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James: Neonatal RDS case study

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ABSTRACT

This case study reviews the neonatal journey of James and includes analysis of participation in the POLAR (positive end-expiratory pressure levels during resuscitation at birth) trial, comparing dynamic positive end-expiratory pressure (PEEP) (new intervention) to static PEEP (current standard of care); he received dynamic PEEP at delivery. James was born at 23 + 5 weeks gestation via spontaneous vaginal delivery. His mother received one dose of antenatal steroids and intravenous magnesium sulfate ($MgSO_4$). James weighed 628 g at birth. The pathophysiology, care provided, and ethical legal and professional issues are explored. The survival of preterm infants has increased, however, the prevalence of neonatal morbidities associated with premature birth such as BPD and neurodevelopmental impairment remains high. In James' case, being part of a clinical trial has had no apparent negative consequences; At the time of writing this trial continues, potentially improving future PEEP management at delivery and the incidence of chronic lung in preterm neonates.

1. Case study

The pseudonym "James" will be used throughout this manuscript to maintain confidentiality and no identifying information will be used, as required by the Nursing and Midwifery Council (NMC) (NMC, 2018). James was born at 23 + 5 weeks gestation via spontaneous vaginal delivery. His mother received one dose of antenatal steroids and intravenous magnesium sulfate ($MgSO_4$). James weighed 628 g at birth (see Tables 1 and 2).

James is part of the POLAR (positive end-expiratory pressure levels during resuscitation at birth) trial, comparing dynamic positive end-expiratory pressure (PEEP) (new intervention) to static PEEP (current standard of care). James received dynamic PEEP at delivery. When James was brought to the resuscitative bed, he had a heart rate of less than 60 beats per minute (bpm) and had no respiratory effort. James received 5 inflation breaths and 30-s ventilation breaths before his heart rate was above 100 bpm. Significant work of breathing remained so he received one dose of surfactant via LISA (less invasive surfactant administration) and PEEP and FiO_2 (Inspired oxygen fraction) were able to be weaned. James was started on non-invasive spontaneous-continuous positive airway pressure support (SPN CPAP) and transferred to the Neonatal Intensive Care Unit (NICU).

After 12 h James' condition deteriorated with increased work of breathing and repeated apnoeic and bradycardic episodes, requiring increased FiO_2 to maintain oxygen saturation. His observations and blood gas were followed.

The observations of James showed poor blood gasses and an increased oxygen requirement. James had a chest x-ray and was diagnosed with respiratory distress syndrome (RDS). He was intubated and ventilated on Pressure Controlled Assist Control with volume guarantee (PC- AC + VG).

2. Pathophysiology

At 23 weeks James' lungs are immature having undergone only two of five stages of organogenesis: embryonic and pseudoglandular (Copland and Post, 2004). James was born during the third stage, the canalicular stage [see Fig. 1] (Boxwell, 2019). During this, the acinus is contributed to by two or three generations of respiratory bronchioles and a great increase in lung capillaries which cohere to the epithelium to form the alveolar blood barrier (Gao et al., 2016). This allows for pulmonary gas exchange to become possible (Kairamkonda, 2010). As an extreme preterm, James will have an immature gas exchange surface with only alveolar ducts and few elemental alveolar buds present (Warburton, 2017).

Neonatal RDS affects most premature neonates due to surfactant deficiency or inactivation (Pickerd and Kotecha, 2008). At 22–24 weeks, type I and type II pneumocytes are differentiated from cuboidal

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Table 1
James' blood gas 12 hours post birth.

Blood Gas Value	Patient value	Normal Values	High or Low
pH	↓7.02	7.35–7.45	Low
pCO2	↑14.5	4.6–6.0	High
pO2	↓5.7	7.0–12	Low
Glucose	↓1.0	2.6–6.0	Low
Lactate	↑5.6	0.5–2	High
BE	↓-8.2	−2 - +2	Low
Bicarbonate	↓10	18–25	Low

Table 2
James' observations 12 hours post birth.

