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Review

Weaning oxygen in infants with bronchopulmonary dysplasia

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Educational Aims

The reader will come to:

- Understand that sustained and intermittent hypoxia (IH) has adverse consequences for respiratory, growth and neurodevelopmental outcomes in preterm infants.
- Be aware that the implementation and weaning of oxygen therapy in preterm and term infants should refer to age appropriate oximetry reference ranges.
- Be aware that data output from pulse oximeters and oxygen desaturation indices are influenced by technological features of recording devices.
- Recognise that modern oximeters have shorter averaging times and have the ability to exclude motion artefact.
- Understand that a structured approach to home oxygen weaning is associated with improved outcomes in preterm infants with BPD following discharge from the neonatal unit.

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ABSTRACT

Bronchopulmonary dysplasia (BPD) is a form of chronic lung disease commonly seen in preterm infants as the sequelae following respiratory distress syndrome. The management of evolving BPD aims to minimise lung injury and prevent the impact of hypoxia and hyperoxia. Proposed morbidities include respiratory instability, pulmonary hypertension, suboptimal growth, altered cerebral oxygenation and long-term neurodevelopmental impairment. The ongoing management and associated morbidity present a significant burden for carers and healthcare systems. Long-term oxygen therapy may be required for variable duration, though there is a lack of consensus and wide variation in practise when weaning supplemental oxygen. Furthermore, a shift in care towards earlier discharge and community care underlines the importance of a structured discharge and weaning process that eliminates the potential risks associated with hypoxia and hyperoxia. This review article describes recent evidence outlining oxygen saturation reference ranges in young infants, on which structured guidance can be based.

INTRODUCTION

Despite advances in neonatal care over the last decade with various prevention strategies, the incidence of chronic lung disease (CLD) remains high. For extremely preterm infants (birth before 28 weeks of gestation) at risk of respiratory distress syndrome

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(RDS), the incidence of bronchopulmonary dysplasia (BPD), defined as requiring supplemental oxygen for at least 28 days or continued respiratory support at 36 weeks post conceptual age (PCA), ranges from 48 to 68% between centres [1,2]. Almost one third of babies <32 weeks' gestation that were admitted to a UK neonatal unit in the period 2016–2018, developed BPD (6931 infants) [3]. BPD accounts for 68% of children in the UK who receive home oxygen [4].

This resultant morbidity causes a huge burden on both carers and healthcare systems, with 49% of infants with BPD requiring rehospitalisation in the first year of life. Poor respiratory health and impaired lung function have been shown to persist beyond infancy into childhood and adolescence [5,6]. Although the relationship between BPD and neurodevelopment is complex, there is evidence that in extremely preterm infants BPD is associated with adverse neurodevelopmental outcome [7,8].

More recently, care has shifted from inpatient provision of respiratory support and an associated prolonged hospital stay, to earlier discharge and integration with parents/carers in the community. The ready availability of oxygen provision in the home has facilitated this practise and supported wider opportunity for infant social stimulation as well as reducing financial demand. The role of healthcare providers is to ensure a smooth discharge process whilst reducing the potential risks associated with hypoxia or hyperoxia at a time when these infants are no longer on continuous cardiorespiratory monitoring. The potential for subsequent complications if these infants are ineffectively managed is high [9].

Whilst the impact of sustained lower baseline oxygen saturations is increasingly clear [10–12], the effect of brief hypoxic events to which infants are particularly susceptible is only beginning to become evident. These are caused by short central apnoeas as a result of respiratory instability in early infancy which reduce over the first few months of life as respiratory patterns mature and stabilise [13,14]. The consequences of oxygen deprivation may include pulmonary hypertension (PHT) [15,16], altered somatic growth [17,18] adverse effects on neurodevelopment [7,10] and an increased risk of acute life-threatening events.

