Oxygen titration and compliance with targeting oxygen saturation in preterm infants

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Chapter 5

The effect of a smaller target range on the compliance in targeting and distribution of oxygen saturation in preterm infants

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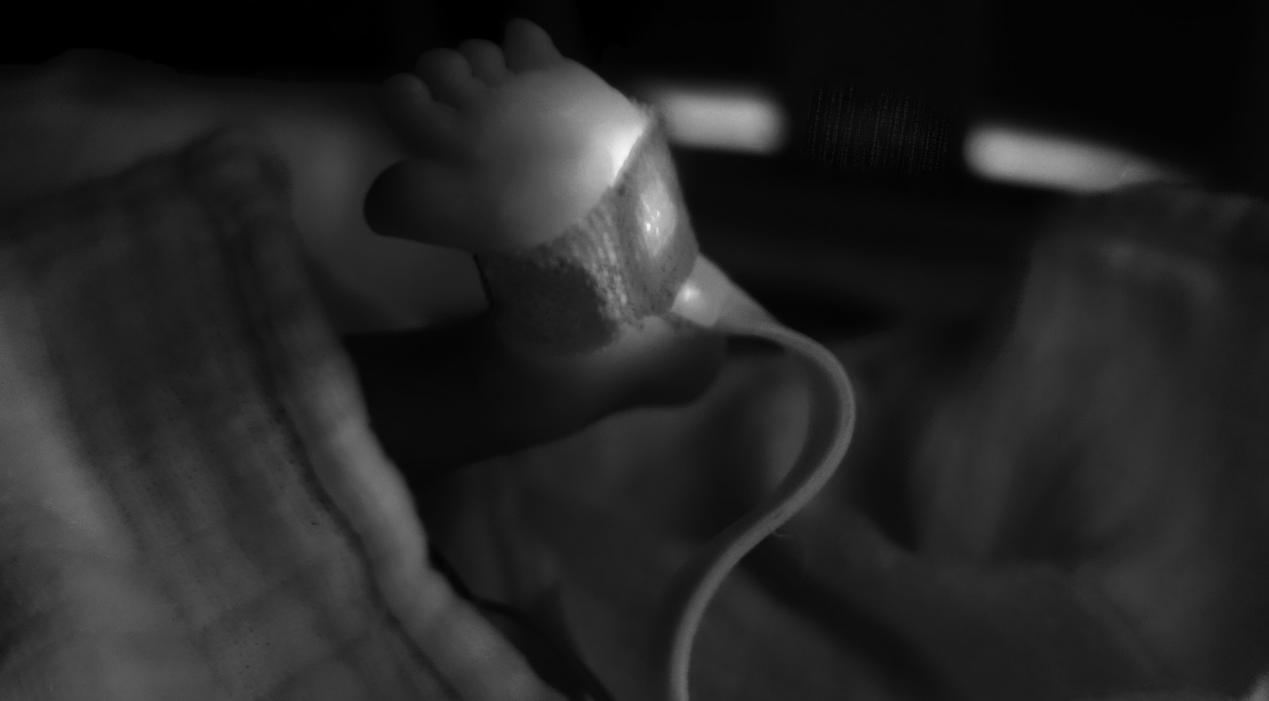

ABSTRACT

Background: Following recent recommendations, the oxygen saturation (SpO_2) target range (TR) for preterm infants in our nursery was narrowed towards the higher end from 85-95% to 90-95%.

We determined the effect of narrowing the SpO_2 TR on the compliance in TR and distribution of SpO_2 in preterm infants.

Methods: Infants <30 weeks of gestation receiving oxygen were retrospectively compared, before and after changing the TR from 85-95% to 90-95%, during their admission on the neonatal intensive care unit (NICU). For each infant distribution of SpO_2 was noted by collecting SpO_2 samples every minute, and the percentage of time spent with SpO_2 within and outside TR was calculated. During both periods oxygen was manually adjusted. Hypoxaemic events (SpO_2<80%) where oxygen was titrated were identified and analysed.

