Chapter 10

Structured approach to monitoring and weaning off home oxygen therapy in neonatal respiratory disease

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There is widespread variation in the implementation and monitoring of and weaning off home oxygen therapy (HOT) in neonatal respiratory disease, and current guidance is based predominantly on expert consensus and clinical experience. The potential adverse consequences associated with hypoxia underline the importance of a structured approach to the management of HOT. Evidence suggests that a structured pathway for night-time and daytime weaning confers advantages for infants, families and healthcare services. Family-centred care and shared decision making are key to the discharge process and transition from the neonatal unit into the community. The technological advancements of oximeters require consideration for the analysis and interpretation of data. Further research is required to establish evidenced-based target mean S_{pO_2} values and to determine the impact of different targets on long-term infant outcomes.

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There is widespread variation in the implementation and monitoring of and weaning off home oxygen therapy in neonatal respiratory disease. A structured approach to this confers advantages for infants, families and healthcare services. https://bit.ly/3cYXWUy

Despite the increasing prevalence of home oxygen therapy (HOT) in the community, there remains an absence of guidelines for the management of home oxygen and uncertainty regarding an optimal approach [1, 2]. Accordingly, there is inconsistency in the implementation and monitoring of and weaning off HOT for infants with neonatal respiratory disease [3–5], and weaning is unsupervised in as many as one-third of infants [6].

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Alongside advancements and practice in neonatal care, the survival of preterm infants has increased [7], with implications for healthcare services. Chronic neonatal lung disease is now the most common diagnosis requiring HOT, and thus home oxygen is increasingly prescribed [8]. Other conditions requiring HOT in infants and children include interstitial lung disease, PH, CHD and CF (interstitial lung disease, PH and CF are discussed elsewhere in this *Monograph* [9–11]). Within the UK, BPD accounts for 68% of home oxygen use in infants and children [12].

Current practice

A shift in care over more recent years from inpatient provision of oxygen therapy to earlier discharge and integration in the community has been facilitated by the ready availability of home oxygen. These changes have had significant implications for infants, children and their families. The potential detrimental impact of hypoxia for the infant is significant, and poorer outcomes are associated with respiratory [13, 14], growth [15–17] and neurodevelopmental [18–20] impairment.

In 2019, the American Thoracic Society (ATS) clinical guidelines for HOT in children highlighted a striking lack of empirical evidence in the implementation, monitoring and discontinuation of HOT [1]. Analogous to the most recent British Thoracic Society (BTS) guidelines [2], ATS clinical recommendations are based predominantly on expert opinion and clinical experience [1]. The BTS guidance published in 2009 continues to influence practice most commonly in 45% of UK centres [21]. Over recent years, there has been a progressive expansion in the evidence base, particularly regarding age-adjusted reference ranges for S_{pO_2} parameters in term and preterm infants [22–27]. Acknowledgement of an urgent need for informed guidance is widespread, and was more recently echoed by the European Respiratory Society [5] and the position statement issued by the Thoracic Society of Australia and New Zealand 2020 [3].

A structured approach

The decision regarding initiation of HOT and timing of discharge requires careful consideration of the advantages and potential risks for the infant *versus* a more prolonged period of hospitalisation. Discharge planning encompassing shared decision making, parental education and involvement of key healthcare professionals facilitates the transition process from hospital to the community setting [28]. Parents should be aware of how to access and navigate healthcare services in the event of clinical concern. The importance of providing written information detailing an individualised pathway for the monitoring and weaning process cannot be overemphasised, and contributes to enhanced parental understanding and expectation.

Monitoring and weaning of oxygen therapy is associated with better outcomes and more rapid weaning in the community [6, 29]. In centres with frequent use of HOT, a reduction in length of stay on neonatal units has been reported when adjusting for illness severity and gestational age [30]. Batey *et al.* [29] reported a 10-month reduction in duration of HOT utilising a structured approach to weaning without adverse consequences. However, this more structured approach with sleep studies prior to discharge has been associated with an increase in the number of infants receiving oxygen at the time of neonatal discharge, with potential implications for infants, families and healthcare services [31]. Notably, a reduction in the duration of HOT is associated with enhanced parental quality of life [32].

