Oxygen titration and compliance with targeting oxygen saturation in preterm infants

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Title: Oxygen titration and compliance with targeting oxygen saturation in preterm infants
Issue Date: 2017-03-15

Chapter 8

General Discussion

The neonatal staff at LUMC observed that although a TR for oxygen saturation (SpO_2) was set for preterm infants admitted to the NICU, the actual SpO_2 often fell outside this range, frequently leading to hypoxaemia and/or hyperoxaemia. This was particularly prevalent when oxygen desaturation occurred during apnoea, when additional oxygen was administered as part of the intervention. To verify this observation, we performed an audit to evaluate targeting SpO_2 and to determine how oxygen was titrated. In this first audit, we investigated the occurrence and duration of hyperoxaemia (defined as SpO_2 >95%) after additional oxygen was administered to treat for ABC (apnoea with bradycardia and cyanosis). This audit led to the conclusion that performance with respect to oxygen titration should be improved, which would significantly improve outcome in these infants. In the subsequent three years, we implemented a series of policy changes in order to improve compliance with respect to targeting SpO_2 and to reduce the occurrence and duration of hypoxaemia and hyperoxaemia in these infants. The effect of each of these policy changes was assessed by performing subsequent audits. It is important to note that these audits were designed to test how often a nurse was able to maintain SpO_2 within TR during and following ABCs, as well as the effect on SpO_2 distribution during oxygen therapy.

For these audits, we performed observational pre/post cohort studies. To define the outcome, we used the parameters that were used for standard care, which included the vital signs and treatment parameters that were stored in our patient data management system at one-minute intervals. This approach enabled the caregivers to compare the results during daily rounds.

In the first audit, we were interested in determining how ABC is treated when oxygen therapy was given. We found that nurses were often unable to achieve the target oxygenation range when oxygen was given during an ABC event. We found that when a nurse performed oxygen titration during ABC, post-ABC hyperoxaemia developed in 79% of cases, and the duration of hyperoxaemia was significantly longer than the duration of both bradycardia and hypoxaemia. The duration of oxygen supplementation was also significantly longer in cases in which the ABC included hyperoxaemia compared to cases in which no hyperoxaemia occurred. Strikingly, we found that hyperoxaemia lasted longer when the patient was in ambient air before the ABC occurred; this was likely the consequence of not adjusting the alarm limits for SpO_2 when oxygen therapy was initiated. Our medical and nursing staff were understandably alarmed by these findings, and it was obvious that quality improvement was needed.

Although the results of our first audit were alarming, poor compliance with respect to targeting SpO_2 is not unique to the NICU. Several studies reported low compliance with respect to targeting SpO_2 in terms of both TR[19 20 29 31 37] and alarm settings.[18 30] Moreover, many factors can influence this compliance, including knowledge regarding the adverse effects of hypoxaemia and hyperoxaemia, the nurse-patient ratio, and the availability of a suitable guideline regarding oxygen titration practices.[29 30 37 48-50 68]

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In the years following this initial audit, policy changes were implemented with respect to oxygen titration and targeting SpO_2. After each change in the policy, a new audit was performed, and the results obtained in the post-change audit were compared to the results obtained before the change. For training the staff, in addition to explaining the results of the audit we also educated the staff with respect to the risk associated with hypoxaemia and hyperoxaemia. To guide the nurses in terms of oxygen titration, we also introduced a specific guideline. When we presented the results of the first audit, we found that the nurses were highly motivated to improve the way in which they titrate oxygen. After we evaluated the effect of training, we found that we needed to comply with the new international recommendation; therefore, we narrowed the SpO_2 TR by increasing the lower value. This change could have decreased compliance with respect to targeting SpO_2, thereby changing SpO_2 distribution and influencing the effect of the training and guidelines. We performed an audit to evaluate this change. Compliance with a narrow TR can be extremely challenging, particularly in a busy neonatal care unit. We therefore determined whether compliance could be improved by introducing automated oxygen control, after which we performed a final audit.

First, we discuss compliance with respect to targeting SpO_2 and the effect on SpO_2 distribution. We then discuss how ABC was handled, including how oxygen was titrated. Because the strengths and weaknesses associated with these studies are quite similar among the studies, these are discussed at the end of the chapter.