PROPOSED MORBIDITY RELATING TO SUSTAINED AND INTERMITTENT HYPOXIA

Bronchopulmonary dysplasia and pulmonary hypertension

Pulmonary hypertension develops in 20–40% of infants with BPD and contributes to morbidity and mortality [15,16,19]. The risks are greatest in very preterm (born <32 weeks of gestation) and extremely low birth weight infants (<1000 g), as well as infants with additional cardiovascular anomalies [20,21]. Retrospective studies of infants with BPD and associated PHT suggest mortality rates range from 14% to 38% [22]. Chronic hypoxaemia is a well-established cause of PHT and lack of a structured oxygen weaning programme is associated with increased prevalence of PHT in infants with BPD [9]. With appropriate oxygen supplementation this is reversible in the majority of cases [23].

Hypoxia and growth

Despite aggressive nutritional support with both enteral and parenteral nutrition in more recent years, a large proportion of infants born <28 weeks gestation demonstrate growth failure at 36 weeks post conceptual age (PCA).

Evidence suggests that mean saturations <92%, are associated with suboptimal growth [18] and necrotising enterocolitis [24] in infants with CLD. However targeting higher saturations (95–98% versus 96–99%) from 32 weeks PCA onwards in extremely preterm infants conferred no significant benefit on growth in either the Benefit Of Oxygen (BOOST) initial trial [25] or Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity (STOP-ROP) multicentre trial [26].

However, once discharged infants with BPD receiving supplementary home oxygen have demonstrated small improvements in growth compared to those managed in room air [27]. Considering that growth failure is common in infants with BPD, any small improvements in growth may potentially support lung recovery.

Infants with lower mean saturations are predisposed to episodes of IH [12] and this is exacerbated in infants with BPD (see Table 2) [28,29]. Certainly, infants with severe lung disease are more predisposed to hypoxic events with exertional activities. Wang et al examined the impact of BPD severity on oxygen saturations during feeding at 2, 4 and 6 months CGA, and growth of very low birth weight (VLBW, <1500 g) preterm and term infants during infancy. Studies were undertaken in room air. During rest immediately prior to feeding mean saturation in all groups were >97%. VLBW infants with severe BPD exhibited significantly lower mean saturations during feeding and more significant desaturations <90% presumably due to increased respiratory demands. These infants displayed slower growth compared to term and VLBW infants with mild BPD at all time points [17]. Animal models have demonstrated that even in the absence of respiratory disease IH events are associated with impaired growth in the first few weeks of postnatal life [30]. It is thus possible that both IH events and increased respiratory demands contribute to impaired growth in infants with BPD.

Whilst the impact of hypoxia on growth may reflect a complex mix of increased metabolic demand alongside increased vulnerability to respiratory infection, this data supports the need to ensure adequate oxygenation during periods of activity. Optimising the growth of these infants with increased metabolic requirements, and eliminating the potential adverse effect of hypoxaemia in the first few months of life may aid successful oxygen weaning. Regular monitoring to ensure adequate growth and nutrition is advised [17].

Neurodevelopmental outcome

The importance of avoiding prolonged hypoxaemia in early neonatal life cannot be over emphasised. Pooled meta-analysis data of the Surfactant Positive Airway Pressure and Pulse Oximetry Trial (SUPPORT), Canadian Oxygen Trial (COT), and BOOST studies observed no significant difference between different oxygen saturation targets (85–89% versus 91–95%) on the primary composite outcome of death or major disability at a corrected age of 18–24 months. However, lower saturations were associated with a higher risk of death, albeit with a lower risk of interventions for retinopathy of prematurity (ROP) [24].

The relationship between BPD and neurodevelopment is complex. There is evidence that in extremely preterm infants BPD is associated with adverse neurodevelopmental outcome including cognition, motor performance, speech and language, behaviour, and often poor academic attainment [7,8,31].

Data on the impact of short hypoxic events is emerging. Horne et al utilised daytime polysomnography and near infrared spectroscopy to demonstrate that short hypoxic events (defined as apnoea >3 second duration) in ex-preterm infants are associated with decreases in heart rate and cerebral oxygenation, which were more marked at 2–3 months and 5–6 months than at 2–4 weeks post term corrected age [32]. These greater oxygen deficits coincide with rapid brain growth and metabolic brain activity as well as physiological anaemia. Whilst supplemental oxygen post-discharge from the neonatal unit does not appear to impact on neurodevelopmental outcomes measured using the Bayley Scales

of Infant Development [33], these brief hypoxic events may lead over time to adverse behavioural and neurocognitive functioning similar to that associated with sleep disordered breathing (SDB) [32].