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Parental preference

Parental involvement and family-centred care are beneficial for infant and parent outcomes in the NICU setting [33]. Shared decision making between healthcare professionals and parents/carers is key to this approach and promotes family well-being and satisfaction [34]. Decreased parental stress and anxiety, as well as a higher frequency of exclusive breastfeeding and improved infant weight gain, were reported in a multicentre randomised controlled trial that delivered family-integrated care and empowered parents to become primary care givers in the NICU [33].

While home oxygen use may have the potential to increase readmission rate [31], a reduction in emergency department attendances is reported with implementation of a patient-orientated and family-centred discharge planning process in infants born between 27 and 33 weeks of gestation [35]. Parental satisfaction may impact future service utilisation and treatment adherence, and this has implications for longer-term patient outcomes. Lau *et al.* [36] examined parental preferences regarding HOT and timing of discharge in infants with BPD. Other than gestational age, perceived fear and comfort in the hospital *versus* at home were the greatest determinants of parental decision making. The importance of a structured and supported transition from hospital into the community setting cannot be overemphasised.

Pulse oximetry

Oximetry is a noninvasive, widely available and commonly used tool that allows continuous or intermittent estimation of arterial oxygenation.

Polysomnography is arguably superior in assessing pulmonary reserve [37] and may identify infants with immature cardiorespiratory centres at risk of future hypoxic events. In addition, it can accurately determine sleep stages, in particular periods of rapid eye movement (REM) sleep, which are most susceptible to central apnoeas and desaturations [38]. However, polysomnography is expensive and is not readily available across centres [39].

The accessibility of oximetry facilitates reactive weaning in infants receiving HOT [40]. In the absence of electroencephalogram monitoring, heart rate variability is used as a surrogate marker to detect episodes of REM sleep, and is usually referred to as periods of active sleep (see example in figure 3). Nocturnal pulse oximetry (NPO) should capture at least two episodes of active sleep to ensure that periods of vulnerability are assessed. Notably, periods of wakefulness and other key events should be documented during the study to facilitate data analysis and interpretation.

Oximeters

New-generation oximeters, which have become widely available over recent years, benefit from shorter averaging times and have artefact rejection algorithms that can eliminate the effect of motion. These technological advancements influence data output and thus require consideration for data interpretation. Shorter averaging times, typically <3 s, can reliably detect transient drops in S_{pO_2} and therefore avoid the smoothing out of brief desaturation

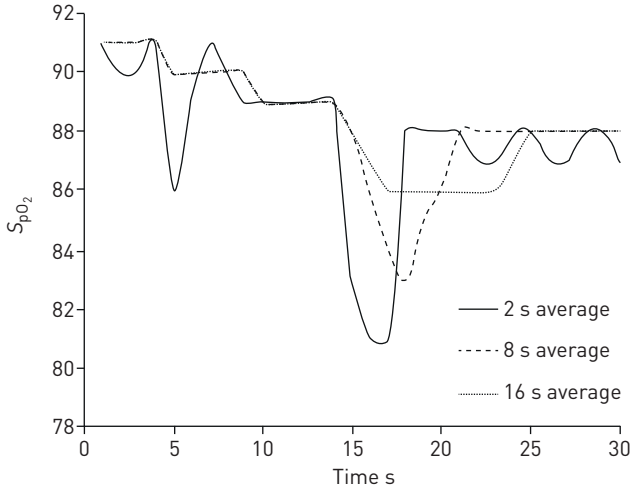

Figure 1. The impact of S_{pO_2} averaging time on the number of desaturation events in a preterm, low-birthweight infant over a 30-s time period with averaging times set at 2 s, 8 s and 16 s. Reproduced and modified from [41] with permission.

events that may artificially lower mean saturations (figure 1) [42]. For infants who regularly display brief hypoxic events secondary to central apnoea, and also in restless young children, such features significantly impact data output [42, 43]. Furthermore, the recent literature based on age-specific reference ranges utilises oximeters with shorter averaging times and artefact rejection algorithms. This is an important consideration when initiating and weaning off oxygen around set target thresholds.