Observation	Observations 12 hours post birth	Optimal observations for >34 + 6 week neonate (NHS Trust, 2020)	High or Low
Heart Rate (bpm)	153	110–180	Within limits
Respiratory rate (breaths per minute)	90	30–70	High
Blood pressure	52/26 (35)	Mean BP = gestation + 5 (>28)	Within limits
Saturations	92 (in 90% FiO2)	91–95%	In range (however in 90% FiO_2 to maintain this
Temperature	36.5 °C	36.4 °C–37.2 °C	In range
Humidity of incubator (%)	90%	90% (for >29–30 weeks' gestation on day one).	

epithelial cells (Schittny, 2017). Surfactant is produced by Type II pneumocytes in the alveoli and is stored in lamellar bodies (Schitty, 2017) but not secreted in an efficient amount until 30–34 weeks (Kairamkonda, 2010). Therefore, at 23+5-week gestation, James may produce small amounts of surfactant but not release a sufficient amount.

Due to low surfactant and reduced number of alveoli, James is at higher risk of pulmonary atelectasis from alveolar collapse (Santos et al., 2019). This causes underventilation leading to hypoxia; James had repeated apnoeas. Alveolar ventilation (V) and pulmonary capillary blood flow (Q) need to be balanced in James' lungs (Rennie and Kendall, 2013). As blood returns to the left atrium of the heart without oxidisation, this hypoxia causes pulmonary vasoconstriction (PV) (Rennie and Kendall, 2013). Hypoxic PV is a mechanism that

optimises gas exchange when there is V/Q mismatch. This causes hypoxemia, as shown by James' low PO_2 of 5.7. Blood flow is diverted from poorly ventilated to well-ventilated lung segments to balance V/Q ratio (Dunham-Snary et al., 2016). As blood is diverted, there is increased difficulty in transporting oxygen to unventilated segments of the lung, causing a vicious cycle until oxygen is supplemented.

Hypoxemia and tissue hypoperfusion lead to anaerobic cellular respiration (Yadav et al., 2022). During anaerobic respiration glucose is metabolised into two pyruvate molecules with net production of adenosine triphosphate (ATP) and limited nicotinic adenine dinucleotide (NADH) via glycolysis; Glycolysis does not require O_2, with NADH being re-oxidized to NAD + via the metabolism of the pyruvate to lactate; this is shown as the high lactate of 5 on James' blood gas. ATP is used for all energy cellular reactions (Rennie and Kendall, 2013); however, anaerobic respiration produces two ATP molecules compared to the more efficient aerobic respiration producing thirty-six (Ward and Linden, 2013). When oxygen is present, products of glycolysis can be oxidized through the Krebs cycle and oxidative phosphorylation. This increases the efficiency of ATP production and produces carbon dioxide (CO_2) as a waste product (Ward and Linden, 2013). When there is insufficient oxygen, there is a build-up of pyruvate which is converted into lactic acid (Coad et al., 2020). Excessive anaerobic glycolysis results in a build-up of lactic acid causing metabolic acidosis. Lactic acid reacts with bicarbonate, with bicarbonate ions being used to balance H+ (Ranson and Pierre, 2016), causing the bicarbonate level to fall, resulting in a base deficit (Goldsmith and Karotkin, 2004). This is shown within James' blood gas by high lactate, low bicarbonate and a base deficit.

James' blood gas showed a low pH and high level of carbon dioxide in the blood (pCO_2) indicating respiratory distress. When CO_2 enters red blood cells (RBC), it is broken down by an enzyme, carbonic anhydrase, and hydrated with water (H_2O) into carbonic acid (H_2CO_3) (Marieb and

$$\underset{\text{water}}{H_2O} + \underset{\text{carbon dioxide}}{CO_2} \rightleftarrows \underset{\text{carbonic acid}}{H_2CO_3} \rightleftarrows \underset{\text{hydrogen ions}}{H^+} + \underset{\text{bicarbonate ions}}{HCO_3^-}$$

Fig. 2. Figure demonstrating carbonic acid formation.