Results: Data were analysed for 104 infants (57 before and 47 after the range was narrowed). The narrower range was associated with an increase in the median SpO_2 (93 (91–96)% vs 94 (92-97)%;*p*< 0.01), but did not lead to an increase in median (IQR) time SpO_2 within 90-95% (49.2 (39.6-59.7)% vs 46.9 (27.1-57.9)%;ns). The distribution of SpO_2 shifted to the right with a significant decrease in SpO_2 <90%, but not <80%, and a trend towards a higher occurrence of SpO_2 >95%. There was no difference in the frequency, depth and duration of hypoxaemic events and the titration of oxygen.

Conclusion: Narrowing the TR from 85-95% to 90-95% in preterm infants caused a shift of the SpO_2 distribution to the right with less occurrence of a low SpO_2, no change in time spent between 90-95%, but a trend towards more time with SpO_2 >95%.

What is already known

1. Titrating oxygen manually to maintain SpO_2 within intended target range can be challenging.
2. A higher SpO_2 target range (91-95%) leads to a lower mortality, but also more retinopathy of prematurity (ROP) when compared to a lower SpO_2 target range (85-89%).

What this study adds

1. Implementing a narrower TR from 85-95% to 90-95% did not lead to a change in duration of a SpO_2 level between 90-95%.
2. The distribution of SpO_2 shifted towards the right, with less lower SpO_2, but no decrease in hypoxaemia (SpO_2 <80%), and a trend towards hyperoxaemia (SpO_2 >95%).

INTRODUCTION

Oxygen therapy in preterm infants is routinely monitored by pulse oximetry during their admission in a neonatal intensive care unit (NICU). In order to prevent the risk of hypoxaemia and hyperoxaemia, neonatal caregivers in most units titrate fraction of inspired oxygen (FiO_2) manually in order to stay within the set oxygen saturation (SpO_2) target range (TR). Recent randomised trials in evaluating lower SpO_2 TR (85%-89%) versus higher SpO_2 TR (91%-95%) in preterm infants[25 43 44] have shown that using a higher SpO_2 TR led to a reduced mortality but increased the rate of retinopathy of prematurity (ROP) when compared to a lower SpO_2 TR.[25 44] Although the groups in the studies[25 43 44] had a substantial overlap in SpO_2 levels and the optimal TR remains undefined, European and Dutch guidelines now recommend a SpO_2 TR of 90–95% for preterm infants.[76]

Maintaining SpO_2 within TR during oxygen therapy requires compliance with alarm limit settings, prompt responses and careful oxygen titration of caregivers which can be a difficult task to perform.[18-20] Hyperoxaemia can easily occur, especially when supplemental oxygen is given after hypoxaemic events.[24] The workload of caregivers, education and awareness about the hazards of hypoxaemia and hyperoxaemia, and appropriate alarm settings, can also influence the caregivers compliance in SpO_2 targeting.[18 31 40]

We recently reported that the compliance in SpO_2 targeting significantly improved after creating more awareness by training and implementation of a guideline for manual oxygen titration.[77] However, following the recommendation of European and Dutch guidelines our TR for SpO_2 was recently changed from 85-95% to 90-95%. This could lead to more intrinsic stability in infants[74] but we also recognised that complying with this smaller range could be challenging for the NICU-nurses.[18 30 74] We audited the effect of narrowing TR towards the higher end on the distribution of SpO_2 and compliance in SpO_2 targeting during oxygen therapy.

METHODS

A prospective designed, retrospective pre-post implementation study was performed in the NICU of the Leiden University Medical Centre (LUMC), which is a tertiary level perinatal centre with an average of 550 intensive care admissions per year. In the Netherlands, no ethical approval is required for anonymised studies with medical charts and patient data that were collected and noted for standard care. The LUMC Medical Ethics Committee provided a statement of no objection for obtaining and publishing the anonymised data. All

preterm infants born <30 weeks of gestation (GA) admitted to the NICU in LUMC between February 2014 and October 2014 (SpO_2 TR 85-95%) and November 2014 and March 2015 (SpO_2 TR 90-95%) receiving respiratory support (endotracheal and non-invasive ventilation) in the NICU. For respiratory support the AVEA ventilator (CareFusion, Yorba Linda California) was used. Data were collected until infants were transferred from the NICU. Preterm infants with major congenital heart disease were excluded. All preterm infants received, as part of standard care, a loading dose of 10 mg/kg caffeine base followed by 5 mg/kg/day. Doxapram hydrochloride (2 mg/kg/hr) was added in case of refractory apnoeas.