Healthcare utilisation

Associations between supplemental oxygen use, respiratory and healthcare utilisation are conflicting. Greenough et al. reported a significantly lower total cost of care over a two-year period for infants discharged from centres with high rates of home oxygen therapy (HOT) [34]. Longer desaturation events in extremely preterm infants at TEA are associated with greater healthcare utilisation over the first two years of life [29].

Conversely DeMauro et al reported a higher rate, and greater duration of hospitalisation, in extremely preterm infants with BPD over a 2-year period receiving supplemental oxygen following propensity score matching at 36 weeks PCA. Infants receiving oxygen were also more likely to have increased medical resource use (respiratory medication and equipment) and undergo tracheostomy insertion during the first two years of life, suggestive of respiratory morbidity. The STOP-ROP RCT observed as a secondary outcome that pneumonia and pulmonary exacerbations occurred more frequently in infants assigned to higher saturations (96–99% versus 89–94%) from 35 weeks PCA [26]. Importantly, a third of infants in the supplemental arm discontinued oxygen at a mean PCA of 37 weeks as they had reached the study endpoint and thus may not be applicable to babies discharged in oxygen.

The perceived vulnerability of an infant requiring supplemental oxygen may influence parental health seeking behaviours and healthcare attendance. Children receiving home oxygen are more likely to have home pulse oximeters [27] which may affect thresholds for presentation with respiratory symptoms. HOT commonly facilitates a more direct and 'open access' pathway to secondary healthcare services and clinicians may consider these infants vulnerable contributing to cautious management and hospital readmission. The impact of oxygen supplementation on growth and respiratory outcomes at 6 months on infants discharged from the Neonatal Intensive Care Unit (NICU) is currently the focus of an RCT [35].

Prescribing supplemental home oxygen clearly requires a careful balance between the potential risks and benefits for infants with BPD. The uncertainties around the benefits or otherwise of supplemental oxygen support the need for supervised weaning for infants discharged from NICU in oxygen.

A STRUCTURED APPROACH TO WEANING

Current practise

National guidelines for initiating, monitoring and weaning infants from supplemental oxygen following discharge from NICU lack an evidence base [36,37], which has changed little over the past decade. Historic guidance has been subject to weak evidence and influenced by observational data.

This lack of an evidence base has led to wide variation in international practise with both a lack of consensus for initiating oxygen therapy particularly around mean saturation thresholds for prescribing oxygen and optimum target saturations [38,39]. Variation in target saturations impacts on weaning preterm infants from supplemental oxygen therapy [40]. Rhein et al. surveyed weaning practise in the USA and reported that only 8% of pulmonologists followed a standardised weaning protocol. Growth was felt to be an important consideration when weaning infants but other variables such as hospitalizations lacked consensus [41]. Notably, there is a limited understanding of technological considerations that affect data output from oximeters [41].

In the absence of a structured weaning plan, the median age at which infants are weaned off oxygen ranges from 10 to 15 months [9,42] and is unsupervised in as many as one third of infants [9]. Importantly, structured weaning targeting oxygen saturation levels within recommended ranges has been demonstrated to reduce the duration of oxygen supplementation with the rate of weaning being more rapid in those infants having more regular episodes of continuous saturation monitoring [42]. Active weaning and a shorter home oxygen duration treatment is associated with enhanced parental quality of life [43].

Batey et al demonstrated a 10-month reduction in duration of home oxygen following introduction of a structured weaning programme without adverse effects. Close initial monitoring of infants pre-discharge did lead to an increase in the number of infants receiving supplemental oxygen at discharge, however, there was an overall reduction in HOT. No significant difference was observed between hospital readmission rates following the intervention [42]. Supervised weaning is associated with a lower incidence of PHT [44].