Compliance with respect to targeting SpO_2 and SpO_2 distribution
Several studies have described efforts designed to increase nurses' compliance with respect to targeting SpO_2. These efforts included training and/or the implementation of guidelines, and they had various degrees of success.[29 37 48-50 66] Here, we opted for both approaches (i.e. training and the implementation of guidelines); we therefore developed a training programme designed to teach all caregivers in our NICU regarding the risks associated with hypoxaemia and hyperoxaemia, and we implemented an oxygen titration guideline. There was a change in pulse oximeter use in the unit (Masimo instead of Nellcor) and to compare two cohorts using similar algorithm for pulse oximetry, a new cohort before training was needed. This was a cohort that was admitted 10 months after the implementation of the new pulse oximeters in our unit.

Both the training and implementation of a guideline led to a small but significant decrease in median SpO_2, but did not affect the interquartile range. However, compliance with respect to targeting SpO_2 improved, which was reflected in the SpO_2 distribution. Specifically, the amount of time in which SpO_2 was within TR increased from 46% to 62%. This improvement was primarily reflected in a reduction in the prevalence of hyperoxaemia; however, the amount of time below TR was unchanged, and the prevalence of hypoxaemia did not decrease.

It is likely that the combination of the teaching programme and oxygen titration guideline made the nurses more aware of the hazards associated with hyperoxaemia, which ultimately led to more careful and timely titration of oxygen levels. The lack of an effect with respect to hypoxaemia could be explained by the fact that our nurses already respond to hypoxaemia as promptly as possible, meaning that there was little room for improving recovery time. It is difficult to determine which – if any – component in the policy changes (i.e. training and/or guideline) played the largest role in this improvement; it is also possible that the positive effect was the result of the combined approach. Indeed, previous studies reported less improvement when either training or a guideline was implemented.[37 40 49 70] We recognise that the guideline regarding oxygen titration was likely not followed precisely, and we did not measure compliance with respect to the precise timing and steps taken. Nevertheless, we believe we were successful in terms of giving our nurses guidance with respect to oxygen titration. This initiative had a clear positive effect, and if the observed reduction in hyperoxaemia can be maintained through repetitive training, outcome among preterm infants will likely improve. In addition to performing repeat training sessions, both oxygen titration and SpO_2 distribution are now evaluated daily during rounds.

Recent randomised trials comparing a lower SpO_2 TR (85%-89%) with a higher TR (91%-95%) in preterm infants[25 43 44] revealed that using the higher TR led to reduced mortality, but increased the prevalence of retinopathy of prematurity (ROP) compared to using the lower TR.[25 44] These results led to the development of new European and Dutch guidelines, and we therefore changed the TR for SpO_2 in our NICU from 85-95% to 90-95%. Although this new TR was implemented in order to prevent low SpO_2, we also expected that nurses would be less able to comply with the narrower TR. Therefore, the effect of narrowing the TR towards the higher end was evaluated with respect to SpO_2 distribution and compliance in terms of targeting SpO_2 during oxygen therapy. We observed that the new, narrower TR resulted in a small increase in median SpO_2 and a rightward shift in the distribution. This led to a decrease in the prevalence of SpO_2 at values ranging from 80% to 89%, but had no effect on hypoxaemia (i.e. SpO_2 <80%). Changing TR did not affect the duration at which SpO_2 was 90-95%, although it did cause a trend toward an increasing occurrence of hyperoxaemia. These results indicate that the nurses attempted to comply with the new TR, but found it difficult to titrate oxygen sufficiently to stay within the narrow TR.

The change in median SpO_2 values after TR was narrowed was relatively small. This finding – together with the observation that the time during which SpO_2 was 90-95% did not change – suggests that the nurses in our NICU already tended to maintain SpO_2 at the higher end of the intended TR when the wider range (i.e. 85-95%) was used. This is consistent with previous reports that nurses are generally less compliant with respect to alarm settings for the upper SpO_2 limits.[18 19 74 78] Indeed, clinical trials comparing lower vs. higher TR also reported that the median SpO_2 levels exceeded the intended TR in both treatment groups.[25]

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[43] [44] It is therefore likely that caregivers favour an SpO_2 value that is closer to the higher end of TR, as infants are intrinsically more stable when maintained at higher SpO_2 levels. Nevertheless, given that we were able to reduce the prevalence of SpO_2 values below 90%, narrowing TR in our unit may have beneficial effects similar to those reported in recent trials.[25] [43] [44] However, caution must be exercised, as the lower prevalence of SpO_2 values <90% coincided with a trend towards an increased prevalence of hyperoxaemia.