The characteristics of each infant as well as clinical parameters and ventilator settings (including FiO_2 and SpO_2) were sampled every minute and routinely collected in the patient data management system (PDMS) (Metavision; IMDsoft, Tel Aviv, Israel). During both periods the heart rate and SpO_2 were collected using a Masimo pulse oximeter (Masimo Radical, Masimo Corporation, Irvine CA, USA) integrated in a Philips bedside Intellivue monitor (Philips Healthcare Nederland, Eindhoven, The Netherlands) with an averaging time set at eight seconds. The pulse oximeter probe was placed around the hand or foot of the infant (right hand in case of a patent ductus arteriosus). During both periods caregivers titrated the supplemental oxygen manually following local guidelines (Figure 1). During both periods the alarm was activated when SpO_2 was below or above the set TR. Before the start of each shift the TR and alarm settings were checked by the nurse.

We were interested in the extent to which nurses were able to comply with the narrower TR, and compared the percentage of time spent with SpO_2 between 90-95% when FiO_2 >0.21. Additionally the percentage of time spent with SpO_2 85-95%, >95%, >98%, <90%, <85% and <80% were calculated. To evaluate whether the SpO_2 distribution changed when no oxygen therapy was given to the infant, the percentage of time that SpO_2 was <90%, <85% and <80% when infants were breathing room air was also calculated.

In addition, all hypoxaemic events during non-invasive ventilation were identified in PDMS and analysed starting at the occurrence of SpO_2 <80% accompanied with bradycardia (<80 beats per minutes (bpm)), until the administered oxygen returned to the baseline oxygen level before the hypoxaemic event occurred. As data is sampled every minute, every hypoxaemic event where supplemental oxygen was titrated were evaluated by documenting the following characteristics: lowest stored minute value (depth) and count in low minute values (duration) of HR <80 bpm, lowest stored minute value (depth) and the count in low minute values (duration) of SpO_2 <80%, ΔFiO_2 (maximum additional FiO_2 minus baseline FiO_2), the count in minute values with additional oxygen, occurrence and count in minute values with SpO_2 >95%. Hypoxaemia was defined as SpO_2 <80% and hyperoxaemia as SpO_2 >95%.