Since publication of the American Thoracic Society (ATS) guidance providing a 'strong recommendation based on very low-quality evidence' for the prescription of home oxygen in patients with BPD complicated by chronic hypoxaemia [37], there has been a progressive increase in evidence providing reference oxygen saturation data for preterm infants. More recently, the European Respiratory Society (ERS) recognised the urgent need for evidence to support guidance in the long term management of BPD [36] and the Thoracic Society of Australia and New Zealand delivered a position statement to address the considerable variation and limited objective evidence for the use of long term supplemental oxygen in CLD [45].

SETTING CRITERIA FOR OXYGEN REQUIRMENT AT DISCHARGE

Since publication of the ATS guidance [37] in 2018 the evidence base has expanded in relation to reference ranges for oxygen saturation parameters in healthy preterm and term infants [13,28,29,46–48]. Using this data, we propose a structured weaning programme for infants with BPD at term equivalent age (TEA), receiving supplemental oxygen post- discharge from NICU. This guidance aims to define target oxygen saturations relative to otherwise healthy infants and importantly demonstrates the influence of rapid maturation both in tidal volumes and saturation indices in the first few weeks of life beyond term and how these can impact on oxygen weaning.

Baseline mean saturations

British Thoracic Society (BTS) (2009) guidelines are most commonly used to wean oxygen in 45% of UK centres [49]. This guidance suggests maintaining oxygen saturations at ≥93% and allowing <5% of the study time with saturations <90% during a stable recording period [50].

However, this predates the widespread use of new generation oximeters which can reliably detect brief drops in oxygen saturations due to shorter averaging times and also effectively remove artefact due to motion. Such features are vital in infants who regularly exhibit brief hypoxic events secondary to central apnoeas [51], and restless young children [41]. These oximeters are now widely available and are important advances in the investigation of children for SDB [14,51]. Shorter averaging times (usually maximum 3 seconds) avoid smoothing out of brief desaturation events (Fig. 1) [41].

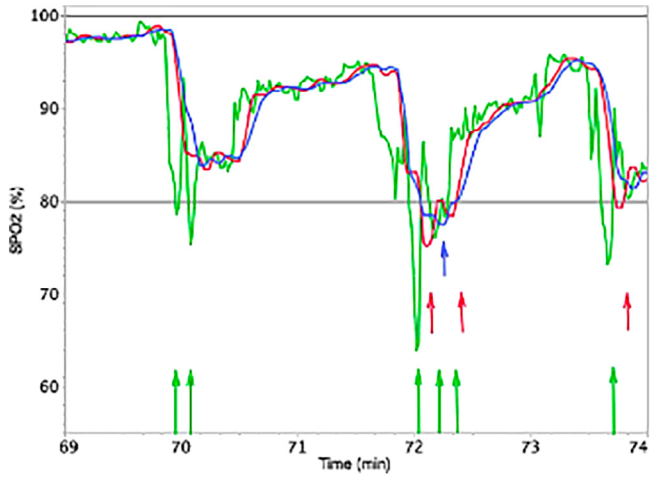

Fig. 1. Influence of the averaging time on the number of desaturations for an alarm threshold at 80% SpO_2. An averaging time of 3 s (green) results in six desaturations, while an averaging time of 10 s (red) or 16 s (blue) results in three and one desaturation(s), respectively. Reproduced from Vagedes et al. [52].

Additionally, this smoothing may artificially lower mean saturations resulting in the delivery of a higher oxygen concentration to maintain target range [53], and more infants perceived to reach agreed thresholds for supplemental oxygen. Technological aspects of oximeters that affect data output must be considered to avoid misinterpretation [41].

Studies using new generation oximeters demonstrate that both healthy term-born [13,48] and healthy preterm infants at TEA [28,29,46] have mean oxygen saturations >95%. Similarly, extremely preterm infants with significant lung disease also have mean saturations >95% [28,29], although it should be noted that in these cases mean saturation data is likely to have been influenced by the respiratory support (CPAP and oxygen) delivered to some infants at the time of oximetry studies (Tables 1 And 2).