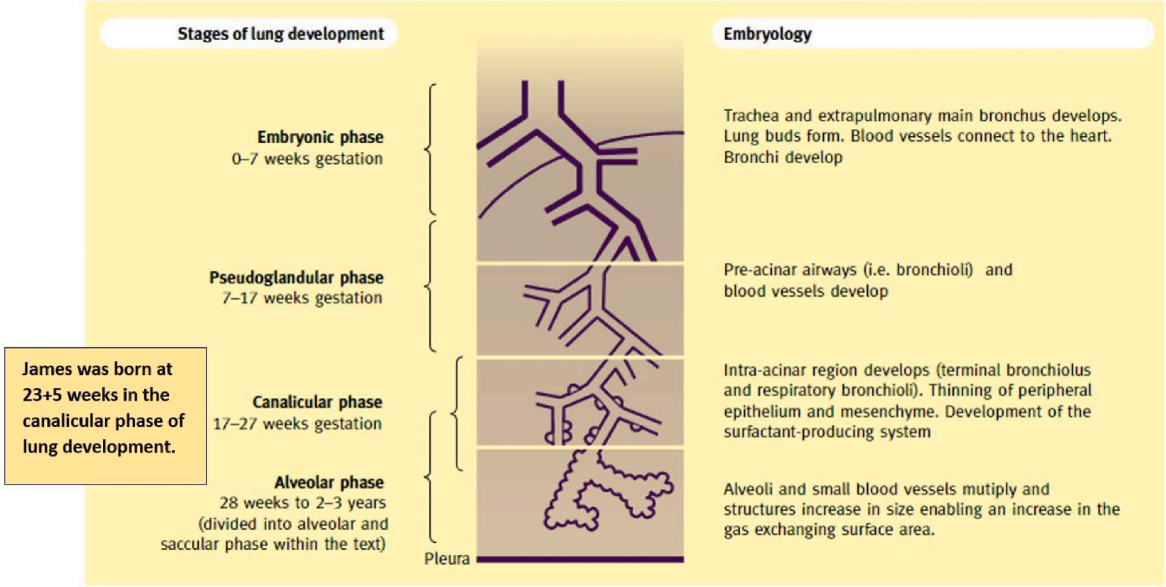

Fig. 1. Shows lung development (Holme and Chetcuti, 2012) with James' developmental stage annotated. Both stage 4 (saccular) and stage 5 (alveolar) of lung development come under the "Aveolar phase" in this figure.

Hoehn, 2018). As shown in Fig. 2, H_2CO_3 dissociates into hydrogen (H+) and bicarbonate ions (HCO^-); an increase in H+ ions lower blood pH (Coad et al., 2020) causing respiratory acidosis.

Central chemoreceptors are stimulated by an increase in CO_2 and H+ within blood plasma. Chemoreceptors increase impulse frequency via afferent nerves to the respiratory regularity centre located in the medulla oblongata (Marieb and Hoehn, 2018). In turn, the dorsal respiratory group in the medulla increase contractions of the intercostal and diaphragmatic muscles, increasing rate and depth of breathing (Ward and Linden, 2013). James is unable to clear high levels CO_2 (hypercapnia) from his blood due to reduced surface area and underdeveloped alveolar capability. Hypercapnia stimulates hyperventilation which is clinically shown in James as tachypnoea (Yadav et al., 2022).

3. Nursing care

James' mother received antenatal steroids. The National Institute for Health and Care Excellence (NICE, 2019a) recommends the use of antenatal corticosteroids for mothers with threatened preterm birth (24–33 + 6 weeks) to reduce the severity of RDS in the infant.

However, a meta-analysis investigating administration before 24-weeks found corticosteroids were associated with lower mortality. Corticosteroids is an anti-inflammatory medication that accelerates lung maturation (McGoldrick et al., 2020); The formation of thin gas-exchanging walls of alveoli is accelerated, resulting in fast alveolisation, as well as maturation of surfactant-producing type-II pneumocytes (Vafaei et al., 2021). Resulting in increased lung volume and compliance (Wapner, 2013).

RDS is caused by surfactant deficiency; surfactant is a lipoprotein that acts to reduce surface tension of the alveoli and improve compliance of the lungs (Ramanthan et al., 2013). It is a mixture composed of 90% lipid: dipalmitoyl phosphatidyl-choline (DPPC) and phosphatidylglycerol (PG). The other 10% is made up of four proteins: SP-A, SP-B, SP-C and SP-D (Sardesai et al., 2017; Zuo et al., 2008). Multilayers of phospholipids are created at the air-liquid interface. Formation is assisted by both SP-B and SP-C which are hydrophobic, allowing adsorption and spreading of DPPC, maintaining the stability of the lipid film during respiration (Sardesai et al., 2017). With hydrophilic heads in the water and hydrophobic tails facing the air, DCCP reduces surface tension. In turn, this reduces the energy required to inflate the lungs, increasing lung compliance (Zuo et al., 2008).