The persistent use of older oximeters may influence thresholds for the initiation of and weaning off supplemental oxygen therapy. Recent survey data suggest that the influence of technological features on data output are poorly understood, contributing to a wide variation in pulse oximeter settings across home oxygen services [21]. Furthermore, there is wide variation in clinicians' understanding and interpretation of oximetry traces for the initiation of and weaning off oxygen therapy [44–47].

Normative data

Target saturations

Maintaining mean S_{pO_2} ⩾93% and allowing <5% of the oximetry study time with S_{pO_2} <90% are currently recommended by the BTS guideline [2]. However, there is widespread agreement regarding the limited evidence base to guide these reference ranges [1, 2, 5]. Since publication of the ATS guidance in 2018 [1], there has been a progressive increase in evidence regarding age-adjusted reference ranges for S_{pO_2} parameters, particularly in term and preterm infants.

Normative study data obtained using modern-generation oximeters with motion artefact extraction technology suggest that healthy term infants have a mean S_{pO_2} >95% [22, 25, 27]. Notably, these findings are also replicated within the preterm cohort, in which both healthy

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preterm infants at term [25], and also extremely preterm infants with lung disease at term [23, 24], have an S_{pO_2} >95% (albeit some extremely preterm infants were receiving respiratory support during data collection) (table 1).

Accordingly, oxygen weaning in term and preterm infants at a term-corrected age should target mean S_{pO_2} >93%, and arguably this could be higher at 95%. Suggested target thresholds are outlined in table 2.

Desaturation indices

The oxygen desaturation index (ODI), defined as the number of times·h^{-1} of sleep that S_{pO_2} drops by a certain percentage from baseline, are typically reported as a 3% or 4% ODI, referring to a drop of >3% and >4% from baseline, respectively, with the former increasingly referenced in recent guidance.

HOT

The duration of HOT and the associated impact on parental quality of life underline the importance of a planned approach with regular review. RHEIN *et al.* [32] reported the impact of HOT on parental quality of life in a randomised controlled trial examining the use of recorded home oximetry data on duration of home oxygen in preterm infants. Transmitted home oximetry data performed between standard monthly clinic visits at the parents' discretion reduced the duration of home oxygen use in comparison with standard monthly clinic visits alone (mean±SE: 78.1±6.1 days *versus* 100.1±8.0 days). An improvement in parental quality of life was observed in both groups following discontinuation of oxygen, and the importance of structured, regular titration to optimise weaning in a timely manner and its associated impact on quality of life were highlighted [32].

The average duration of HOT for infants with BPD is variable (table 3). Most infants discontinue home oxygen by 12 months of age [54]. Failure to wean from oxygen therapy by this time prompts referral to a paediatric respiratory specialist for review and consideration of further investigations to identify underlying problems.

The weaning pathway

Pre-discharge

Performing an NPO study when clinically stable in the week prior to discharge ensures an up-to-date assessment of the infant's optimal oxygen flow rate to maintain targeted S_{pO_2} levels. PH is a recognised sequela of chronic hypoxia, with extremely preterm and low-birthweight infants at greatest risk, and higher mortality rates are observed in infants with BPD and associated PH [55, 56]. PH and unsupervised weaning off supplemental oxygen in infants with BPD are associated with higher mortality rates [57]. An ECG should be performed prior to discharge so that management can be optimised.

