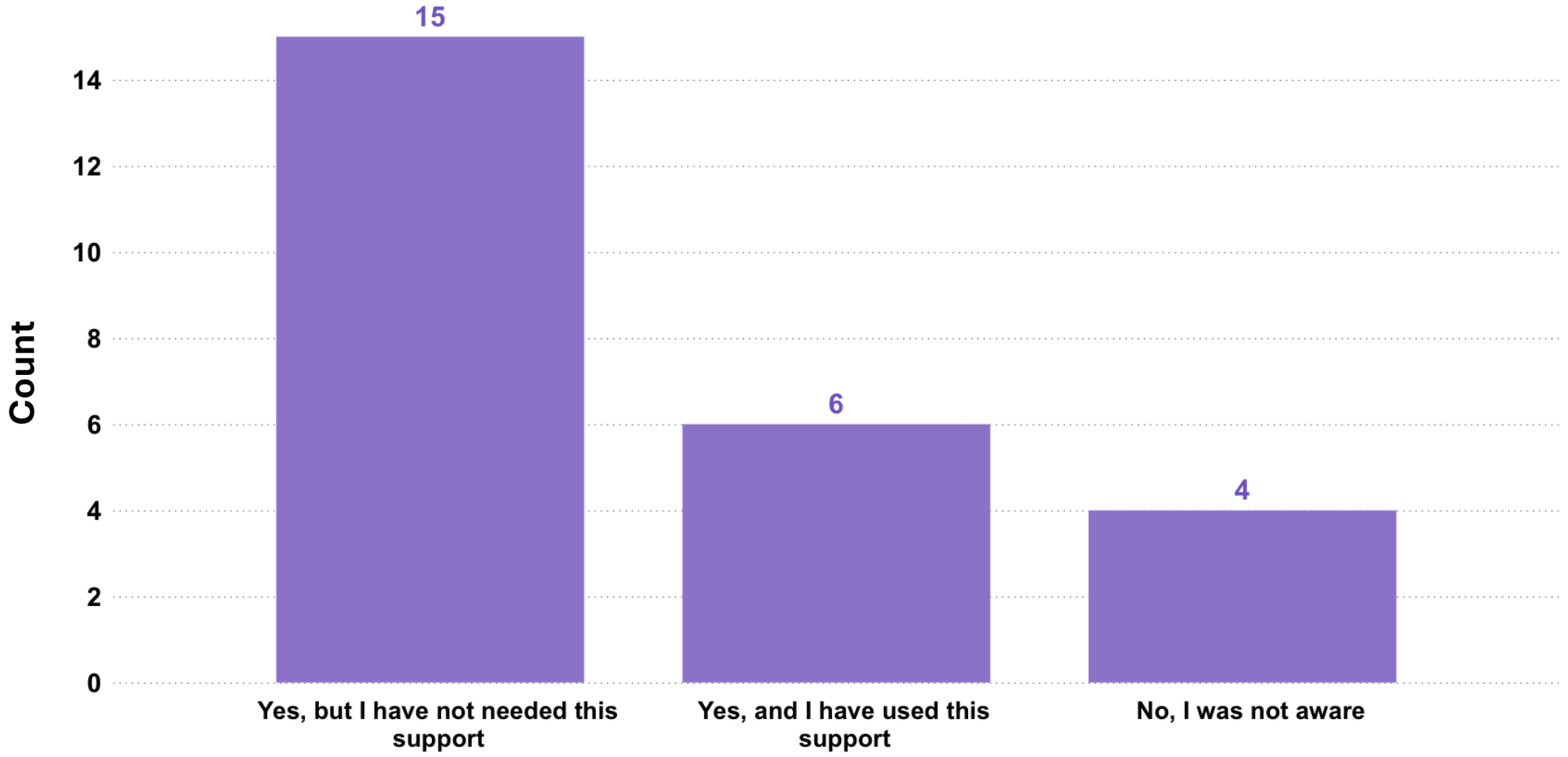


Qualtrics Survey Responses

Q11. Compared with traditional assessment methods, how does eScreener affect…

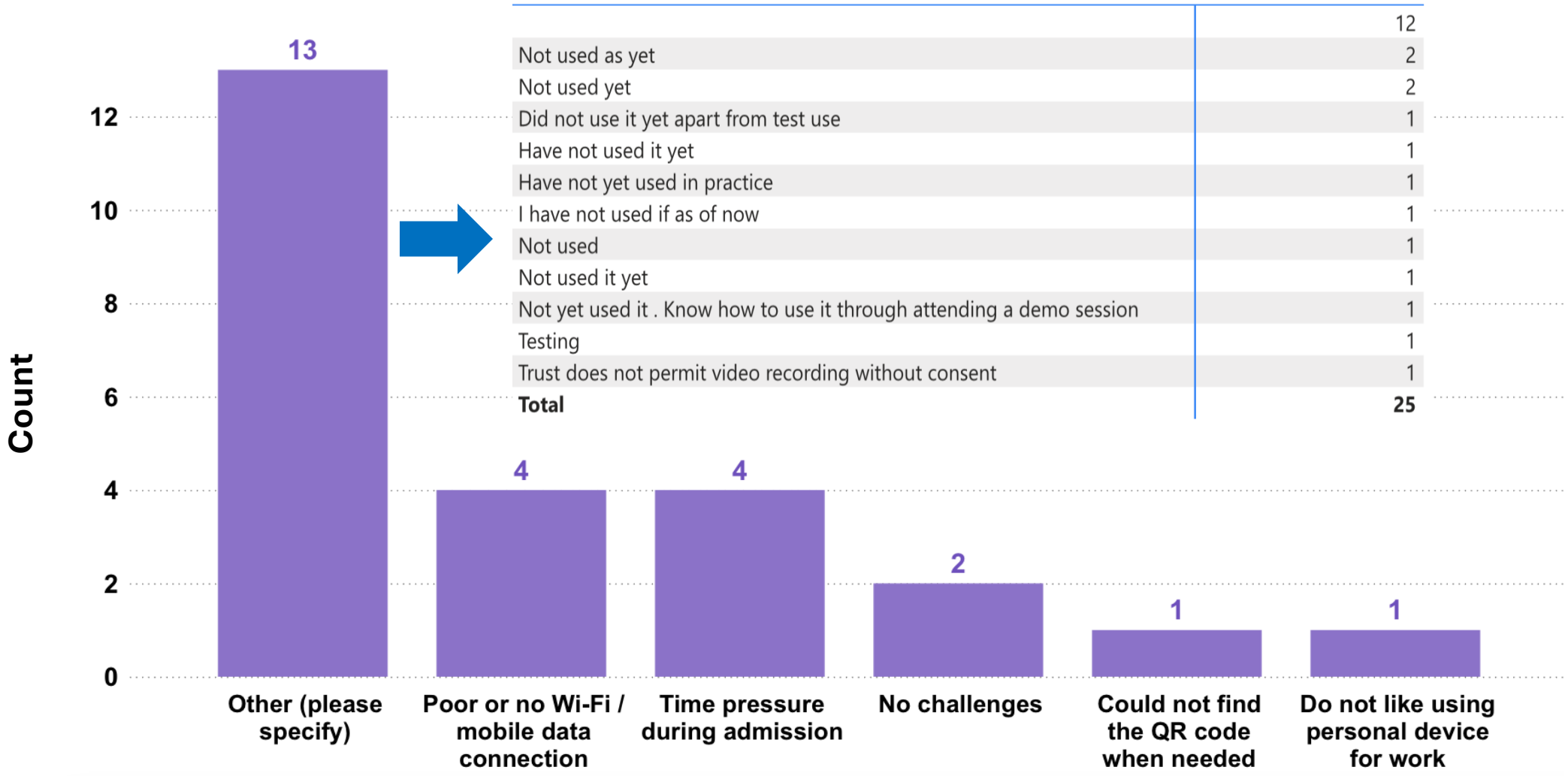
Qualtrics Survey Responses

Q12. Are you aware that completing the eScreener alerts the COMET trial team for 24/7 support?



Qualtrics Survey Responses

Q13. What challenges (if any) have you faced when using the eScreener?



	12
Not used as yet	2
Not used yet	2
Did not use it yet apart from test use	1
Have not used it yet	1
Have not yet used in practice	1
I have not used if as of now	1
Not used	1
Not used it yet	1
Not yet used it . Know how to use it through attending a demo session	1
Testing	1
Trust does not permit video recording without consent	1
Total	**25**

Qualtrics Survey Responses

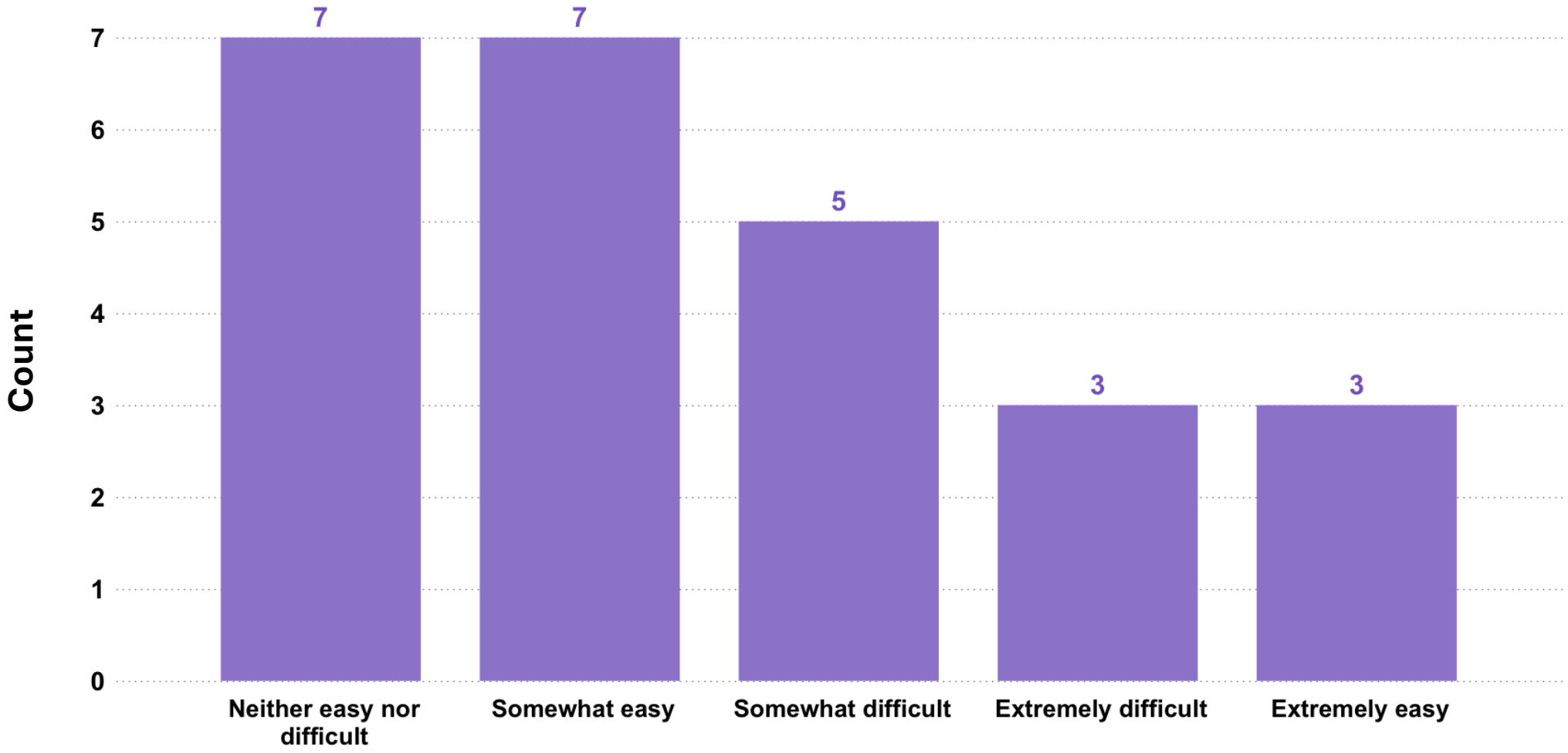
Q14. Thinking about your overall experience with the eScreener, what aspects have been most helpful, and what aspects could be improved?