Once an infant with BPD reaches term and achieves mature retinal vascularisation (as documented by ophthalmologic examination), a target saturation value of greater than 93% is recommended. This provides a "buffer" zone against dips in oxygen saturations and hypoxaemia that lower targets <92% do not. Proposed recommendations are in accordance with BTS guidance [50], and the recent Australian and New Zealand Thoracic Society positional statement [11,45], as well as normative oximetry data for healthy preterm infants (see Table 2) [28,29,46]. Considering these reference data, it is possible that the proposed baseline target saturations outlined are conservative and should conceivably be higher at 95%.

Desaturation indices

Oxygen desaturations indices (ODI) are defined as the average number of desaturation episodes per hour and are typically reported as ODI3 and ODI4, referring to the number of times per hour where the oxygen saturation falls by at least 3% and 4% from baseline respectively. At less deviance from baseline, ODI3 incorporates ODI4 and is therefore equivalent or greater in value (Tables 1 And 2). ODI are increasingly reported by clinicians largely due to the increasing relevance they play in the diagnosis of SDB [41]. In 2012, the American Academy of Sleep Medicine (AASM) revised the scoring criteria for SDB referring to ODI3 rather than ODI4; a shift has been recently replicated in the Australasian Sleep Association (ASA) pulse oximetry guidelines.

Importantly, reference ranges for desaturation indices in older children are not applicable to young infants who regularly exhibit brief hypoxia events secondary to central apnoeas [14,51]. Recently, normative oximetry data has been reported for preterm infants at TEA [28,29,46] and healthy term infants at birth [46], 2 weeks [13], 1 [48], and 3 months [13,48] post term (Table 1).

Mean Oxygen Saturations, Oxygen Desaturation Index >3% (ODI3) and >4% (ODI4) from baseline/hour, Minimum Saturations (Sat Min), percentage time with saturations below 90% (% time <90%).

These data clearly demonstrate maturation in ODI over the first 4 months of life post term [14], presumably due to maturational stability of breathing patterns. Williams et al demonstrated that healthy preterm infants at term have similar 3% ODI to term infants [46], thus suggesting that prematurity alone does not markedly impact on central apnoea and ODI3.

A feature of 3% and 4% ODI is the marked heterogeneity between infants. This may reflect relatively small infant numbers in the published literature [46,48]. Certainly, larger studies would be beneficial to determine whether reference ranges can be defined more tightly.

Extremely preterm infants with BPD appear to be particularly susceptible to brief hypoxic events and higher ODI3 are observed at TEA (Table 2) [28,29,47]. These data most likely reflect greater

Table 1
Normative oximetry data for healthy term infants. Mean Oxygen Saturations, Oxygen Desaturation Index >3% (ODI3) and >4% (ODI4) from baseline/hour, Minimum Saturations (Sat Min), percentage time with saturations below 90% (% time <90%).

Author	Gestation (weeks) (number)	Timing of oximetry (post conceptual age, weeks)	Mean saturations (%)	Sat Min (%)	ODI3	ODI4	% time <90%
Williams LJ (2019) Preterm at day 2/3	35 (34–36) (*N* = 43)	35 (34–36)	97.8 (97.1–98.3)				
Williams LJ (2019) Preterm at term equivalent	35 (34–36) (*N* = 43)	40	98.8 (98.4–99.4)		32.8 (25.9–41.4)		
Williams LJ (2019) Term at day 2/3	40 (39–42) (*N* = 42)	40 (39–42)	97.9 (96.7–98.9)		29.3 (23.5–36.6)		
Terrill PI (2015) Term at 2 weeks	40 (38–42) *N* = 30	(40–44)	97.8 (95–99)		27.2 (21.2–33.1)		1.3 (<92%) 0.0–6.3
Evans HJ (2018) Term at 1 month	39 (37–42) (*N* = 45)	44 (43–44)	97.1 (13.7–18.6)	80.4 (78.8–82.0)	25.4 (22.0–28.8)	16.2 (13.7–18.6)	0.39 (0.26–0.55)
Terrill PI (2015) Term at 3 months	40 (38–42) *N* = 25	(51–56)	98.9 (97–100)		10.0 (7.4–12.6)		
Evans HJ (2018) Term at 3 months	39 (37–42) (*N* = 38)	56 (54–57)	97.7 (97.2–98.1)	84.7 (83.3–86.1)	13.9 (11.4 –16.5)	8.12 (6.46–9.77)	0.11 (0.06–0.20)

Table 2
Normative oximetry data for extreme preterm infants and healthy late preterm infants. Mean Oxygen Saturations (SAT50), Oxygen Desaturation Index >3% (ODI3) and >4% (ODI4) from baseline/hour, Minimum Saturations (Sat Min), percentage time with saturations below 90% (% time <90%).