Prior to discharge, parents/carers should receive training in basic life support and education regarding the signs and symptoms of clinical deterioration and how and when to

Table 1. Normative oximetry data for healthy preterm and term infants and extremely preterm infants

	Cases n	Gestational age weeks	Timing of oximetry (PCA) weeks	S_{pO_2} %	Minimum S_{pO_2} %	3% ODI %	4% ODI %	Time S_{pO_2} <90% %	First author [ref.]
Healthy preterm and term infants									
Preterm at day 2/3	43	35 (34–36)	35 (34–36)	97.8 (97.1–98.3)					Williams [25]
Preterm at term equivalent	43	35 (34–36)	40	98.8 (98.4–99.4)		32.8 (25.9–41.4)			Williams [25]
Term at day 2/3	42	40 (39–42)	40 (39–42)	97.9 (96.7–98.9)		29.3 (23.5–36.6)			Williams [25]
Term at 2 weeks	30	40 (38–42)	(40–44)	97.8 (95–99)		27.2 (21.2–33.1)		1.3 (<92%) 0.0–6.3	Terrill [22]
Term at 1 month	45	39 (37–42)	44 (43–44)	97.1 (96.6–97.5)	80.4 (78.8–82.0)	25.4 (22.0–28.8)	16.2 (13.7–18.6)	0.39 (0.26–0.55)	Evans [27]
Term at 3 months	25	40 (38–42)	(51–56)	98.9 (97–100)		10.0 (7.4–12.6)			Terrill [22]
Term at 3 months	38	39 (37–42)	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)	Evans [27]
Extremely preterm infants									
Preterm at term equivalent	38	32 (24–36)	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)	Wellington [23]
Preterm at term equivalent	37	24 (23–25)	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)	Terrill [24]

Results are shown as median (range), unles otherwise stated. PCA: post-conceptual age; ODI: oxygen desaturation index, *i.e.* number of times·h^{-1} of sleep that S_{pO_2} drops by the given percentage from baseline. Reproduced and modified from [48] with permission.

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Table 2. S_{pO_2} targets for weaning off oxygen using motion-resistant oximeters with short averaging times

Corrected age post-term	Minimum mean S_{pO_2} %	Time S_{pO_2} <90% %	3% ODI
37–40 weeks	>93	<3	35
40–44 weeks	>93	<3	30
44–56 weeks (1–4 months)	>9	<3	15
>56 weeks (>4 months)	>93%	<3	7

3% ODI: 3% oxygen desaturation index, *i.e.* number of times·h^{-1} of sleep that S_{pO_2} drops by 3% from baseline. Reproduced and modified from [48] with permission.

seek help. Enabling open access to paediatric services offers a structured pathway for timely review in the event of parental concern and respiratory deterioration. Consideration of safe infant transport and associated monitoring should be performed [2].

Post-discharge

Clinical review by the neonatal community team within 48 h of discharge provides a timely opportunity for reassurance and support in the home setting, as well as addressing any practical and equipment-related issues. Growth is an important consideration in infants receiving supplementary oxygen therapy, and inadequate growth is commonly encountered in infants with chronic lung disease. Regular monitoring to ensure adequate growth, dietetic involvement where appropriate and optimisation of nutrition are recommended [17].

Timing of studies

Oximetry studies, performed at regular intervals within the home setting, ensure that an oxygen prescription is appropriate and titrated accordingly. The Australian and New Zealand positional statement proposes approximately monthly weaning off oxygen therapy [3],

Table 3. Comparison of the duration of home oxygen therapy

First author [ref.]	Cases n	Flow rates L·min^{-1}	S_{pO_2} target %	Duration months
Saletti [38]	93	0.06 (0.03–0.5)	92–98%	Daytime: 1 (0–13) Night-time: 2 (0–13)
Hudak [49]	30	0.125–0.5	⩾95%	4.5 (0.5–17)
Bertrand [50]	20	NA	NA	5.7±3[#]
Silva [51]	56	0.125 (0.03–0.85)	⩾95%	Daytime: 3 (1–23.5) Night-time: 5 (1–28.5)
Norzila [52]	32	NA	⩾94%	3.5 (3–6)[¶]
Oliveira [53]	46	NA	⩾93%	11 (4–51)
Yeh [6]	154	<0.125 to ⩾0.5	NA	7.6 (6–9.3)
Batey [29]	44	0.08–1.5	⩾93%	5 (2–24)

Data are presented as median (range) unless otherwise stated. NA: not available. [#]: data presented as mean±SD; [¶]: data presented as median (interquartile range). Reproduced and modified from [29] with permission.

while other studies have suggested that a more frequent and rapid approach is preferable [32] and is possible without adverse consequence [29, 58]. Accordingly, titration studies should be performed within a time frame of 3–5-week intervals, and more rapid weaning may be possible. Following a reduction in the oxygen flow rate, further weaning off night-time oxygen is not usually advised within 7 days.