Being able to video and have screener tool on same device ie split screen would be better
Disclaimer on front page stating parental verbal consent sufficient
Great
Have not used it yet
i have not used it before
I have not used this e screener yet
Missed using it in a baby who was obviously unlikely to be recruited to the COMET trial as was severe HIE
Na
Not applicable
Not in Use yet
Not sure
Not tried it yet but will do
Not used yet
Not yet used in practice
Really good and supports juniors in assessment
Support from the team and ease of use
Testing
The most difficult part is making the team share their attention to e screening in between high pressure of handling a critically sick baby.
Very good
Video and screen simulatoiusly
Works well
Yet to use this

Video recording

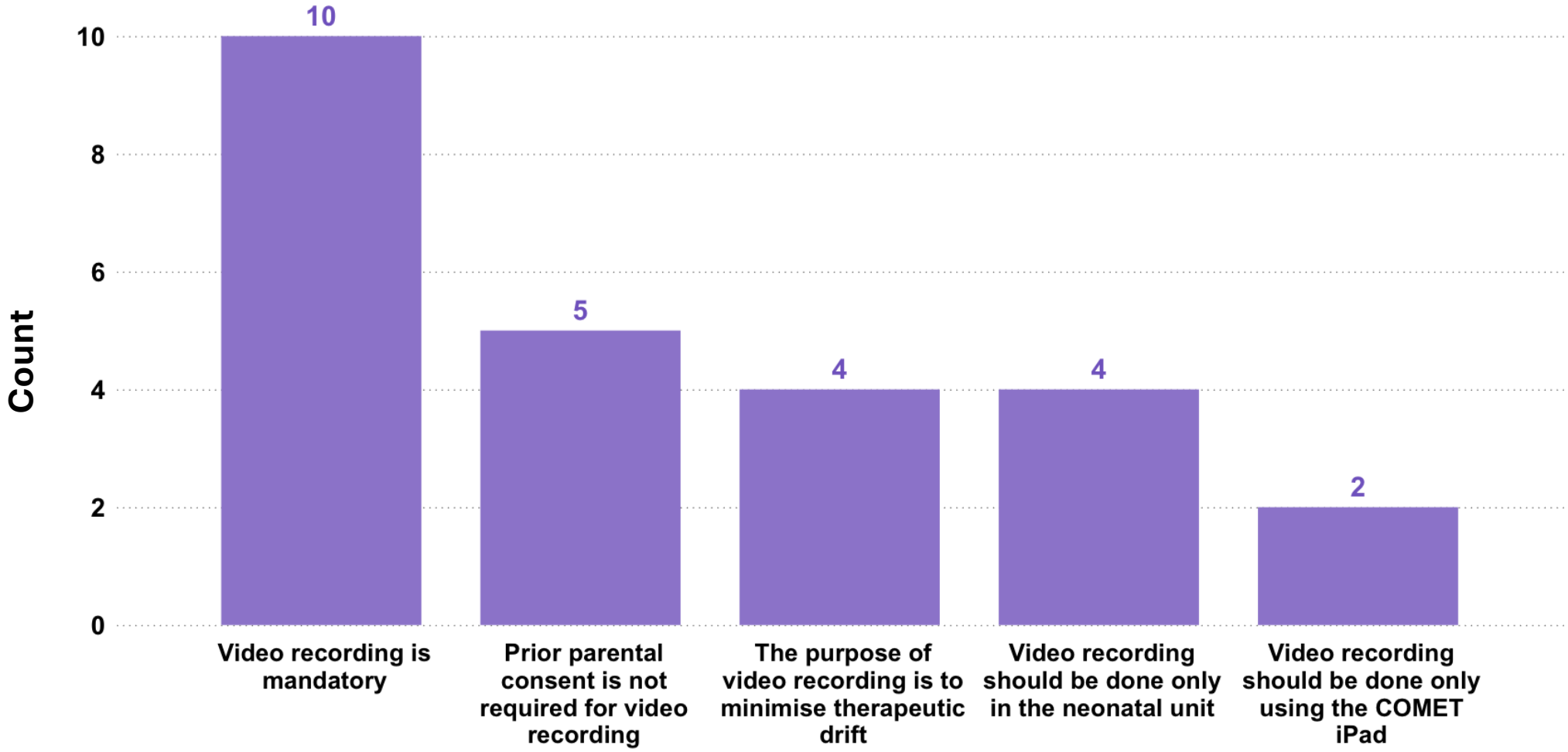
Qualtrics Survey Responses

Q15. How easy or difficult is it to incorporate video recording of the neurological assessment into your workflow?



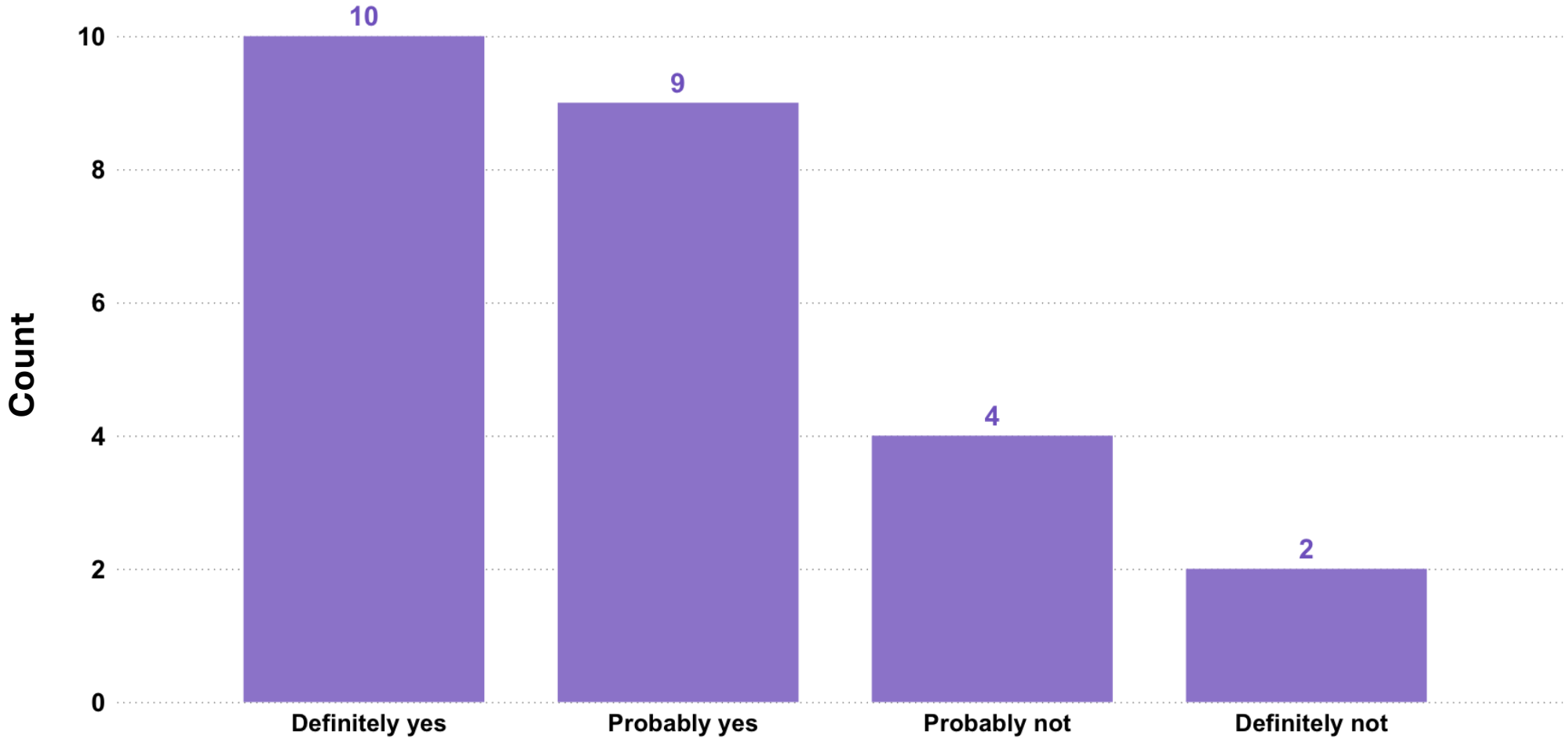
Qualtrics Survey Responses

Q16. Which of the following statement is false regarding video recording of the neurological assessment?



Qualtrics Survey Responses

Q17. Is video recording before parental consent (deferred consent) feasible in your neonatal unit?



Neurological Examination for COMET Trial Eligibility

The Expanded Modified Sarnat Staging

Prof Sudhin Thayyil MD. FRCPCH, PhD
Chair of Perinatal Neuroscience and Consultant Neonatologist
Imperial College London

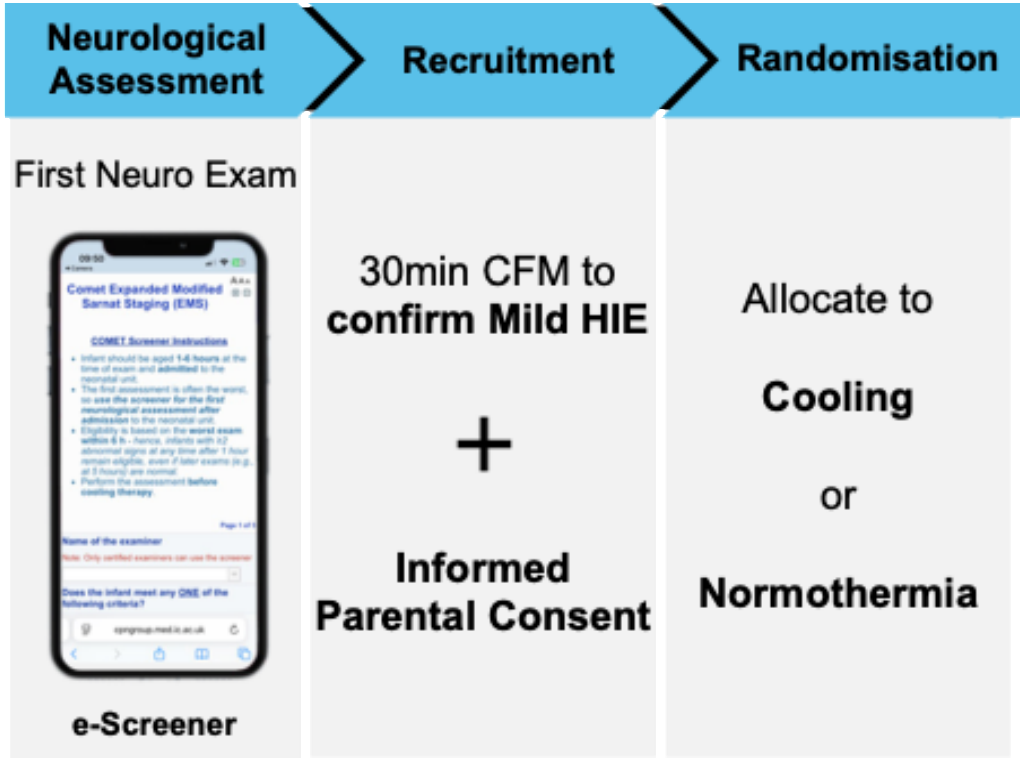
Training and Certification Agenda

- Pre-course reading
  - Sarnat Staging: Original, Modified and Expanded
  - Definitions used in Expanded Modified Sarnat (EMS) staging