Author	Gestation (weeks) (number)	Timing of oximetry (post conceptual age, weeks)	Mean saturations (%)	Sat Min (%)	ODI3	ODI4	% time < 90%
Wellington G (2018) Preterm at term equivalent	32 (24–36) ($N = 38$)	37 (35–42)	97.8 (97.1–98.7)	60 (45.5–66)	80 (55–105)	53 (34–76)	1.95 (0.8–4.68)
Terrill PI (2018) Preterm at term equivalent	24 (23–25) $N = 37$	40 (37–42)	96.1 (95.4–96.8)		54.8 (47.2–62.5)	43.8 (37.0–50.6)	7.56 (5.1–10.0)

vulnerability to hypoxaemia from central apnoeas. This may be as a result of lung damage contributing to PHT and impaired diffusion.

These data confirm the need for an approach to initiation and weaning of oxygen which takes in to account age specific reference ranges alongside the severity of lung disease.

Weaning infants from oxygen

The amount of oxygen inspired by an infant on supplemental oxygen depends on the amount of extraneous room air that is inspired. In infants weighing <1.5 kg, the amount of extraneous room air that dilutes supplemental oxygen with inspiration is minimal. However, this dilutional effect increases with growth. Finer et al demonstrated that at an oxygen flow of 0.2 l/min, an infant weighing <1.5 kg can achieve a fraction of inspired oxygen (FiO_2) of up to 95% when measured at the back of the oropharynx whereas infants >1.5 kg will achieve a maximum FiO_2 of approximately 70% (mean 47%) [48]. Accordingly, very small changes in inspired oxygen can have large effects on saturations in infants <1.5 kg, but >2.5 kg changes of 0.1 l/min oxygen result in only small changes in oxygen saturations [54]. On this basis, oxygen