Night-time weaning

While an infant is receiving HOT throughout the day and night, NPO performed on two consecutive nights provides an opportunity to assess the S_{pO_2} profile and desaturation indices at baseline (night 1) and then, if appropriate, at a reduced flow rate that is typically reduced by 0.1 L·min^{-1} (night 2) in infants >2.5 kg [58]. Oximeter alarms, set in accordance with age-specific reference ranges for the monitor being used, help guide the decision for a reduced flow rate on the second night. A safe reduction in oxygen flow rate decrements of 0.1 L·min^{-1} for infants >2.5 kg is supported by the influence of extraneous air, which dilutes the actual inspired oxygen concentration as tidal volumes increase with body weight [59]. Repeating titration studies at regular 3–5-week intervals until a flow rate of 0.1 L·min^{-1} is reached has been demonstrated to achieve timely weaning without adverse effect [29, 32]. A weight-based oxygen flow rate with weaning rates of <20 mL·kg^{-1}·min^{-1} was predictive of successful weaning off HOT in a large cohort of infants with BPD [60]. Once weaned to 0.1 L·min^{-1} at night, the infant may be gradually weaned onto air during the daytime. In infants >5 kg with mild to moderate BPD, evidence suggests that withdrawal of both daytime and night-time oxygen may be possible following successful completion of a night-time study in accordance with age-adjusted reference ranges (table 2) [60].

Daytime weaning

Feeding and activity are recognised times of exertion most likely to stress respiratory reserve. Wang *et al.* [17] observed a reduction in S_{pO_2} during infant feeding, and accordingly the initiation of gradual weaning may be suggested during this time. At the onset of daytime weaning, coordination of community review towards the end of a period of time in air enables observation and saturation monitoring to ensure that the infant has tolerated the daytime weaning period. A structured approach to daytime weaning involving regular monitoring and supervision may provide less confusion for parents/carers and may manage expectations. A proposed framework for daytime oxygen weaning (once an infant reaches 0.1 L·min^{-1} at night-time) is shown in table 4.

Once weaned onto daytime air, NPO should be repeated, as a transient recording of S_{pO_2} while an infant is awake does not accurately predict S_{pO_2} during prolonged sleep (figure 2). This can be undertaken at home as a two-night study with alarms on: night 1 performed with 0.1 L·min^{-1} and night 2, if appropriate, in air. Night-time oxygen may be discontinued

Table 4. Proposed daytime oxygen weaning schedule for infant time in air

	Time in air h (consider weaning every 3–4 days as tolerated)							
a.m.	1	1	2	2	3	3	4	4
p.m.	0	1	1	2	2	3	3	4