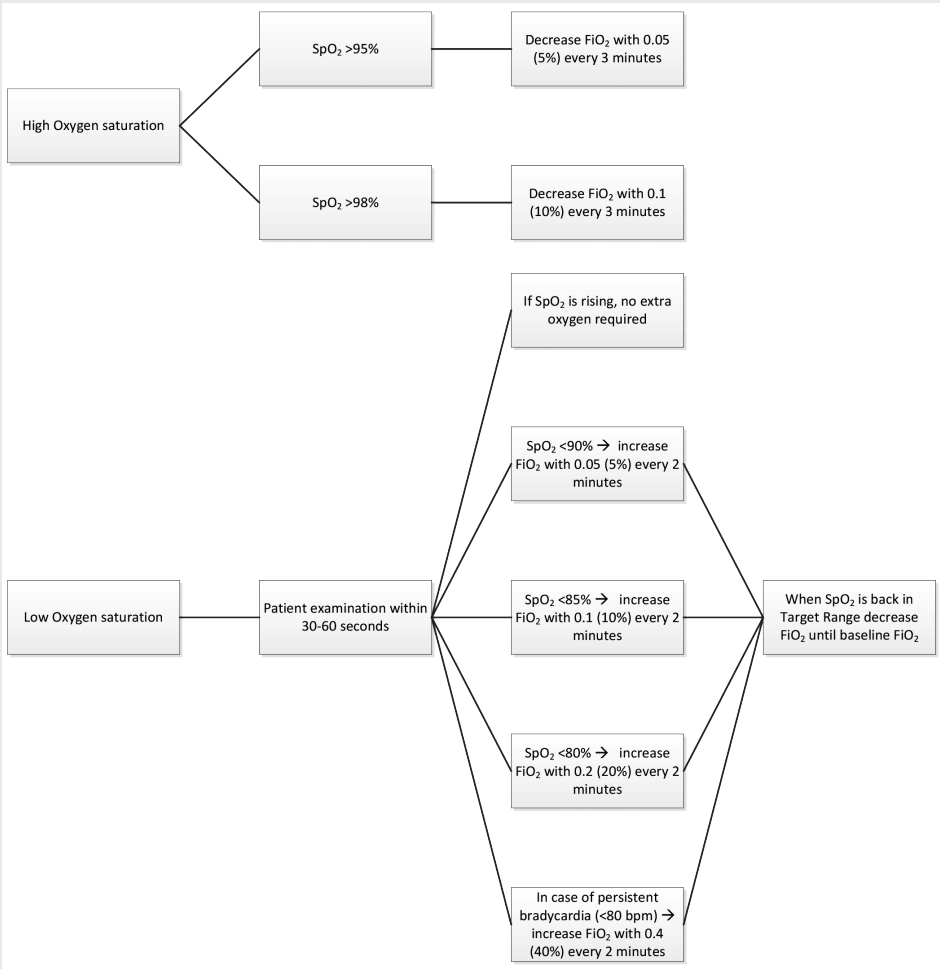

Figure 1. Oxygen Titration guideline

Statistical analyses

For this study a convenience sample was used. For the first period, infants were included that were born one month after the implementation of staff training and an oxygen titration guideline was implemented until TR was changed. For the second period, infants were included after implementing the new TR, until the time point automated oxygen control was implemented in our unit. Quantitative data are presented as median (IQR), mean ± SD or number (percentage) where appropriate. The total time with SpO_2 levels within various ranges for FiO_2 >0.21 was collected for each infant individually before and after implementation of a narrowed TR and was aggregated as a percentage of recorded time (median (IQR)). The

Mann-Whitney-U test for non-parametric comparisons for continuous variables is used, to compare the patient characteristics and the hypoxaemic event characteristics. The Kruskal-Wallis rank sum test was used to compare proportions of recorded time with SpO_2 within various ranges for each patient individually. A Chi-square test was used to analyse discrete variables. If one of the cells had an expected count of less than five the Fisher's exact test was used. P-values < 0.05 were considered to indicate statistical significance. Statistical analyses were performed using IBM SPSS Statistics version 23 (IBM Software, NY, USA, 2012) and R 3.2.0 (R Core Team (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

RESULTS

During the study period of 13 months, a total number of 104 infants born <30 weeks of gestation were admitted to our NICU. Of these infants, 57 were born before changing the SpO_2 TR, and 47 infants after this change. No infants were excluded for congenital abnormalities. There were no differences in median (IQR) GA (28+3 (26+4 – 29) vs 27+5 (26+1 – 29) weeks; ns) and birth weight (1000 (855 – 1206) vs 900 (740 – 1153) grams; ns) or other characteristics (Table 1).

Table 1. Patient characteristics

	SpO2 TR 85-95% N= 57	SpO2 TR 90-95% N= 47	*p*-value
Gestational age (wk)	28+3 (26 +4 – 29)	27+5 (26+1 – 29)	0.25[a]
Birth weight (g)	1000 (855 – 1206)	900 (740 – 1153)	0.17[a]
Male, no (%)	32 (56)	26 (55)	0.93[b]
Caesarean delivery, no (%)	31 (54)	25 (53)	0.90[b]
Singletons, no (%)	39 (68)	26 (55)	0.17[b]
Apgar 5 min.	7 (6-9)	7 (7-9)	0.49[a]

[a] Independent samples Mann-Whitney U test
[b] Chi square test

Effect on compliance and SpO_2 distribution

During the TR 85-95% period 630.244 data points were collected and during the TR 90-95% period 402.993 data points of SpO_2 measurements were collected when oxygen therapy was given. The median (IQR) number of data points per infant were not significantly different (2359 (377 - 14129) vs 3082 (1352 – 15024) data points; ns).