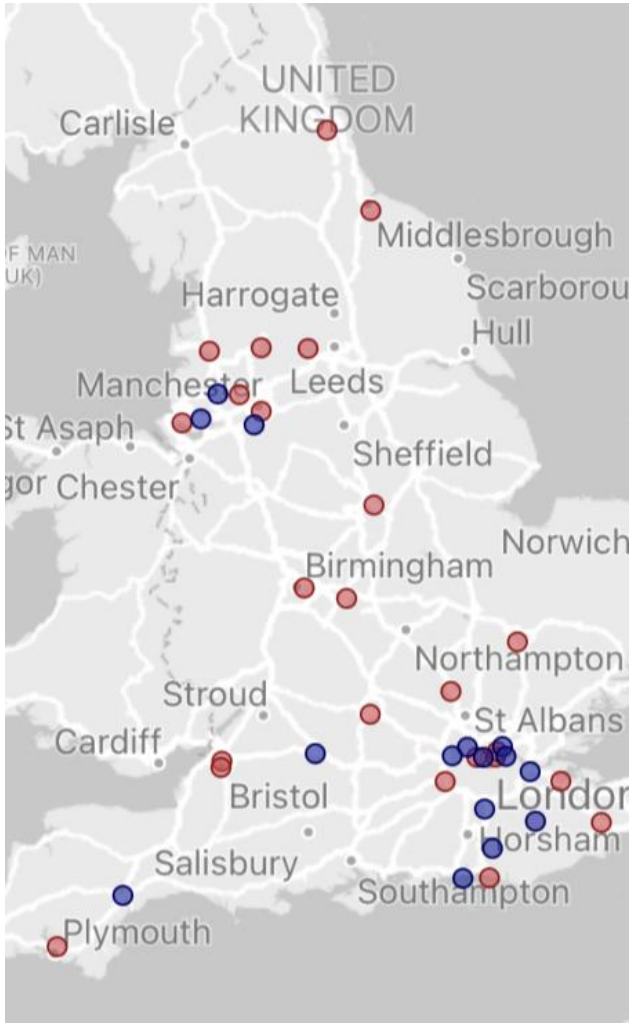
  https://www.imperial.ac.uk/comet-trial

- Current course
  - Animated and actual videos of the nine signs
  - Full videos of assessments and discussion
  - Exam videos (x2)

The COMET Trial e-Screen



Hospital	Level
Birmingham Heartlands	NICU
Bradford Royal Infirmary	NICU
Burnley General Hosptial	NICU
Darent Valley Hospital	SCBU/LNU
Derriford Hospital	NICU
East Surrey Hospital	SCBU/LNU
Gloucestershire Royal Hospital	SCBU/LNU
Great Western Hospital	SCBU/LNU
Hillingdon Hospital	SCBU/LNU
Homerton Hospital	NICU
James Cook Hospital	NICU
John Radcliffe Hospital	NICU
Liverpool Women's Hospital	NICU
Luton and Dunstable Hospital	NICU
Medway Maritime Hospital	NICU
Newham General Hospital	SCBU/LNU
Northwick Park Hospital	SCBU/LNU
Princess Royal Hospital (Haywards Heath)	SCBU/LNU
Queen Charlotte's Hospital	NICU
Queens Medical Centre Nottingham	NICU
Rosie Maternity Hospital, Addenbrookes	NICU
Royal Albert Edward Infirmary	SCBU/LNU
Royal Bolton Hospital	NICU
Royal Devon and Exeter Hospital	SCBU/LNU
Royal London Hospital	NICU
Royal Preston Hospital	NICU
Royal Sussex County Hospital	NICU
Royal Victoria Infirmary	NICU
Southmead Hospital	NICU
St Mary's Hospital (Manchester)	NICU
St Mary's Hospital (Paddington)	SCBU/LNU
St Michael's Hospital (Bristol)	NICU
St Peter's Hospital	NICU
Tunbridge Wells Hospital	SCBU/LNU
University Hospital Coventry	NICU
Whipps Cross Hospital	SCBU/LNU
Whiston Hospital	SCBU/LNU
William Harvey Hospital	NICU
Worthing Hospital	SCBU/LNU
Wythenshawe Hospital	SCBU/LNU



Original Sarnat Staging

Neonatal Encephalopathy Following Fetal Distress

A Clinical and Electroencephalographic Study

Harvey B. Sarnat, MD, Margaret S. Sarnat, MD

Arch Neurol—Vol 33, Oct 1976

Table 2.—Distinguishing Features of the Three Clinical Stages of Postanoxic Encephalopathy in the Full-Term Newborn Infant

	Stage 1	Stage 2	Stage 3
Level of consciousness	Hyperalert	Lethargic or obtunded	Stuporous
Neuromuscular control Muscle tone	Normal	Mild hypotonia	Flaccid
Posture	Mild distal flexion	Strong distal flexion	Intermittent decerebration
Stretch reflexes	Overactive	Overactive	Decreased or absent
Segmental myoclonus	Present	Present	Absent
Complex reflexes Suck	Weak	Weak or absent	Absent
Moro	Strong; low threshold	Weak; incomplete; high threshold	Absent
Oculovestibular	Normal	Overactive	Weak or absent
Tonic neck	Slight	Strong	Absent
Autonomic function	Generalized sympathetic	Generalized parasympathetic	Both systems depressed
Pupils	Mydriasis	Miosis	Variable; often unequal; poor light reflex
Heart rate	Tachycardia	Bradycardia	Variable
Bronchial and salivary secretions	Sparse	Profuse	Variable
Gastrointestinal motility	Normal or decreased	Increased; diarrhea	Variable
Seizures	None	Common; focal or multifocal	Uncommon (excluding decerebration)
Electroencephalogram findings	Normal (awake)	Early: low-voltage continuous delta and theta. Later: periodic pattern (awake). Seizures: focal 1-to 1½-Hz spike-and-wave	Early: periodic pattern with isopotential phases. Later: totally isopotential
Duration	Less than 24 hr	Two to 14 days	Hours to weeks

Modified Sarnat Staging

Key Points

- Not for use within the first 6 hours of life
- Tracks encephalopathy over 3 days
- Detailed neurological examination
- Requires full-montage EEG

Table 2.—Distinguishing Features of the Three Clinical Stages of Postanoxic Encephalopathy in the Full-Term Newborn Infant

	Stage 1	Stage 2	Stage 3
✓ Level of consciousness	Hyperalert	Lethargic or obtunded	Stuporous
Neuromuscular control			
✓ Muscle tone	Normal	Mild hypotonia	Flaccid
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✗ Stretch reflexes	Overactive	Overactive	Decreased or absent
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Complex reflexes			
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✗ Oculovestibular	Normal	Overactive	Weak or absent
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Autonomic function			
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✗ Electroencephalogram findings	None	Common; focal or multifocal	Uncommon (excluding decerebration)
✗ Duration	Normal (awake)	Early: low-voltage continuous delta and theta. Later: periodic pattern (awake). Seizures: focal 1-to 1½-Hz spike-and-wave	Early: periodic pattern with isopotential phases. Later: totally isopotential
	Less than 24 hr	Two to 14 days	Hours to weeks

Modified Sarnat Staging

The NEW ENGLAND JOURNAL of MEDICINE

Whole-Body Hypothermia for Neonates with Hypoxic–Ischemic Encephalopathy

N Engl J Med 2005;353:1574-84.

3

Table 1. Criteria for Defining Moderate and Severe Encephalopathy.

Category	Moderate Encephalopathy	Severe Encephalopathy
Level of consciousness	Lethargic	Stupor or coma
Spontaneous activity	Decreased activity	No activity
Posture	Distal flexion, complete extension	Decerebrate
Tone	Hypotonia (focal or general)	Flaccid
Primitive reflexes		
Suck	Weak	Absent
Moro	Incomplete	Absent
Autonomic system		
Pupils	Constricted	Deviated, dilated, or nonreactive to light
Heart rate	Bradycardia	Variable
Respiration	Periodic breathing	Apnea

Modified Sarnat Staging in the TOBY trial

Key differences

N Engl J Med 2009;361:1349-58.

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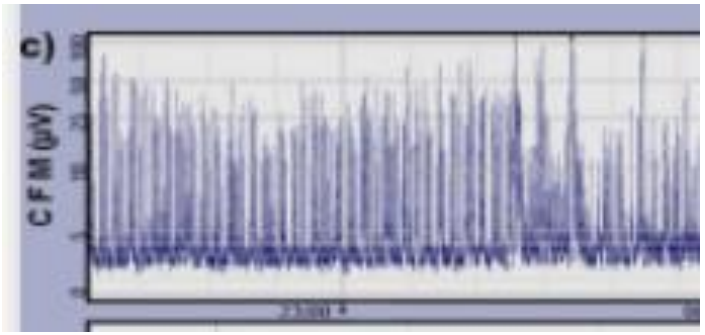


B. *Moderate to severe encephalopathy, consisting of altered state of consciousness (lethargy, stupor or coma) AND at least one of the following:*

- hypotonia
- abnormal reflexes including oculomotor or pupillary abnormalities
- absent or weak suck
- clinical seizures

Infants that meet criteria A & B will be assessed by aEEG (read by trained personnel):

C. *At least 30 minutes duration of amplitude integrated EEG recording that shows abnormal background aEEG activity or seizures. There must be one of the following:*

- normal background with some seizure activity
- moderately abnormal activity
- suppressed acitivity
- continuous seizure acitivity

Moderate or Severe Encephalopathy

Eligible for Hypothermia/Cooling

Key Rules for Cooling Eligibility

- Level of sensorium → assess only by stimulating the baby
- Normal aEEG → not cooling-eligible *unless* ≥3 categories are scored moderate/severe
- Equal scores (moderate vs severe) → assign based on level of consciousness
- Seizure present → baby has at least moderate encephalopathy

Mild Encephalopathy

Eligible for COMET

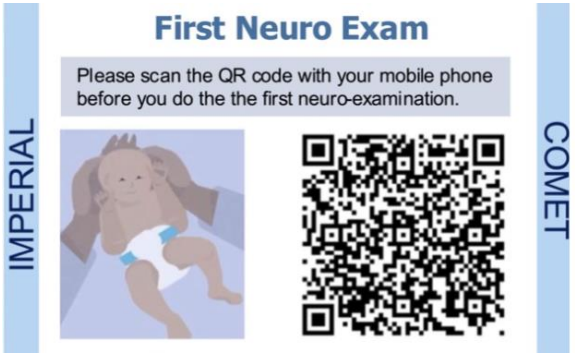
- Have less than 3 categories under moderate or severe
- Have at least 2 neurological abnormalities in any category