At delivery, James demonstrated significant work of breathing (WOB) and therefore was given a dose of surfactant via LISA. Surfactant is administered via a thin catheter inserted into the trachea (Bhayat and Shetty, 2020); this technique was appropriate for James as it allows a spontaneously breathing infant to avoid mechanical ventilation (MV) (Herting et al., 2019). This method is often preferred over techniques such as Intubate-Surfactant-Extubate (INSURE) as it does not require intubation, MV, or sedation (Herting et al., 2019). A systematic review of randomised control trials (RCTs) has shown LISA significantly decreases the risk of future bronchopulmonary dysplasia (BPD) due to less time mechanically ventilated, including low-birth-weight infants (Ge et al., 2021). European consensus guidelines on the management of RDS (Sweet et al., 2019) recommend LISA as the optimal method for neonates stable on CPAP, however, Reynolds et al. (2021) suggest further research.

James did not require intubation for initial stabilization in the delivery room, instead CPAP was initiated to maintain lung recruitment and functional residual capacity (Bohlin, 2012). CPAP is non-invasive respiratory support and allows a gentle transition at delivery (Sweet et al., 2019). It is recommended that spontaneously breathing babies should commence CPAP to reduce BPD (Schmölzer et al., 2013) as MV can cause further lung injury (Bohlin, 2012). James' deterioration prompted intubation and ventilation with PC-AC + VG. PC-AC is pressure-controlled ventilation delivering set breaths per minute. With every breath, both patient-triggered and time-triggered, James receives a set tidal volume (V_T) (Walter et al., 2018) V_T is the estimated volume inspired per breath; increasing V_T will increase minute volume which decreases CO_2, improving respiratory acidosis (Chakkarapani et al., 2020).

PEEP and FiO_2 are two main contributors to oxygenation; FiO_2 ensures oxygen concentration in alveoli is higher than in the capillaries, so oxygen diffuses from alveoli to the

blood. PEEP increases the capillary-alveoli interface for gas exchange (Powers and Dhamoon, 2023). Increasing PEEP or FiO_2 will increase PaO_2, correcting James' hypoxia (Carpio and Mora, 2022). Using VG mode can avoid alveolar overdistention and reduce risk of barotrauma (Kaam et al., 2010). James' responses to changes in ventilation and oxygenation were monitored.

V_T and lung compliance can be further optimised by position of the infant. Research has shown preterms nursed in prone position have improved oxygenation in their blood and improved V_T, resulting in fewer desaturations (Rivas-Fernandez et al., 2016). Correct ventilator settings and appropriate positioning are critical in optimising lung volume, and when used in conjunction with surfactant administration, increases V/Q ratio (Rivas- Fernandez et al., 2016). However, this evidence is low quality, indicating a need for further research. Parental education on safe sleep is important as when James is discharged, he should sleep supine due to the association between sudden infant death syndrome and a prone position (Lullaby trust, 2023).

Involving parents in the care of their baby is imperative as the clinical impact of bonding is significant in both short-term stability and long-term outcomes (Bonner et al., 2017). James was separated from his mother on admission to the NICU, therefore, skin-to-skin contact (SSC) was not offered at delivery. Studies have shown in unstable low-birth-weight infants, cardiorespiratory stability and temperature control is better with SSC than in an incubator at birth (Linner et al., 2019). SSC activates oxytocin release and in response, sympathetic activity reduces, and endorphin levels increase, reducing stress and pain in the infant (Pavlyshyn et al., 2022). Reducing stress improves short-term and long-term outcomes; Improving oxygen saturations reduces the need for supplemental oxygen, but also results in reduced length of hospital stay and improved neurodevelopment outcomes (North et al., 2022). Educating parents on stress is important as preterm infants experience cumulative stress exposure from non-painful caregiving procedures (Nist et al., 2022). Additionally, a study by Maastrup et al. (2017) concluded nurses play a major role in supporting parents to feel comfortable initiating SSC, touch, and involvement in caregiving.

4. Ethical, political or professional issues

The NMC (2018) states that nurses should be able to identify ethical challenges and practice under legal, professional and ethical frameworks. Neonatal care has rapidly advanced, improving morbidity and mortality rates for extreme preterms such as James (Boxwell, 2019). However, James remains at a higher risk for long-term disabilities. This raises ethical questions on whether outcomes for some neonates are too burdensome; financially for the NHS and burnout for both professionals and parents (Boxwell, 2019). Many discussions around care for preterms focus on the infant and family's best interest, however, it has been questioned whether a cost-to-benefit ratio should be considered regarding expensive life-saving treatments (Wilkinson et al., 2018). Based on available data, resuscitation and intensive care is cost-effective at 23-week's gestation due to the longevity of survival (Wilkinson et al., 2018). Further research into neonatal care could help extend the life expectancy of neonates like James and could, in future, assist in reducing the costs of critical care. Clinical research trials are expensive due to recruitment and the vulnerability of these patients; but are cost-effective for the provision of future treatments (Janvier and Farlow, 2015).