After changing the TR, there was a slight, but significant increase in median (IQR) SpO_2 (93 (91 – 96)% vs 94 (92 - 97)%);p<0.02) (Figure 2), while the FiO_2 slightly decreased (0.28 (0.25-0.32) vs 0.26 (0.24-0.30);p<0.01). Narrowing TR did not lead to an increase in median (IQR) length of time SpO_2 was within 90-95% (49.2 (39.6-59.7)% vs (46.9 (27.1-57.9)%; ns) (Table 2, Figure 2). The time SpO_2 was >95% and >98% increased, but did not reach statistical significance (Table 2, Figure 2). Changing the TR led to a significant decrease in both SpO_2 <90% (15.7 (7 - 21)% vs 10.7 (8.4 - 13.7)%;p<0.05) and for SpO_2 <85% (6.2 (2.5 - 8.0)% vs 3.5 (2.6 - 5.3)%;p<0.05), but SpO_2 <80% was similar (Table 2, Figure 2).

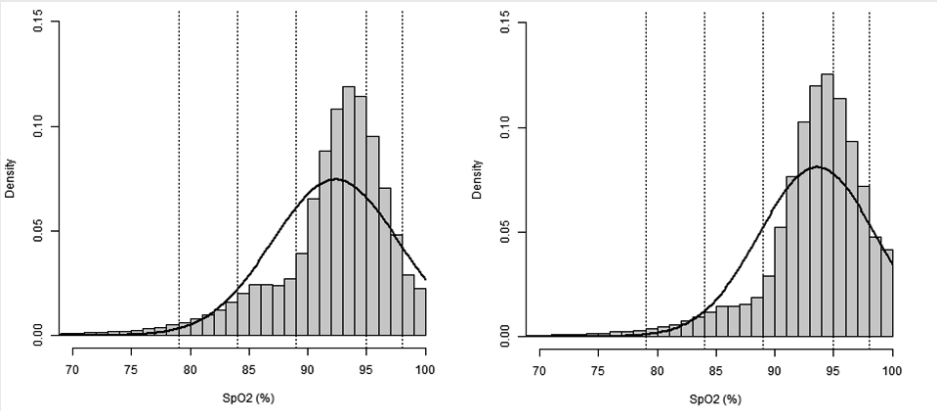

Figure 2. Time with SpO_2 within various ranges collated over all infants and aggregated as total proportion of recorded time

Table 2. Median (IQR) in different saturation ranges

	TR 85-95%	TR 90-95%	*p*-value*
SpO_2 <80%	1.7 (0.8-2.6)	1.5 (0.8 - 2.1)	ns
SpO_2 <85%,	6.2 (2.5 - 8.0)	3.5 (2.6 - 5.3)	<0.05
SpO_2 <90%	15.7 (7 - 21)	10.7 (8.4 - 13.7)	<0.05
SpO_2 85-95%,	61.9 (48.5 – 72.2)	56.5 (32.6 – 64.7)	ns
SpO_2 90-95%,	49.2 (39.6 - 59.7)	46.9 (27.1 - 57.9)	ns
SpO_2 >95	30.8 (22.6 - 44.5)	39.0 (28.8 - 59.2)	ns
SpO_2 >98%,	6.1 (2.3 - 12.1)	8.9 (3.3 - 17.9)	ns

*Statistical analysis comprised nonparametric Kruskal-Wallis rank sum test.

During the TR 85-95% period 471.642 data points were collected and in the TR 90-95% period 424.700 data points of SpO_2 measurements were collected when infants were breathing room air. The median (IQR) number of data points per infant, was not significantly different (5722 (3112 - 10395) vs. 8102 (3635 – 13363) data points; ns). Changing the TR did not lead to significant changes in SpO_2 distribution and SpO_2 <90% was similar when infants were breathing room air (Table 3).