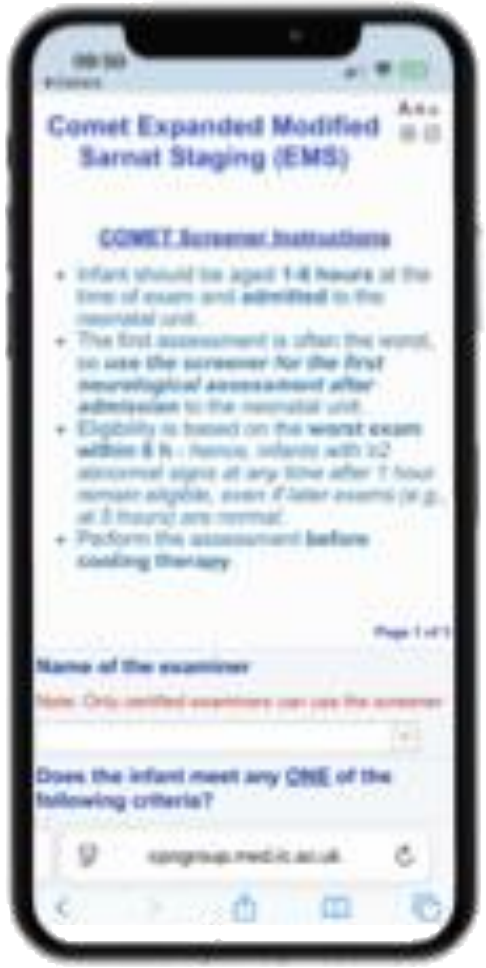
  Multiple combinations possible:

  2 severe, 0 moderate, 4 in mild, 0 normal

  0 severe, 0 moderate, 2 in mild, 4 normal
- Normal aEEG

Neurological Assessment





Neurological Assessment

CATEGORIES (TOTAL 6)	CIRCLE THE COMPONENTS OF NEUROLOGICAL EXAMINATION (TOTAL 9 circles)			
	NORMAL	MILD	MODERATE	SEVERE
1. Level of consciousness				
	Alert, Responsive to external stimuli when awake.	Hyper-alert, has an exaggerated response to minimal stimuli, has a stare, is inconsolable.	Lethargic – i.e. delayed but complete response to a stimulus.	Stupor/coma
2. Spontaneous activity				
	Active (Changes position when awake)	Slightly reduced activity	Markedly reduced activity	Absent
3. Posture				
	Predominantly flexed when quiet	Mild flexion of distal joints (fingers and wrist usually)	Complete extension, frog legged (complete abduction) moderate flexion of distal joints	Decerebrate or decorticate
4. Tone				
	Strong flexor tone in all extremities, including at the hip	Slightly increased peripheral tone in limbs	Hypotonia/floppy (focal or general) or Hypertonia (peripheral + truncal)	Flaccid or Rigid
5. Primitive reflexes (Assign based on the highest of the two sub-categories)				
Suck	Strong, easy to elicit	Weak suck	Suck has a bite	Absent
Moro	Complete	Low threshold to elicit	Incomplete or delayed response	Absent
6. Autonomic system (Assign based on the highest of the three sub-categories)				
Pupils	In dark: 2.5-4.5 mm. In light, reactive: 1.5-2.5 mm	Dilated (Mydriasis) and reacting to light	Constricted (Miosis) and reacting to light	Deviation/ Fixed dilated/ asymmetric/non-reactive to light
Heart rate	100-160 bpm	Tachycardia (HR > 160 bpm)	Bradycardia (HR <100 bpm)	Variable HR
Respiration	Breathing spontaneously	Tachypnoeic (RR >60/min) or requiring supplemental oxygen	CPAP or High flow	Apnoea or requires ventilator
TOTAL SCORE (CIRCLES)				