There is a conflict between the need to protect vulnerable participants and the obligation to protect patients from ineffective routine

interventions; nursing care should be delivered safely with adherence to guidelines (National Quality Board, 2018). There is not enough current knowledge on the optimal PEEP to use at delivery and evidence suggests current set standard PEEP is not sufficient for recruiting the optimal functional residual capacity (Kanaan et al., 2020).

Controlled trials such as POLAR can be used to identify if new practices are better than current "routine" practices and ensure rational allocation of scarce neonatal critical care resources (Kaye, 2019). There are four main ethical principles to apply when including neonates in research: Autonomy, justice, beneficence, and non-maleficence (Purdy and Wadhwani, 2006). The infant's best interest is the focus of NICU care and is considered a priority in decision-making (Boxwell, 2019). The 'best interest' principle is grounded in beneficence, considering a burden versus benefit standpoint (Stanak, 2018); it is unknown whether James will benefit from the trial but is unlikely to cause harm. Legislation set by the United Nations Convention on the Rights of the Child states the best interests of James should be a primary consideration (UNICEF, 2010). Non-maleficence is the principle of doing no harm; It could be argued using interventions in the absence of research (static PEEP at delivery) could be considered a technological form of harm as it may not achieve the best outcome (Boxwell, 2019). Care should be based on the best available evidence to ensure safety and effectiveness (Kaye, 2019). DeMauro et al. (2015) compared clinical outcomes of neonates enrolled in clinical trials to those who were eligible but not enrolled, finding there was no difference between groups. Nonetheless, the trial should be closely monitored for adverse events and safety outcomes to determine whether there is an increased risk of harm to participants such as James (DeMauro et al., 2015).

Autonomy is the basis for informed consent (Varkey, 2020). James would not be considered autonomous (Boxwell, 2019); therefore, any decision-making would be made by parents. under the terms of the Mental Capacity Act 2005, they must be presumed competent unless proven otherwise. Parents must have parental responsibility to have the right to consent (GMC, 2018). Parental consent for the participation of their neonate in research is often influenced by the quality and understanding of the information provided. The decision must be free of coercion with the risks and benefits of trial participation explained (GMC, 2018; Aurich et al., 2020). Parents and their families are a vulnerable population, with consent for trial participation often sought antenatally, a time when parents are stressed and overwhelmed; Bringing into question of whether this is an ethical time to gain consent (Snowdon et al., 2006). The clinical neonatal nurse should advocate for the infant and family, ensuring parents can obtain and understand correct information on the study at any time (Stanak, 2018). Declining to enter a clinical trial must not impact the quality of care that an infant and their family receive (Aurich et al., 2020).

Ultimately, research is ethically necessary to identify better care practices whilst allocating resources appropriately (DeMauro et al., 2015). They can be done in partnership with the infant's family and must be designed to balance potential risks and benefits; with consent processes, and study design to limit harm. The effect of the POLAR trial on James is currently unknown, but this trial will benefit future preterms.

5. Long term outcomes

The survival of preterms has increased, however, the prevalence of neonatal morbidities associated with premature birth such as BPD and neurodevelopmental impairment remains high (Johnson and Marlow, 2017). BPD is the most common complication of prematurity and is a chronic life-long condition (Chen et al., 2020); James is at an increased risk due to the RDS diagnosis, prolonged MV, and supplementary oxygen (Boxwell, 2019). Neonates with BPD are noted to have higher healthcare utilisation, longer initial hospitalization, follow-ups, and long-term effects sustained into adulthood (Homan and Nayak, 2021). Rodriguez-Martinez et al. (2017) reported two-thirds of participants had been hospitalized during their first two years of life due to respiratory problems, including recurrent wheezing and asthma symptoms.

Hospitalization will put an additional emotional and financial strain on James' family as one parent will remain in the hospital with him, losing income plus having less time for personal care and time as a family (Peralta et al., 2023).