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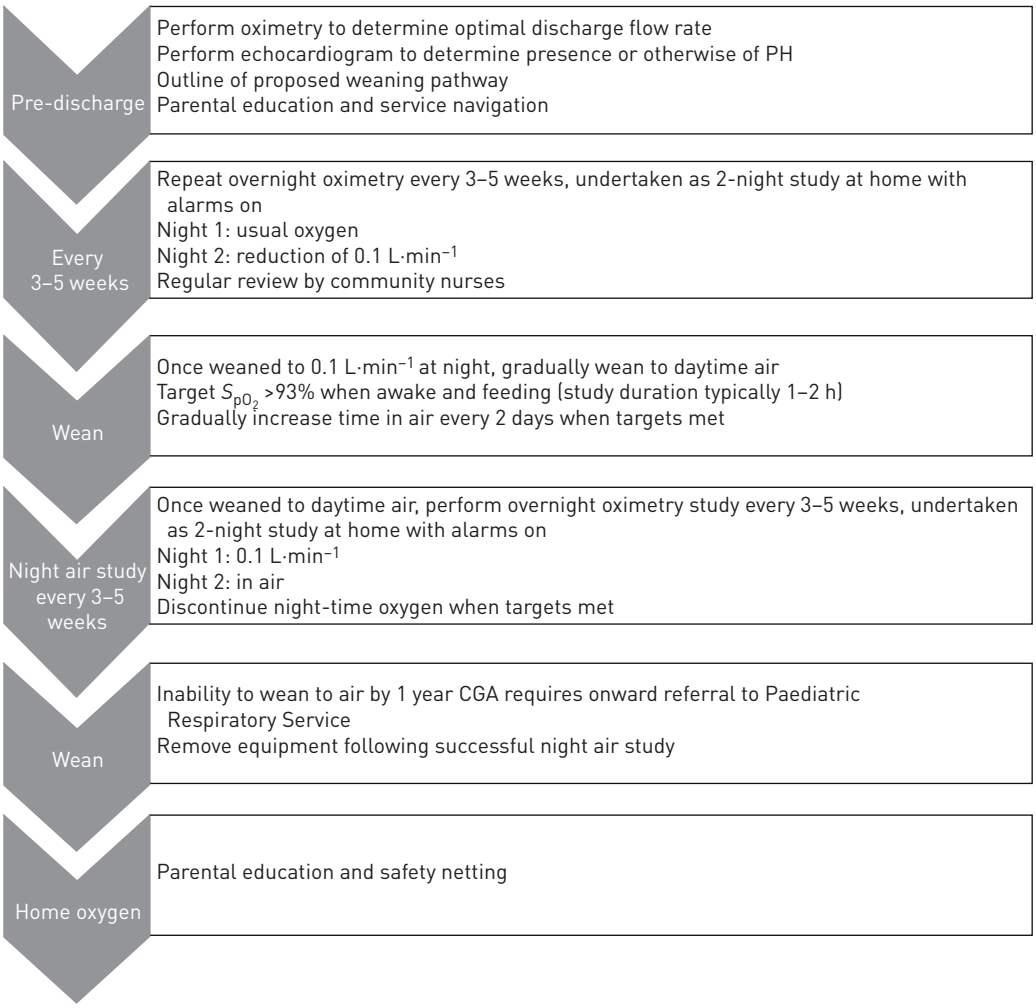

Figure 2. Structured weaning programme for infants requiring supplemental oxygen therapy on discharge into the community. CGA: corrected gestational age. Reproduced and modified from [61] with permission.

when S_{pO_2} targets are met, or NPO is repeated regularly every 3–5 weeks with ongoing oxygen requirement until target thresholds are achieved. Following successful completion of a night-time study in air, equipment may be removed from the home setting.

Home oximeters

The ATS strongly recommends the use of home saturation monitors by consensus agreement for infants with BPD requiring supplemental oxygen therapy [1]. Despite this strong recommendation, there is limited evidence to support their use.

Home oxygen monitoring devices may simply be used to support the weaning process and thus achieve a more rapid weaning through accessibility to equipment [32]. Additional perceived advantages of home oximeters include the potential early indication of worsening respiratory status as well as sudden severe hypoxaemia [61].

However, parents should be cautioned in false reassurance of normative oxygen saturations and encouraged to seek medical attention if they are worried about a change in their child [2]. Parental education regarding the signs and symptoms of deterioration and access to services are integral to discharge planning.

KHETAN *et al.* [61] identified cost as both a positive and a negative factor and, dependent on individual and family circumstances, monitoring devices may either increase or decrease parental anxiety and may have the potential to delay weaning if parents make unnecessary minor adjustments to flow rates, often prompted by false alarms.