Observation

Observation

Active Manipulation

Active Manipulation

Active Manipulation

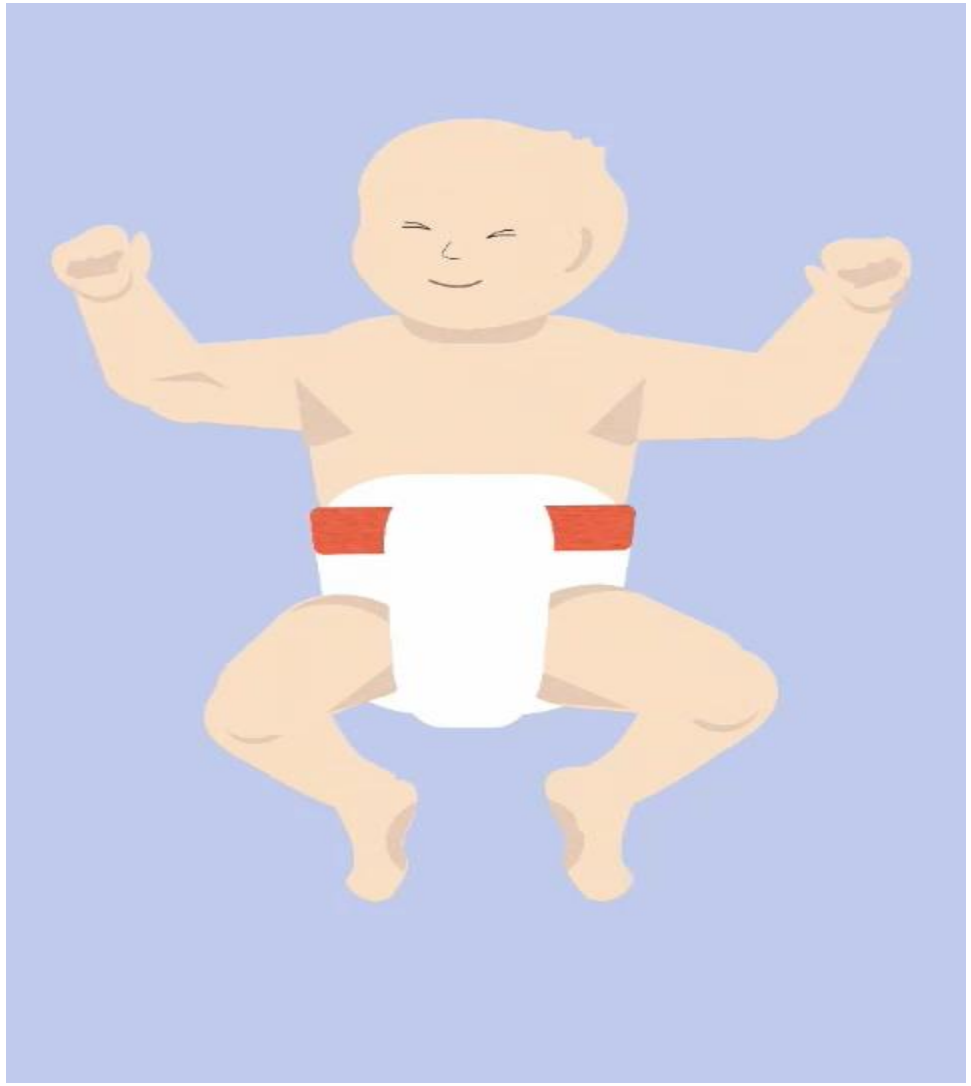
Active Manipulation

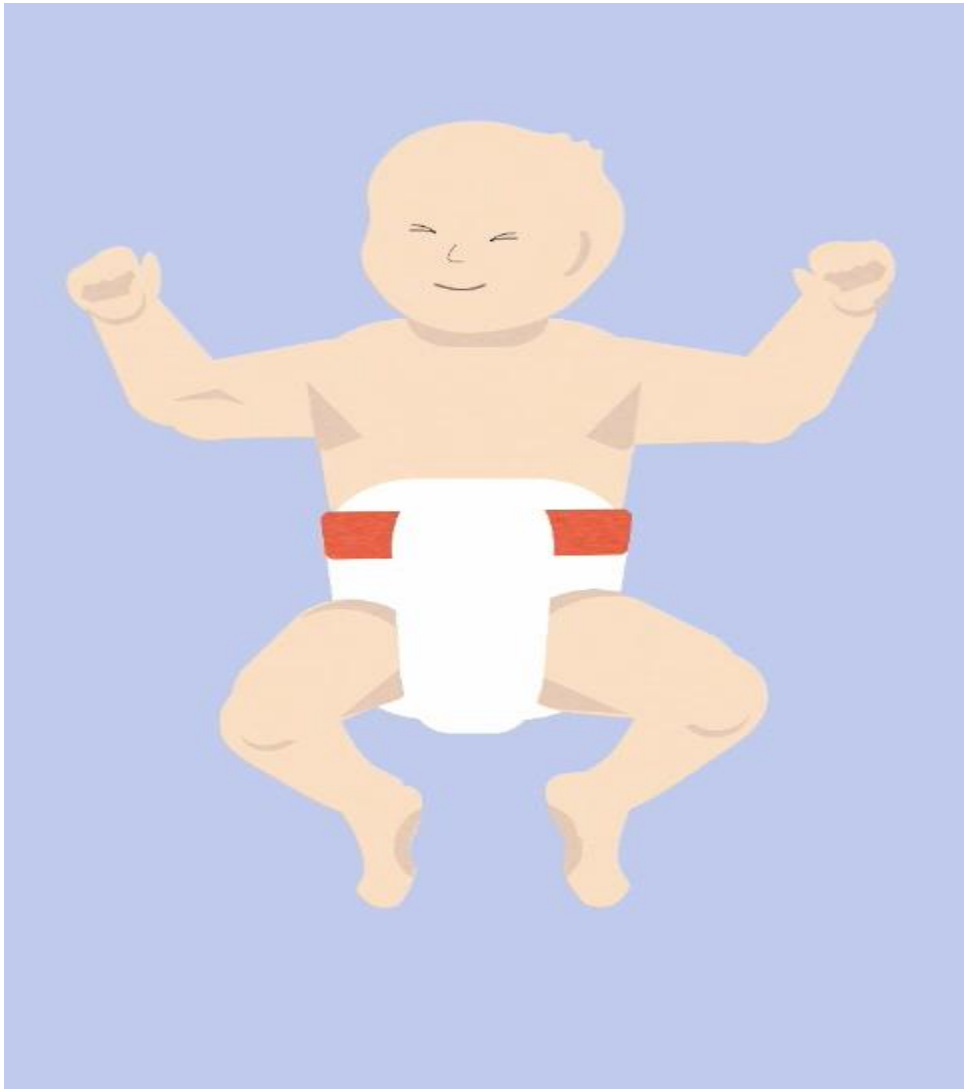
Active Manipulation

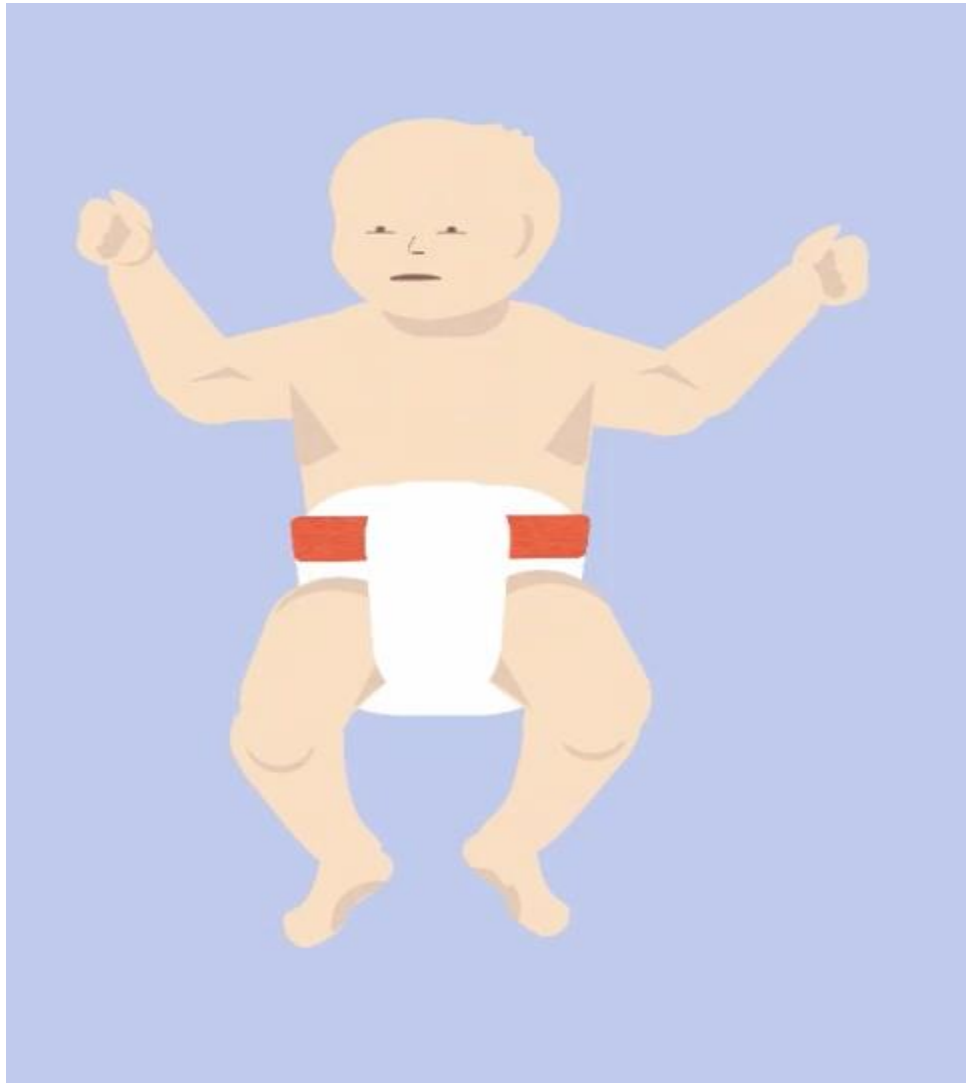
Observation

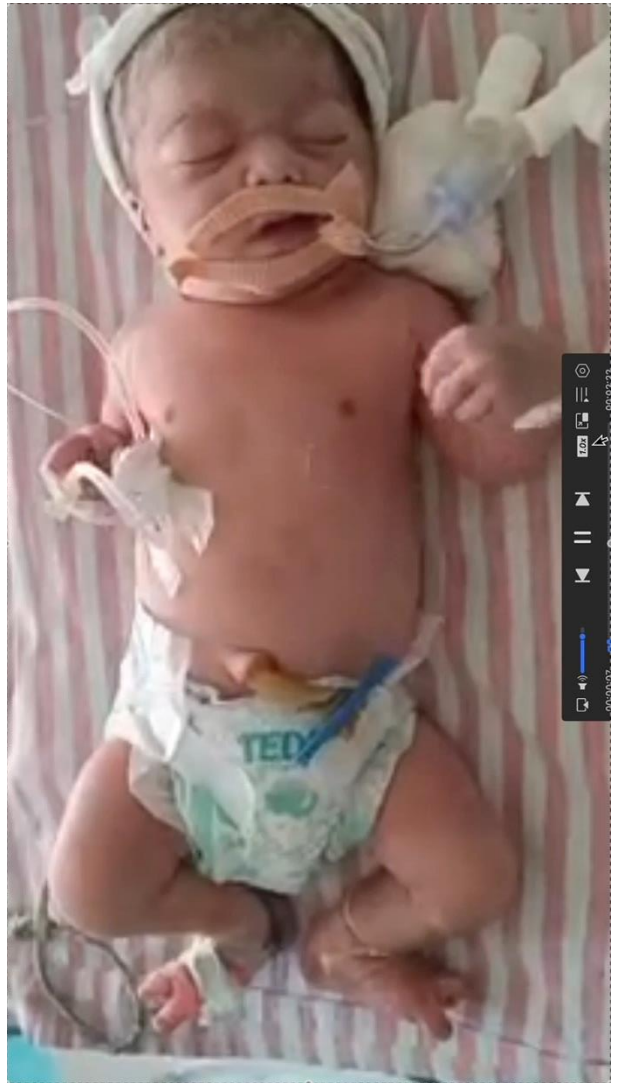