Table 3. Median (IQR) in different saturation ranges when breathing room air

	TR 85-95%	TR 90-95%	*p*-value*
SpO_2 <80%	0.3 (0.1-0.9)	0.3 (0.1 – 0.9)	ns
SpO_2 <85%,	1.1 (0.5 – 2.9)	1.2 (0.7 – 2.7)	ns
SpO_2 <90%	3.6 (1.6 – 11.7)	4.5 (2.1 – 7.9)	ns
SpO_2 90-95%,	29.8 (14.7 – 49.8)	36.5(20.7 – 46.1)	ns
SpO_2 >95%	60.1 (39.5 – 83.2)	58.2 (41.1 – 76.6)	ns
SpO_2 >98%,	14.9 (5.8 – 42.8)	13.9 (6.2 – 27.3)	ns

*Statistical analysis comprised nonparametric Kruskal-Wallis rank sum test.

Effect on hypoxaemic events and how oxygen was titrated

During non-invasive respiratory support 168 hypoxaemic events with supplemental oxygen occurred in 28/57 (49%) infants before TR was changed and 204 events in 32/47 (68%) infants after the TR was changed (ns). There was no difference between the lowest minute value and the count in minute values with bradycardia and SpO_2 <80% (Table 4). There was a trend towards more often hyperoxaemia after the TR was changed (63% (106/168) vs 73% (148/204);*p*=0.051) (Table 4), while there was no difference in ΔFiO_2, duration of titrating oxygen down to the baseline and count in minute values with hyperoxaemia (Table 4).

Table 4. ABC characteristics with oxygen therapy

	TR 85-95% (ABC= 168)	TR 90-95% (ABC = 204)	*p*-value*
ABC with SpO2 >95%	64%	73%	ns
Lowest minute value during bradycardia, bpm (depth)	69 (61-75)	70 (62-75)	ns
Count minute values with bradycardia, min (duration)	1 (1-1)	1 (1-1)	ns
Lowest minute value during SpO_2 <80, % (depth)	72 (61-77)	73 (63-77)	ns
Count minute values SpO_2 <80%, min (duration)	1 (1-2)	1 (1-2)	0.004
ΔFiO_2 (Maximum increase – baseline FiO_2)	0.19 (0.6-0.21)	0.19 (0.7-0.21)	ns
Count minute values of FiO_2 titration to baseline oxygen concentration, min	3 (2-7)	2 (2-6)	ns
count minute value with SpO_2 >95%, min	1 (1-3)	1 (0-2)	ns

DISCUSSION

Our study demonstrated the effect of narrowing the SpO_2 TR of 85-95% to 90-95% on SpO_2 distribution of preterm infants when supplemental oxygen is supplied. We observed a small increase in median SpO_2 and a shift of the distribution to the right with the new TR. This led to a decrease in SpO_2 between 80% and 89%, the occurrence in hypoxaemia (<80%) did not change. Changing the TR did not lead to a change in the time SpO_2 spent between 90-95%, but there was a trend towards more hyperoxaemia. A similar effect was observed around hypoxaemic events. There was no change in occurrence and duration of hypoxaemic events and how oxygen titration was performed, but the occurrence of hyperoxaemia increased, although this raise was not significant.

These results reflect the effort taken by the nurses to comply with the new TR, but it was difficult for them to titrate oxygen in order to stay within the narrow TR. Nevertheless, as we managed to decrease the exposure to SpO_2 <90%, narrowing the TR in our unit could lead to similar beneficial effects as were shown in recent trials. [25 43 44]

To our knowledge this is the first report on the effect when the TR is significantly narrowed to only the upper part of the original TR when oxygen is manually titrated. Laptook *et al*. reported the effect of changing the SpO_2 TR, but the change in range was much smaller (from 90-95% to 88-94%) when compared to ours.[29] It is difficult to compare our results with their findings, but they also reported no change in the time SpO_2 spent within the TR. They also observed no difference in the mean percentage of time spent within the TR, but this might be attributed to the small change in TR.[29] Mills *et al*. reported a lower compliance when a narrow SpO_2 TR was used, except when preterm infants participated in a trial comparing TR.[30]