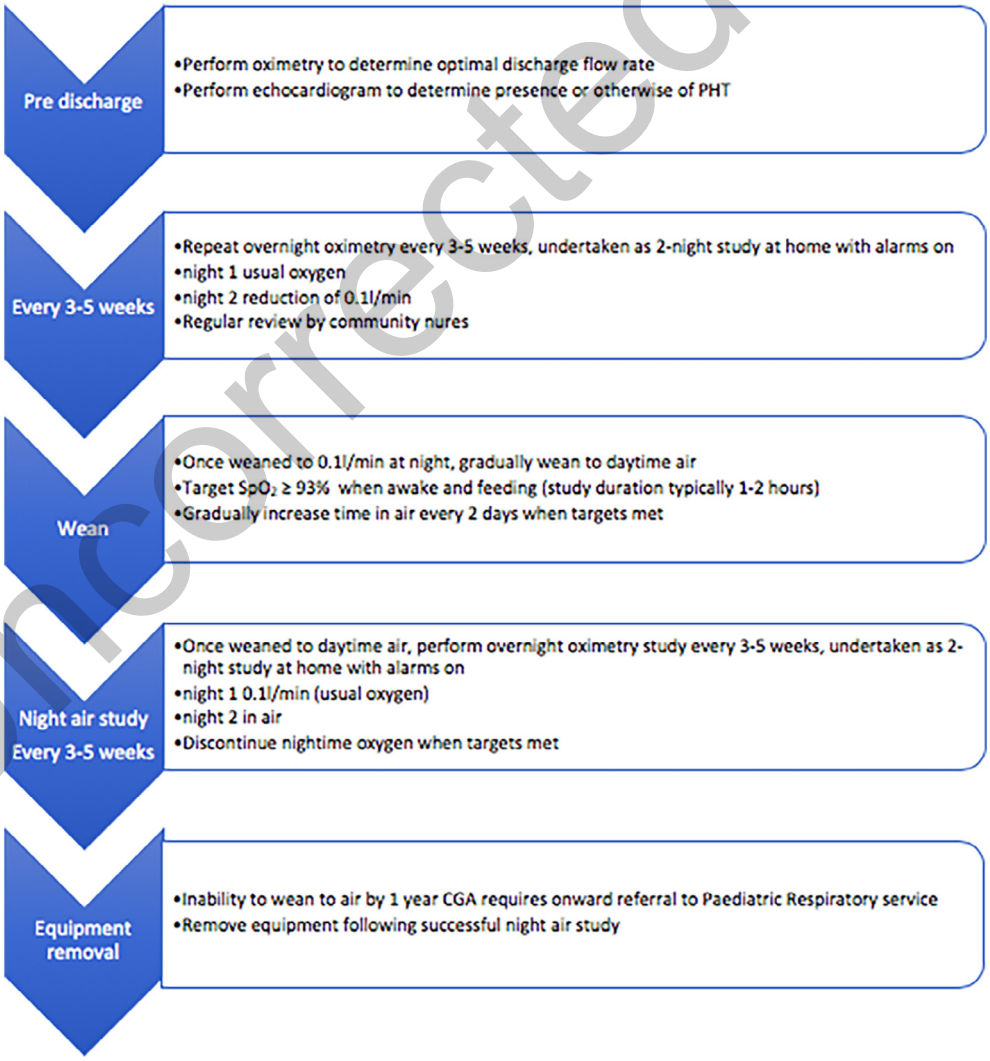

Fig. 2. Structured weaning programme for infants with BPD requiring oxygen on discharge into the community. Adapted from Khetan et al: Advances in Neonatal Care 2016 [61].

can be weaned safely in increments of 0.1 l/min in infants over 2.5 kg and 0.2 l/min in infants >10 kg [42].

Using pulse oximetry to monitor and wean supplemental oxygen

There is much uncertainty regarding the optimal approach to weaning supplemental home oxygen and a lack of consensus regarding best practise [37,50]. Rhein et al. examined the impact of a home oxygen management strategy and the analysis of recorded home oximetry data alongside standard monthly clinic visits on the duration of home oxygen [43]. Recorded home oximetry data was associated with a shorter duration of HOT in preterm infants that required oxygen at discharge. Within this study, the decision regarding oxygen weaning was based on a structured algorithm involving 20 min daytime oximetry challenges to determine whether infants could maintain saturations >93%. Importantly, the level of infant activity at the time of clinic assessment and oxygen weaning was not reported [43].

The duration of infant monitoring during the daytime requires consideration and particularly whether this should contain periods of feeding or activity, that is times most likely to stress respiratory reserve. A reduction in saturations during infant feeding is reported [17], and on this basis it may be appropriate to initially attempt gradual weaning during periods of exertion such as feeding [55]. However, such short term, awake recording of saturations may not accurately predict those during prolonged sleep [18] when episodes of rapid eye movement (REM) sleep predispose to central apnoeas and desaturations [56]. A period of overnight monitoring is therefore crucial in addition to daytime observations and if undertaking regularly has been demonstrated to expedite weaning as respiratory patterns mature [43].

Polysomnography (PSG) is the gold standard tool for diagnosing sleep disorders [57,58] and may be more sensitive in assessing pulmonary reserve than oximetry [59]. The role of PSG in weaning oxygen from infants with BPD is however less clear [9]. Pre discharge PSG may identify infants with immature cardiorespiratory centres and thus those at high risk of hypoxic events in the community [60] and may also be used to exclude nocturnal hypoxaemia prior to oxygen weaning [56,61]. However, PSG is expensive, not readily available in many centres and thus poses a challenge for flexible, reactive weaning. Oximetry may be argued a feasible and inexpensive alternative tool [57].