Observation

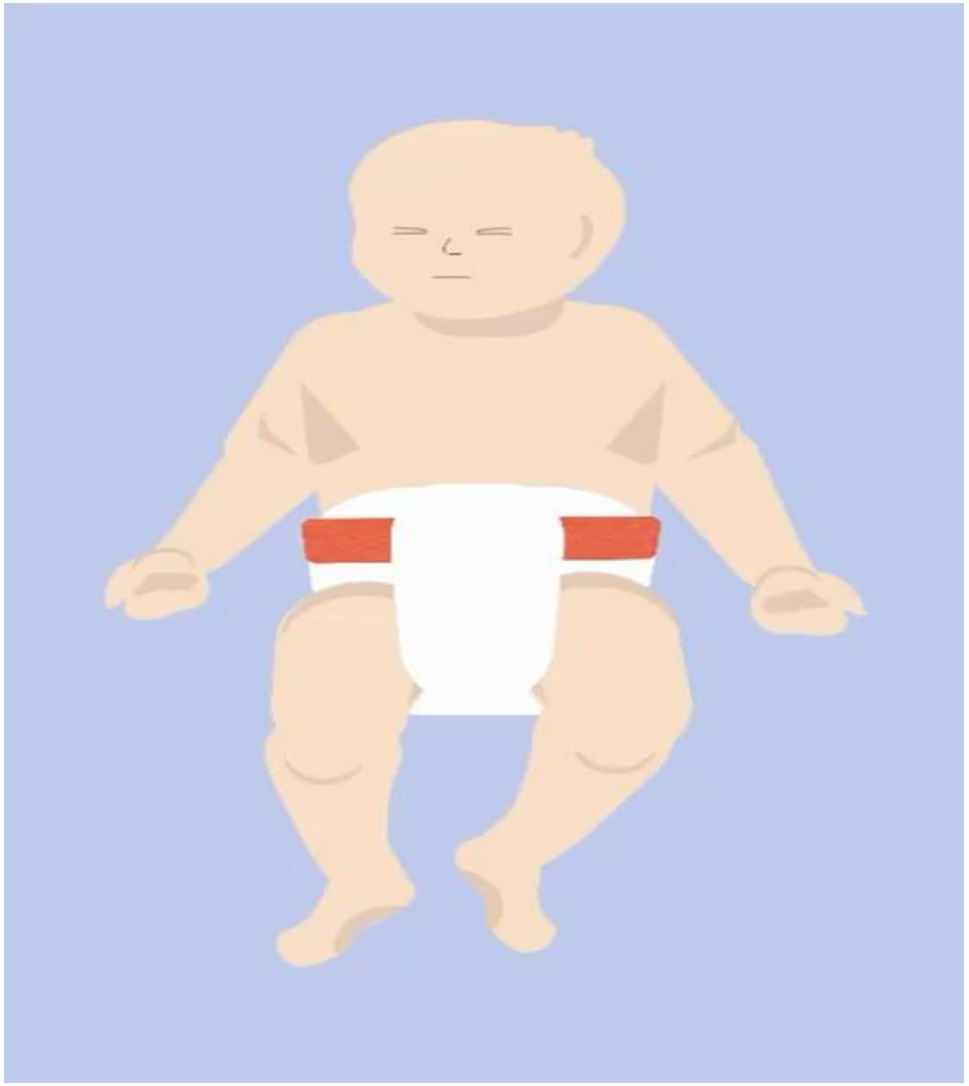
Spontaneous Activity





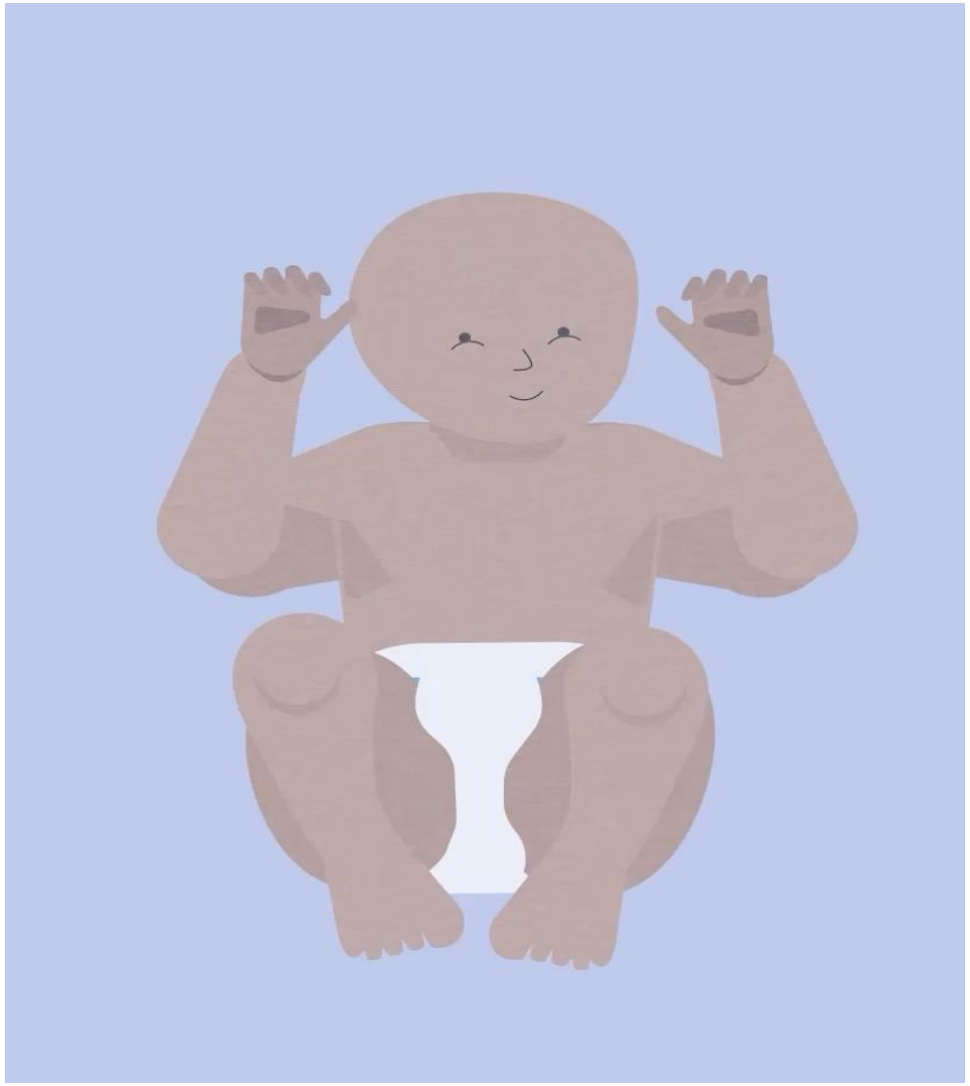


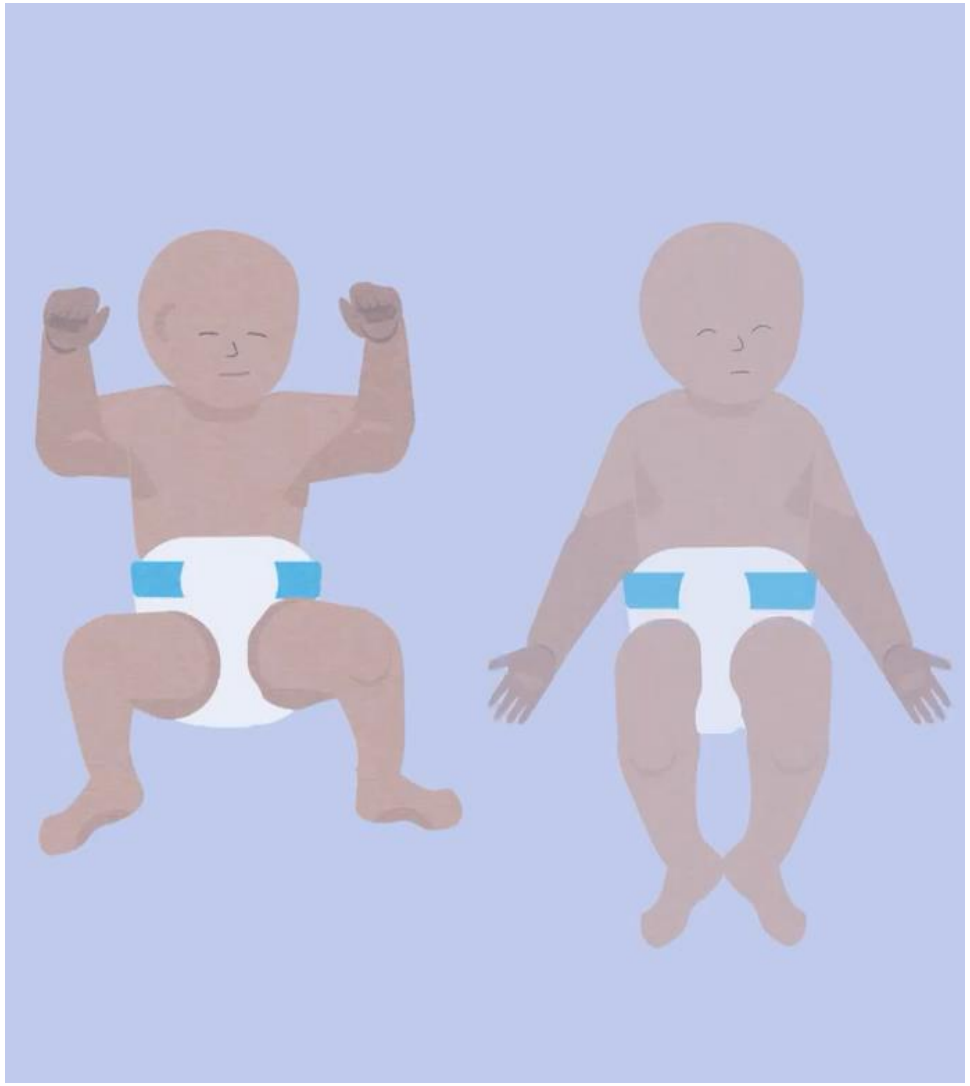


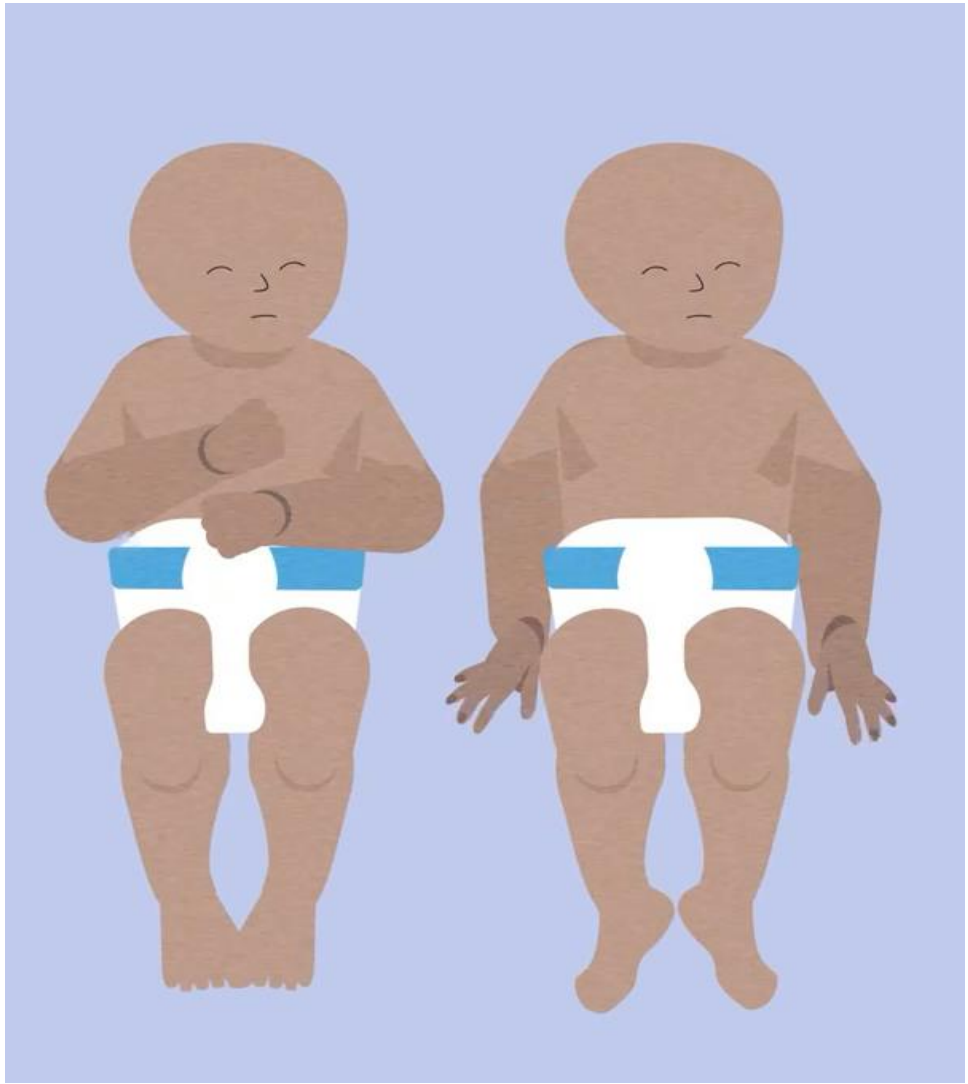


Posture

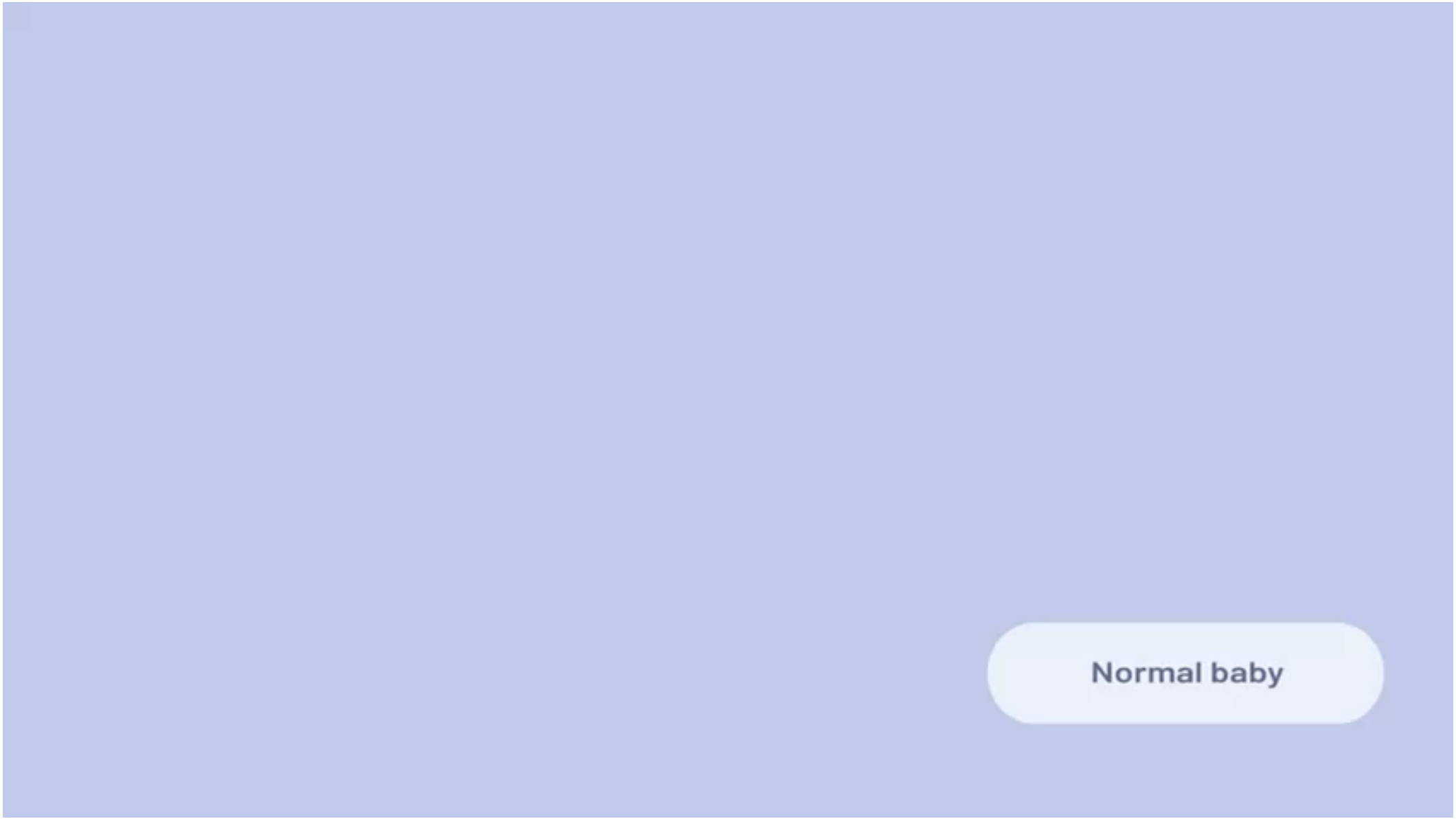
Ensure the baby is awake when assessing posture