Case study

A male infant was delivered by vaginal delivery at 27+3 weeks of gestation weighing 1.2 kg following prolonged preterm rupture of membranes and spontaneous onset of labour. Antenatal steroids and magnesium sulfate were administered prior to delivery. The infant commenced respiratory support shortly after delivery for respiratory distress. A chest radiograph demonstrated a ground-glass appearance in keeping with RDS. He was transitioned from CPAP to high-flow oxygen and this was gradually weaned and discontinued at 32 weeks post-conceptual age (PCA). Multiple desaturation episodes were observed and low-flow oxygen was therefore commenced with a noticeable reduction in events. At 35 weeks PCA, a further trial in air was performed; however, the infant continued to have ongoing desaturations requiring oxygen, and a low flow was continued at 0.2 L·min^{-1}.

The infant established full enteral feeds by 30 weeks PCA, and the management of suspected reflux, which was felt to be contributing to desaturations, was optimised. Bottle feeds were gradually introduced and his growth was satisfactory, tracking along the centiles. A cranial ultrasound scan initially demonstrated mild bilateral periventricular flare and there were no neurological concerns. A repeat cranial ultrasound scan at 36 weeks PCA was within normal limits.

Following discussion with the parents, a decision for discharge with HOT was agreed, and planning for the community transition ensued. NPO was performed prior to discharge to clarify the optimal oxygen flow rate. An echocardiogram performed at this time revealed no evidence of PH. A proposed pathway and time frame for the monitoring of and weaning off HOT was discussed, alongside advice for access to services and parental support. Basic life support training and assessment for safe travel in a car seat were performed. The infant was discharged at 38 weeks PCA receiving 0.2 L·min^{-1} of oxygen and bottle feeding.

Post-discharge, the neonatal community team maintained close telephone contact and regularly visited the home setting for review. There were no clinical or parental concerns. The infant continued to thrive, and NPO was performed at 4 weeks post-discharge (42 weeks PCA) for two consecutive nights using an oximeter with artefact rejection technology and short averaging time. The alarm limits for the oximeter were set to detect falls in S_{pO_2} to 90%. Night 1 was performed at baseline (0.2 L·min^{-1}) and night 2 at a flow rate reduced by 0.1 L·min^{-1} (to 0.1 L·min^{-1}) given there were no first-night concerns. The parents completed an overnight monitoring events diary to aid data interpretation including times and duration of awake periods, probe disconnection and disturbances. Oximetry results from >7 h of recording on both nights, which included episodes of active sleep as determined by heart rate variability, were in keeping with age-appropriate reference ranges for the recording device being used (table 5).

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Table 5. Mean S_{pO_2} and 4% oxygen desaturation index (ODI) performed in 0.2 L·min^{-1} (night 1) and 0.1 L·min^{-1} (night 2) of supplemental oxygen

	Night 1	Night 2
Mean S_{pO_2} %	98	96
4% ODI n·h^{-1}	3.9	7.4
3% ODI n·h^{-1}	5.6	11.4

The ODI gives the number of times·h^{-1} of sleep that S_{pO_2} drops by the given percentage from baseline.

The infant was subsequently weaned to 0.1 L·min^{-1} and gradually weaned to daytime air as per protocol. S_{pO_2} was monitored for initial short periods in air (1 h) while awake and feeding, and he displayed no signs of respiratory distress. The duration and frequency of time in air was gradually increased over a 4-week period, daytime oxygen was withdrawn and he continued with night-time oxygen.