Changing the TR did not lead to a change in SpO_2 distribution when infants were breathing room air and there was no decrease in lower SpO_2. This finding, together with the observation that the time SpO_2 was 90-95% did not change when oxygen was given, could indicate that the nurses in our unit already had the tendency to keep SpO_2 in the higher end of the intended TR when 85-95% was used. This is in line with the observation in previous studies that nurses were less compliant in the upper alarm limits.[18 19 74 78] Indeed, the clinical trials comparing lower vs higher SpO_2 TR also reported that the median levels of oxygen saturations were higher than intended TR in both treatment groups.[25 43 44] It is likely that caregivers favour SpO_2 closer to the higher end of TR because infants are intrinsically more stable in the higher SpO_2 region.

We observed a decrease in time SpO_2 spent <90% when oxygen was given, which is comparable to the findings of recent trials comparing low (85-89%) vs high TR (91-95%). These trials showed that a TR above 90% led to a decrease in mortality.[25 43 44] A low SpO_2 TR has been associated with an increased rate of hypoxaemic events.[29 79] However, we did not observe a change in hypoxaemia, or hypoxaemic events and how these were handled, after we increased the lower limit of the TR. This lack of effect is probably also a consequence of how nurses titrated oxygen before the TR was changed. Changing the TR towards the higher end led to a non-significant increase in hyperoxaemia and more often hyperoxaemia when oxygen was titrated after an hypoxaemic event. This has also been observed in previous studies, as also in the trials comparing lower and higher TRs,[25 43 44] which could then potentially lead to an increase in retinopathy of prematurity (ROP).

Titrating oxygen, using a smaller TR in instable premature infants with fluctuating SpO_2 requires constant nursing intervention.[24] It has been reported that a narrower TR leads to an inevitable increase of SpO_2 alarms.[80] These alarms contribute to all other alarms on a NICU where a high number of alarms are false, or without any clinical relevance.[81] Excessive exposure to alarms can effect alarm response from caregivers and lead to alarm fatigue, which is potentially harmful to patients.[82 83] Although we have not measured the number of alarms in our study, but this can affect the compliance in TR negatively.

While maintaining SpO_2 within a narrow TR is a difficult task to perform when oxygen needs to be titrated manually, automated oxygen regulation could be more effective and lead to the desired compliance in keeping SpO_2 within the narrow range.[33 35 36 38 39] However, when Wilinska *et al*. used automated oxygen control and compared the TR 87-93% with a more narrow TR (90-93%), results similar as in our study were observed. The narrow range of 90-93%, resulted in less time with lower SpO_2 (80-86%), but more time with higher SpO_2 (94-98%). In addition, there were also no differences in the amount and duration of hypoxaemic events.[84]

This study is a report of a quality improvement project, and inherently the retrospective character is a limitation. Although the groups compared were not different in basic characteristics and also there were no further policy changes occurred during the study period, conditions we did not recorded or measure could have led to bias. Also, the Masimo oximeter algorithm could not be updated in the Philips monitors we used in our unit, which is reflected by the well described dip[75] in the frequencies of SpO2 87-90%. However, the same oximeters and monitors were used in both groups and thus did not influence the observed distributions when comparing the groups. Furthermore, we did not adjust for the contribution of the number of hypoxaemic events of each patient, but we considered

every hypoxaemic event as an independent event because all events are handled the same for each infant. Due to the retrospective character, we could only use a one-minute time interval for sampling parameters, which is less frequent than reported in other studies.[14 85] It is possible that in both groups we missed hypoxaemic events that were resolved within one minute. These limitations indicate that the results have to be interpreted with caution, this study was not designed to compare morbidity and mortality but as an audit in SpO_2 targeting.

In conclusion, narrowing the TR from 85-95% to 90-95% in preterm infants did not lead to a change in the time SpO_2 spent within 90-95%. There was however a shift of the SpO_2 distribution to the right with a decrease in SpO_2 less than 90%, no change in hypoxaemia, but a trend in hyperoxaemia. This beneficial effect could be further improved by increasing the compliance to a narrow TR.