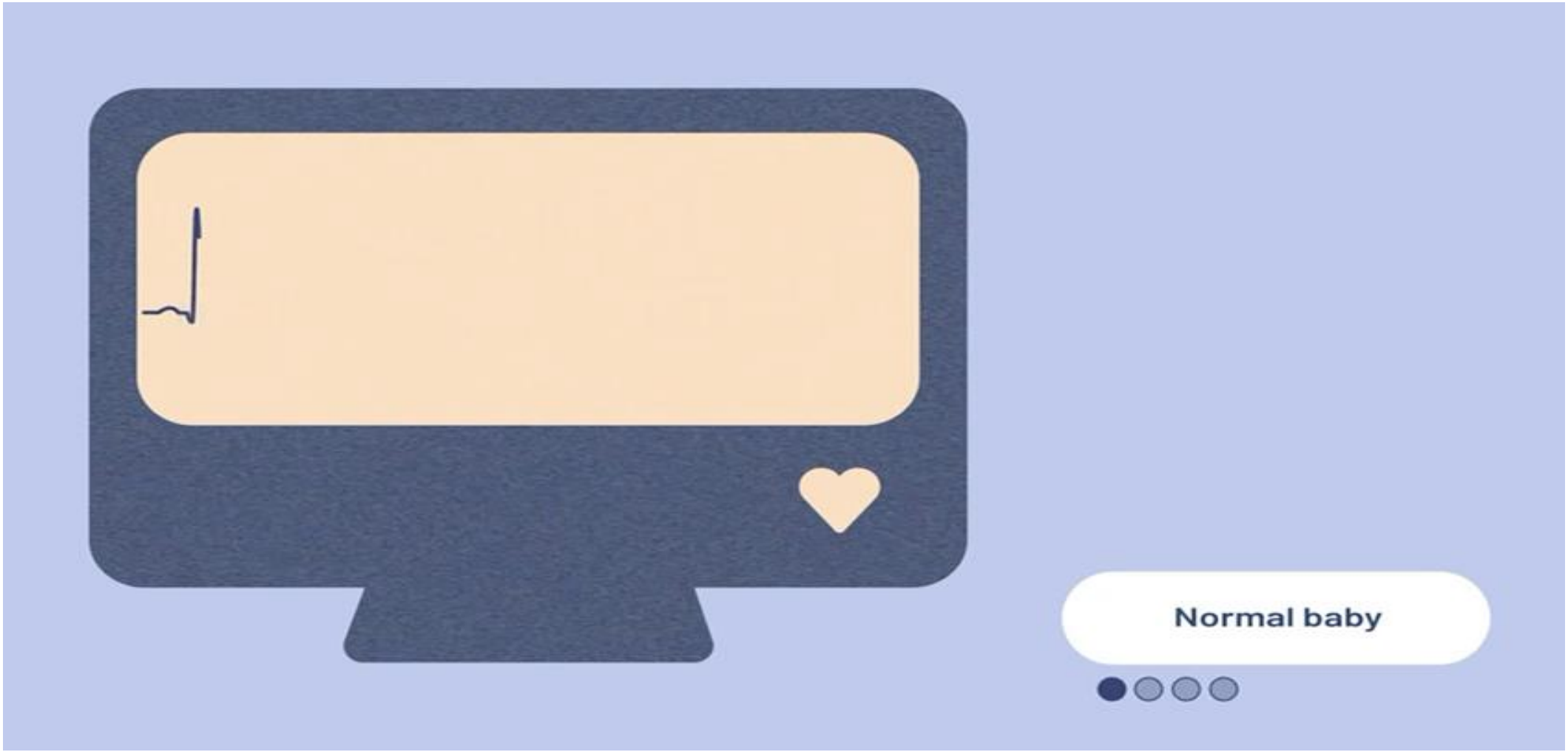




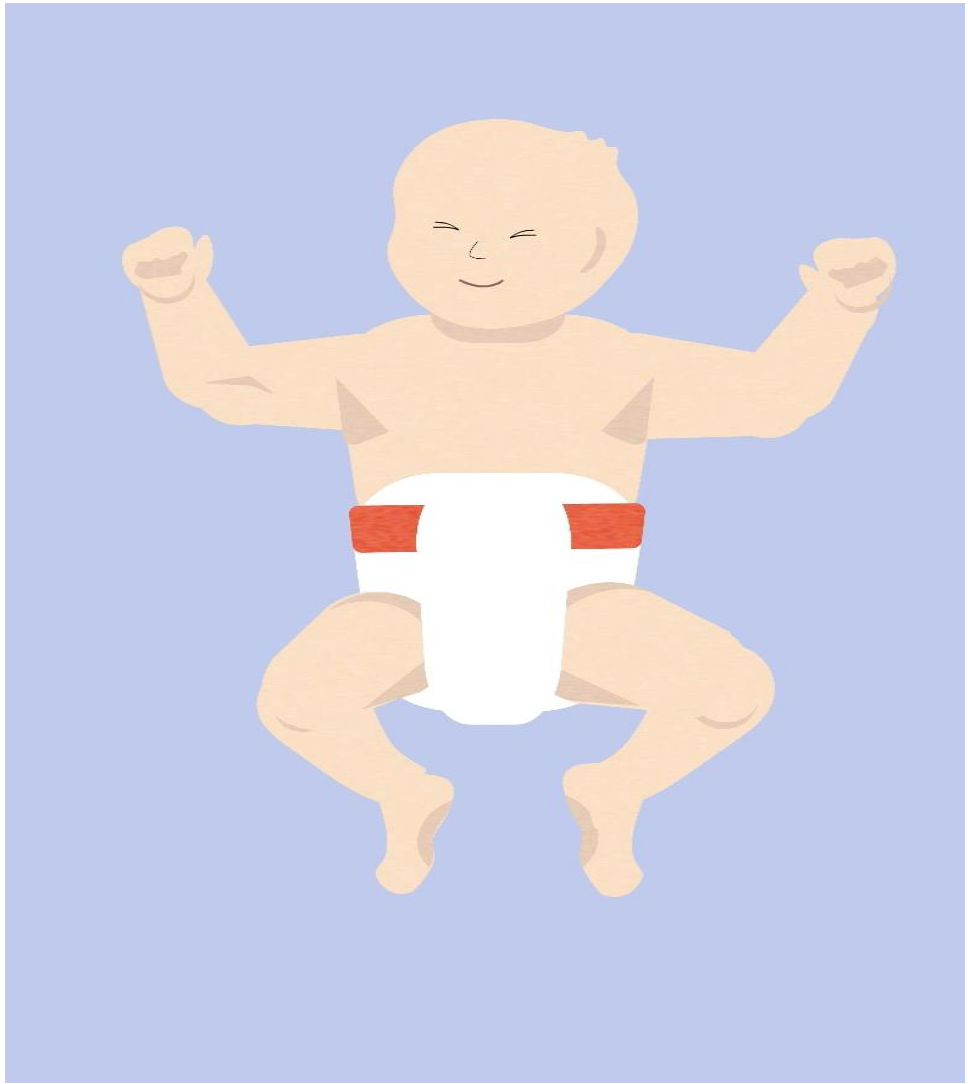
Respiratory Pattern

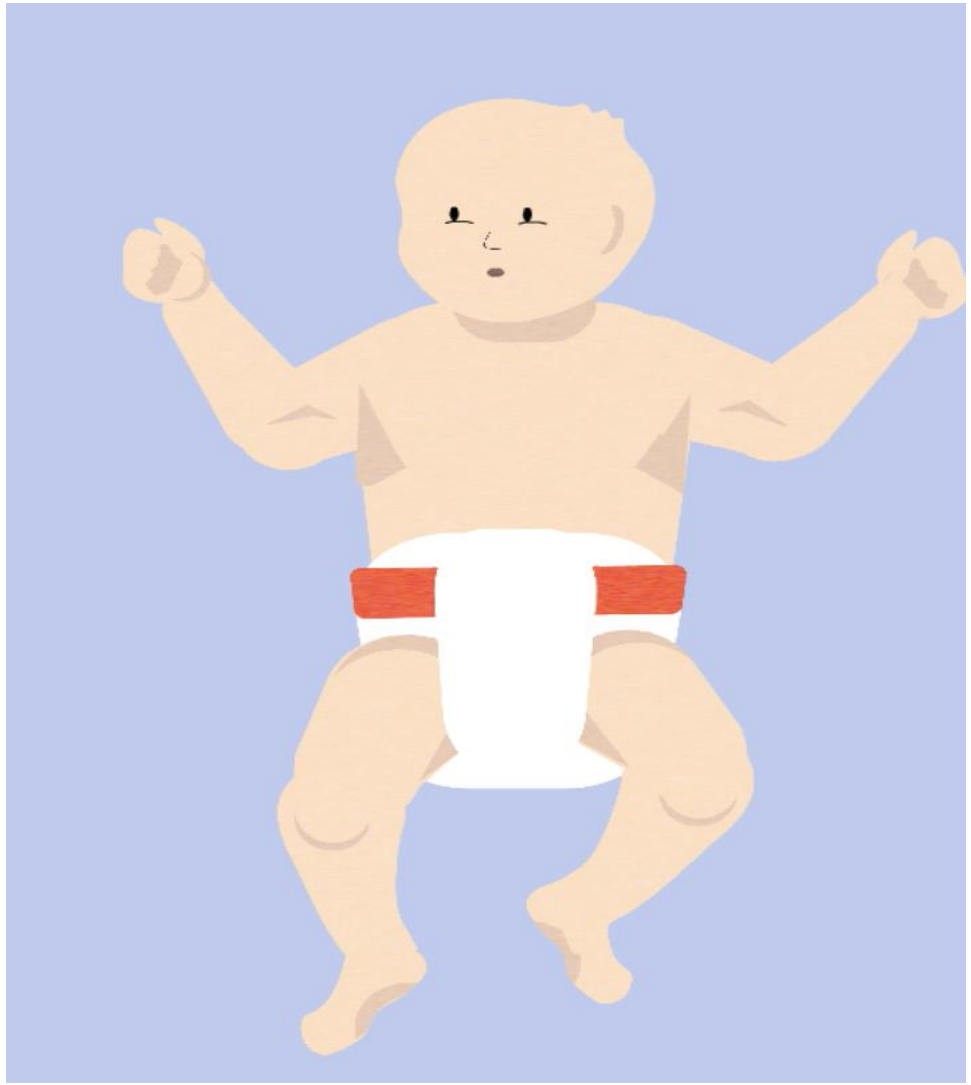

Normal baby

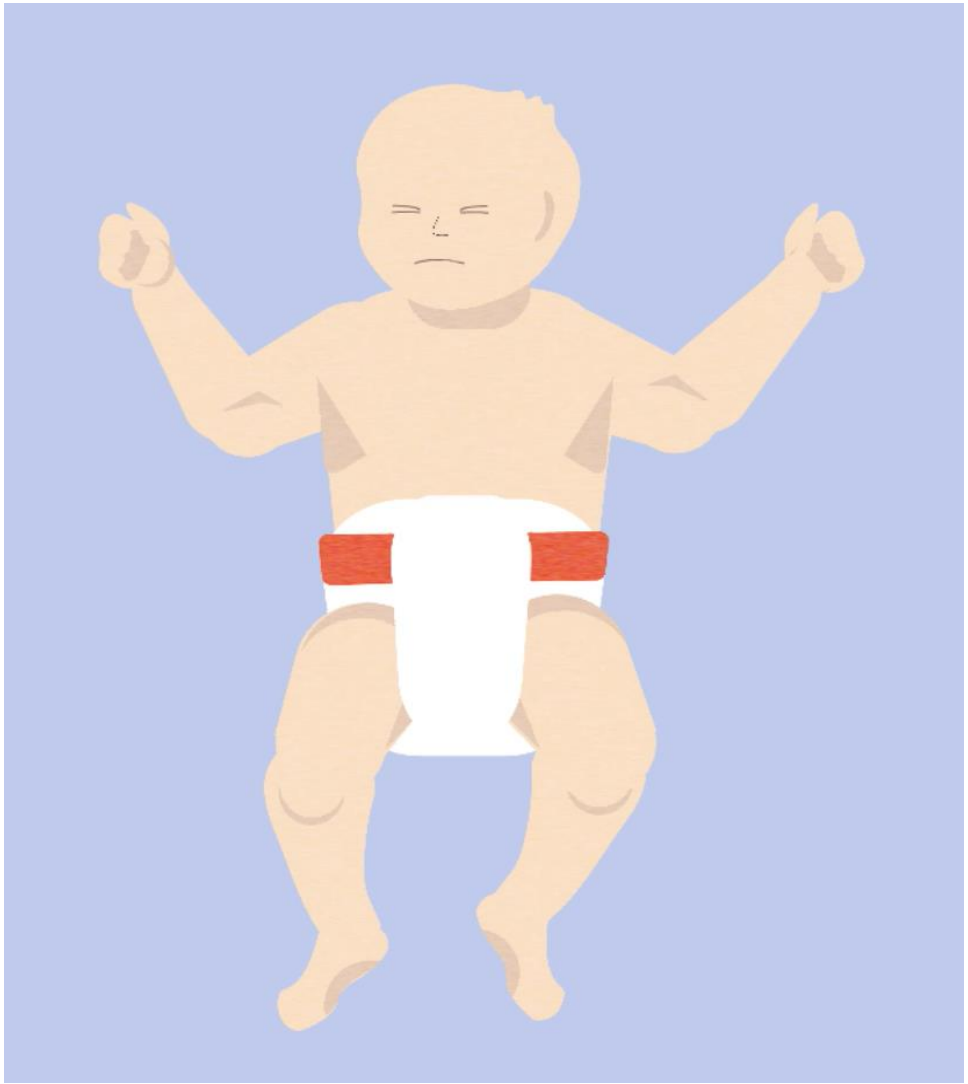
Heart Rate

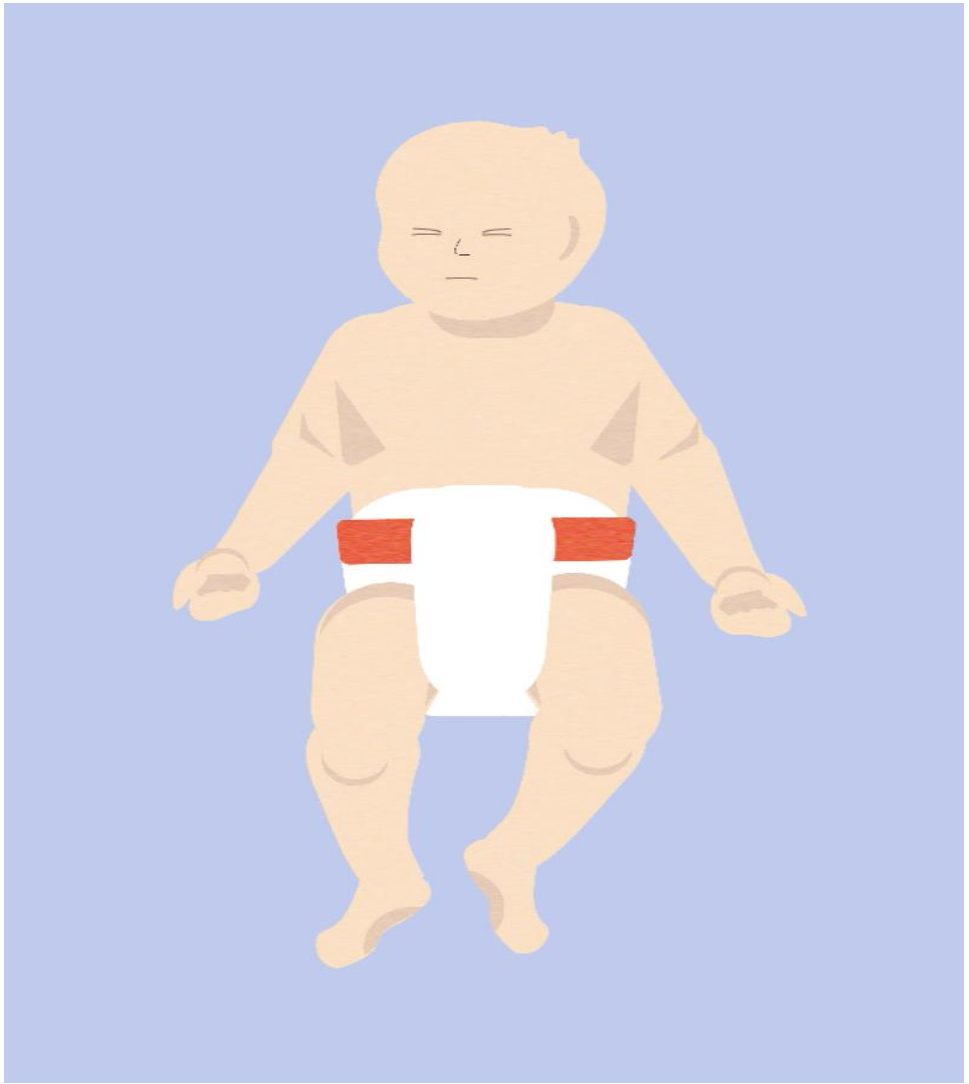

Normal baby

Active Manipulation & Level of Consciousness









Assessing Tone

Tone = baby’s response to passive movement

Evaluate extremities, trunk, and neck tone.

If tone varies → score the predominant state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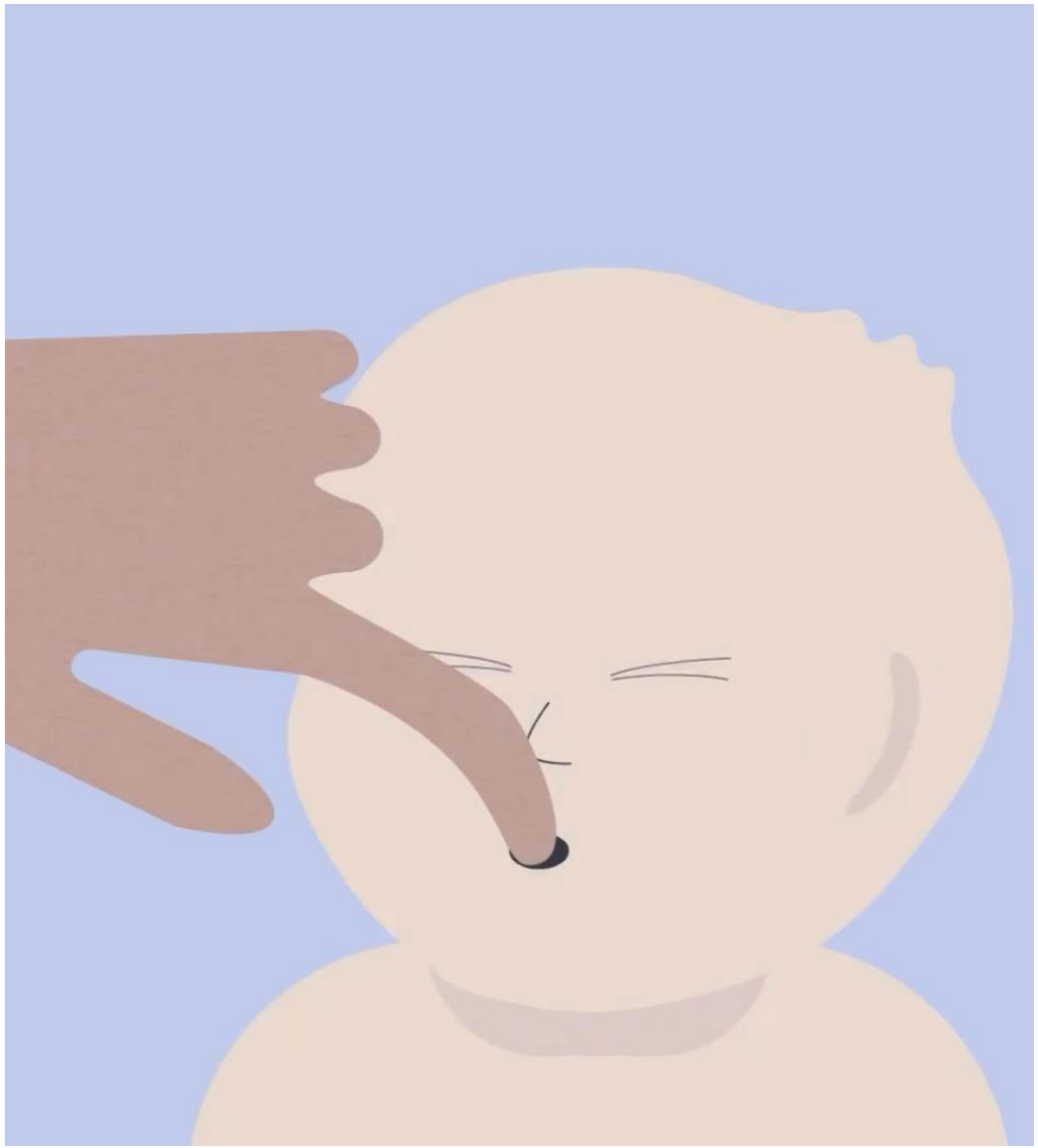
Sucking Reflex



Assessing Moro Reflex

The Moro reflex has two components:

1. Extension and abduction of the arms (throwing arms out)
2. Flexion and adduction of the arms (bringing arms back in)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Pupils


Normal baby

Exam Videos

Video 1 – Admission Data

1. Was the neurological assessment recorded? ▢ Yes ▢ No

2. Criteria A – Did the infant meet at least one of the following?

- ▢ Cord/infant blood gas within 1 hour: pH < 7.0 or base deficit ≥16
- ▢ Apgar score ≤ 5 at 10 minutes
- ▢ Ongoing resuscitation at 10 minutes