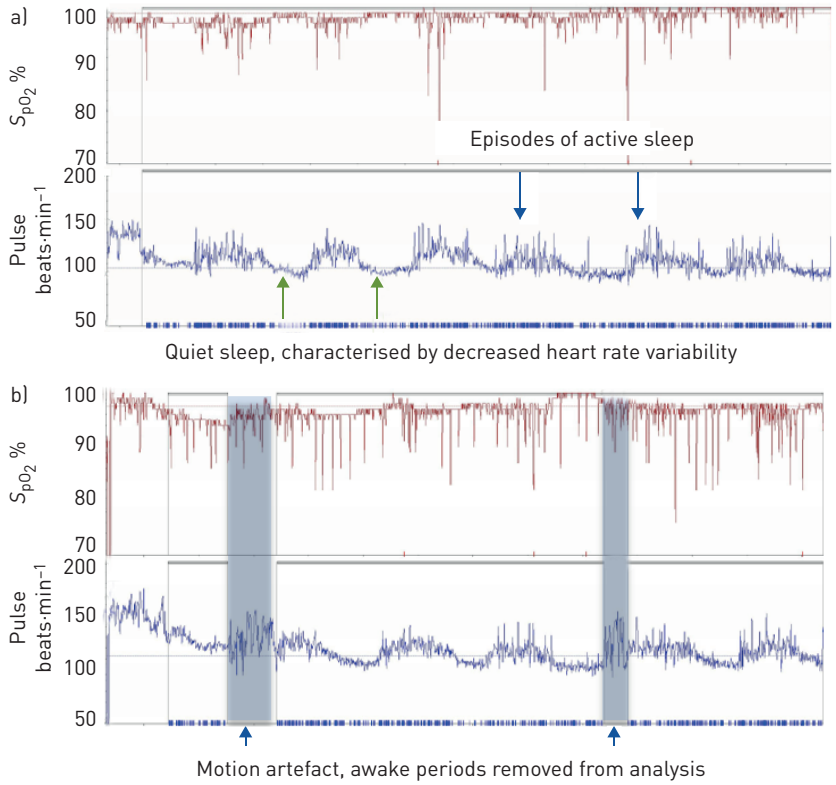

Figure 3. a) Pulse oximetry performed on night 1 in 0.1 L·min^{-1} of supplemental oxygen. Sleep-wave cycling is demonstrated with periods of active and quiet sleep characterised by heart rate variability. Analysis demonstrated intermittent desaturation during active sleep with a mean S_{pO_2} of 98% and 4% oxygen desaturation index (ODI) of 4.64 h^{-1}, appropriate for the post-conceptual age. b) Multiple transient episodes of desaturation clustered throughout night 2 (trial in air), more prominent during active sleep. Suspected awake periods were removed from the analysis. There was a mean S_{pO_2} of 97% and an elevated 4% ODI of 19.89 h^{-1} for the post-conceptual age. Traces provided courtesy of Emily Senior and Paula Lowe, Sleep Physiologists at University Hospital Southampton NHS Foundation Trust (Southampton, UK).

The infant continued to thrive, and at 3 months corrected gestational age, a repeat NPO was performed: night 1 at baseline (0.1 L·min^{-1}) and night 2 trial in air (figure 3). The results demonstrated normal mean S_{pO_2} levels (98% and 97%); however, the night 2 study, performed in air, demonstrated an elevated 4% ODI (19.9 h^{-1}) with clusters of desaturations in active and quiet sleep. Direct communication with the family confirmed that the infant was well with no concerns. The infant underwent monthly NPO, and at 9 months of age, oximetry demonstrated normal S_{pO_2} levels in air, and oxygen was discontinued and removed from the home.

Conclusion

There is inconsistency in the implementation and monitoring of and weaning off HOT for infants with neonatal respiratory disease [3–5]. This variation in current practice and lack of consensus is multifaceted, influenced by little objective evidence, and high-quality prospective studies are required. The potential for adverse consequences associated with hypoxia in infants is high, emphasising the importance of appropriate management on discharge from the neonatal unit. Poorer outcomes are associated with respiratory [13, 14], growth [15–17] and neurodevelopmental [18–20] impairment. A balanced approach considering the potential risks and benefits of HOT is required, and this is best supported by a structured, supervised approach to the initiation and monitoring of HOT for infants discharged from the neonatal unit into the community setting [29]. Further research is required to establish evidence-based target mean S_{pO_2} levels following discharge into the community for infants with BPD and to better understand the impact of mean S_{pO_2} levels and desaturation indices on long-term respiratory, growth and neurodevelopmental outcomes.

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