Neonates with BPD often spend at least their first four months in NICU (Morrow et al., 2018), James' stay was 110 days. A prolonged NICU stay increases James' parents' risk of suffering from posttraumatic stress disorder, anxiety, and depression (Haward et al., 2020). In their British Association for Perinatal Medicine (BAPM) endorsed report, Atkins et al. (2022) state there is no specific guidance on psychological staffing but there are risks to both parents and neonates when no support is offered; There was no psychologist for James' parents, increasing the risk of psychological consequences for their bonding with James (Grunberg et al., 2018). Consideration should be given to making parental mental health support part of routine NICU care (Malouf et al., 2022). It can be difficult for parents to bond with their infant in the NICU due to separation at birth and all of the medical wires and tubes, making the parenting experience different from their expectations (Haward et al., 2020); This can impact the transition to parenthood (Malouf et al., 2022).

James' parents were made aware of the long-term implications and future management (Boxwell, 2019). Having a preterm baby has a significant impact on the family, it is important to support parents leading up to and on discharge to home (NICE, 2019b). Home oxygen therapy plays a big role in the management of BPD, >72% of neonates born before 27weeks with BPD go home on supplementary oxygen (Dassios et al., 2021); National guidelines should be followed alongside the provision of outreach support when implementing this (NICE, 2019b). Early initiation of this process allows the establishment of a safe home oxygen setup without unnecessary delays in discharge (Dassios et al., 2021). Discharge with home oxygen allows families an earlier return to a "normal life", but there is little evidence to support weaning oxygen at home (Fitzgerald, 2023). Usually, weaning from supplemental oxygen occurs by 2 years of age due to alveolar "catch-up" of the lungs; most postnatal alveolar growth occurs during the first two years of life (Bhandari and McGrath-Morrow, 2013).

According to Fitzgerald (2023), additional oxygen may support growth but not alter neurodevelopmental outcomes, thus not reducing James's risk of neurodevelopmental disability (for example, cerebral palsy (CP)), of which both prematurity and BPD have been associated. The severity of BPD is directly linked with an increasing risk of quadriparesis and diparesis (Marter et al., 2011). In James' case, $MgSO_4$, a neuroprotective substance, was administered antenatally. $MgSO_4$ is proven to reduce the risk of cerebral palsy (Burhouse et al., 2017) and is now part of the PeriPrem (Perinatal Excellence to Reduce Injury in Premature

birth) bundle. Periprem is a relatively new bundle of eleven interventions, including antenatal steroids and $MgSO^4$, delayed cord clamping, volume-targeted ventilation, early breast milk, and the use of probiotics, aiming to reduce brain injury and neonatal mortality by 2025 (West of England Academic Health Science Network, n.d.). Neonatal services monitor neurodevelopmental outcomes for up to 3 years of age (Johnson and Marlow, 2017); NICE (2019) suggests that preterms should be offered enhanced developmental support. Follow-ups from the NICU outreach team can assist in the early identification of children not reaching motor milestones and refer the family to appropriate members of the multidisciplinary team to meet individualised needs. Caring for a child with complex needs requires a multidisciplinary approach and partnership between professionals and parents (NICE, 2017). Families must adapt their lives to meet the child's needs; healthcare professionals have a responsibility to provide training to parents, allowing parents to attain control over their child's care.

6. Conclusion

In James' case, being part of a clinical trial has had no obvious negative consequences and at the time of this writing, this trial continues, potentially improving future management and outcomes of preterm neonates. James' parents were encouraged to participate in care and were involved in decisions, both small and large. The built trust between the NICU team and James' parents provided positive collaborative care. Although parents received support from the NICU staff, there was no specific mental health support, potentially leaving James' parents vulnerable to mental health issues that may affect bonding. Future considerations should include a designated psychological support system for parents during and after a NICU stay.

At extremely low gestations, ethical questions are crucial, and the use of advancing technology brings increased moral dilemmas. It is difficult to predict the future outcomes for individual babies and to assess whether the decisions made were in James' best interest. James went home on oxygen therapy and was diagnosed with BPD as a result of RDS and ventilation. For James' parents, this was a positive outcome as they were excited to have him home safe, despite the potential long-term complications they may face. Parents had been well-prepared by nurses, doctors, and community teams for possible outcomes such as this. James received appropriate and evidence-based care during his NICU stay, with positive and supportive relationships developed between the parents and the multidisciplinary team.

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