✓ Yes ▢ No

3. Gestational age ≥36 weeks? ✓ Yes ▢ No

4. Is the infant currently on active cooling? ▢ Yes ✓ No
(Note: Screener should be completed before cooling is started)

5. Infant admitted to neonatal unit? ▢ Yes ▢ No
(If initial exam was on postnatal ward, repeat after NICU admission to generate Screening ID)

6. Infant details: Date of Birth: **[TODAY],** Time of Birth: **12:00**

STERILE EO

Video 2 – Admission Data

1. Was the neurological assessment recorded? ▢ Yes ▢ No

2. Criteria A – Did the infant meet at least one of the following?

- ▢ Cord/infant blood gas within 1 hour: pH < 7.0 or base deficit ≥16
- ▢ Apgar score ≤ 5 at 10 minutes
- ▢ Ongoing resuscitation at 10 minutes

✓ Yes ▢ No

3. Gestational age ≥36 weeks? ✓ Yes ▢ No

4. Is the infant currently on active cooling? ▢ Yes ✓ No
(Note: Screener should be completed before cooling is started)

5. Infant admitted to neonatal unit? ▢ Yes ▢ No
(If initial exam was on postnatal ward, repeat after NICU admission to generate Screening ID)

6. Infant details: Date of Birth: **[TODAY],** Time of Birth: **12:00**

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