Overnight oxygen saturation studies are a common method for weaning. Home oximetry data may enable clinicians to identify infants suitable for weaning. Oximetry does not however accurately predict periods of wakefulness and sleep. It is therefore paramount that parents and carers observe and document this information during the study to enable correct interpretation. Studies should use saturation monitors with data storage facilities to record the oxygen saturation levels and heart rate overnight. A reduction in the duration of HOT was observed with frequent recorded home oximetry data and monthly clinic visits in comparison to standard monthly clinic visits alone, alongside monthly polysomnography [43].

Determining the need for supplemental oxygen pre-discharge is important in order to avoid the potential adverse consequences associated with HOT. We propose that an oximetry study be performed in the week immediately prior to discharge to provide an up to date assessment and ensure the correct amount of oxygen flow will be delivered in the home setting. Ongoing titration studies should be undertaken. Weaning can be achieved on an approximately monthly basis [42,45] and ideally more frequently [43]. A previous, similar structured programme has demonstrated that infants can be weaned more rapidly from oxygen without adverse outcomes [62] (Fig. 2). Target oxygen saturations are age dependent and infants should be weaned according to age specific reference ranges [47,63] for the oxygen saturation monitor that is being used. The suggested percentage time spent with saturations <90% is less than BTS guidance of 5% [50], and considers oxygen saturation profiles of preterm infants recently reported by Wellington et al (percentage time <90% 1.3%) [47]. Suggested target saturations and ODI limits based on the current evidence [64] and using modern generation oximeters able to exclude motion artefact and with averaging times set at 2 seconds are outlined in Table 3.

Table 3
Saturation targets for weaning oxygen using motion resistant oximeters with short averaging times.

Corrected age post term	Minimum mean saturations	% of time below 90%	3% ODI
37–40 weeks	>93%	<3%	35
40–44 weeks	>93%	<3%	30
44–56 weeks (1–4 months)	>93%	<3%	15
Over 56 weeks (Over 4 months)	>93%	<3%	7

CONCLUSION

BPD is responsible for over two thirds of children receiving UK home oxygen, and is associated with significant morbidity and high health care utilisation. Currently, there is much heterogeneity in the implementation, monitoring and weaning of LTOT which reflects a limited evidence base, and the need for higher quality prospective studies. Maintaining healthy oxygen saturations and avoiding the consequences of oxygen deprivation is likely to improve outcomes. Whilst a standardised weaning programme may result in an initial increase in infants receiving oxygen at discharge, the benefits include reduced hospital readmissions, more rapid weaning and the potential effects of unwanted hypoxia such as pulmonary hypertension. Increasingly modern oximeters with short averaging times able to exclude motion artefact are widely available, and offer many advantages particularly in relation to the availability of age specific reference ranges for this cohort of infants.

PROPOSED WORKFLOW

We suggest that initiating and weaning oxygen therapy is done as a staged and gradual process using age appropriate reference ranges for the oximeter that is being used. Targeting mean oxygen saturations greater than 93%, in order to avoid adverse outcomes that may result from hypoxaemia is proposed. Short desaturations occur in healthy term and preterm infants and it is acceptable to wean oxygen in the presence of these within a specified range. The recommendations set out in this article are particularly aimed at infants born prematurely with BPD but could be applied to other infants with CLD and those with SDB such as periodic breathing. However, infants with complex issues such as cyanotic congenital heart disease may not necessarily fit into the suggested pathway and advice should be sought from specialist teams.

DIRECTIONS FOR FUTURE RESEARCH

- Further research to identify and define optimal oxygen saturation indices for infants discharged from the neonatal unit.
- Develop a greater understanding of the impact of differing target oxygen saturations on long term growth, neurodevelopmental and respiratory outcomes.
- Better establish the optimal mode and rates of oxygen weaning in infants with bronchopulmonary dysplasia requiring home oxygen on discharge from the neonatal unit.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Lucy H. Everitt: Conceptualization, Writing - original draft, Visualization. **Adejumoke Awoseyila:** Writing - original draft. **Jayesh M. Bhatt:** Conceptualization, Writing - review & editing. **Mark J. Johnson:** Writing - review & editing. **Brigitte Vollmer:** Writing - review & editing. **Hazel J. Evans:** Conceptualization, Writing - review & editing, Supervision.

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The authors declare that there is no conflict of interest.

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