Titrating oxygen manually in order to stay within a narrow TR can be challenging; in contrast, using automatic oxygen titration can provide superior results.[86] [87] Randomised trials that compared automated oxygen control systems with manual titration for short periods revealed that the amount of time that SpO_2 was within TR increased by 8-24%.[35] [36] [38] [39] The use of an automated oxygen control system can also reduce the amount of time the nursing staff must spend with preterm infants who frequently experience desaturation.[35] [88] [89]

In our NICU, we introduced an AVEA-CLiO$_2$ automated closed-loop oxygen control system (CareFusion, Yorba Linda, CA), and we routinely use this system to improve targeting SpO_2. We therefore performed a new audit in order to compare automated oxygen control with manual titration of oxygen in terms of maintaining SpO_2 within the intended TR. Also in this audit a new cohort for measurements before implementation was needed. The Masimo pulse oximeter in the Philips monitor used the unrevised algorithm, while the Masimo pulse oximeter for the automated oxygen control used the revised algorithm. To use similar algorithms in both groups the Masimo pulse oximeter integrated in the ventilator was used for measuring SpO_2, while the automated oxygen control was turned off in the cohort before implementation.

We found that the introduction of automated oxygen control significantly increased the amount of time spent in which SpO_2 was within TR; in addition, the prevalence of hyperoxaemia decreased significantly. On the other hand, the amount of time in which SpO_2 was <90% increased, although we found no change in the total duration of hypoxaemia. Apparently, using automated oxygen control has no effect on the occurrence or depth of hypoxaemia; however, using an automated oxygen control system provides a more rapid response when SpO_2 is below TR. The response to very low SpO_2 values is similar between the automated oxygen control system and manual titration by a nurse. It is known that nurses have an aversion to very low SpO_2 values.[11] [34] [35] [39] Thus, the gradual but incessant titration of oxygen by the automated oxygen control explains the decrease in hyperoxaemia under these conditions.

There is one item that could have influenced the response to the nurses during the pre/post period of the automated oxygen control. During this period the Masimo oximeter was connected to the AVEA ventilator and SpO_2 values were depicted on the AVEA ventilator and not on the Philips bedside monitor. This indicated that this values where only visible at the bedside of the patient. Adding the pulse oximeter measurements to the AVEA automatically

lead to more acoustic alarms. The acoustic alarms in this ventilator are differentiated on the severity of alarms. However the high priority alarm of having a SpO_2 value below of above the set SpO_2 TR, could not be differentiated from an alarm indicating circuit disconnected or high peak pressure. The alarms needed immediately response from nurses and could only be turned off on the AVEA. It is possible that this also has contributed to good compliance as nurses were more often near the patient for evaluating the alarms.

Apnoea, bradycardia, and cyanosis (ABC)

The incidence of apnoea of prematurity (AOP) is inversely correlated with both gestational age and birth weight; thus, nearly all infants born at <29 weeks gestation and/or weighing <1000 grams at birth develop AOP.[55] Because the respiratory system is not fully developed in preterm infants, AOP is often difficult to treat. Moreover, because apnoea is often combined with bradycardia and cyanosis (leading to the condition known as ABC), preterm infants often receive supplemental oxygen for prolonged periods of time. Given the unpredictability and relative frequency of most forms of ABC, maintaining SpO_2 within the TR is often difficult and time-consuming.[33] Importantly, when a preterm infant experiences intermittent periods of hypoxaemia lasting approximately 1 minute or more, the infant develops an increased risk of adverse outcome.[14] Our baseline assessment in 2012 provided us with key insight regarding how ABC was handled and how oxygen was titrated following ABC. The findings underscored the need for increased awareness and more accurate handling of ABC in our NICU. The effect of our policy changes on both ABC outcome and oxygen titration was audited as part of the quality improvement project, using the minute values that were used for standard care. Although we recognise that this is only a crude measurement, the count in minute values reflect the duration of hypoxaemia, bradycardia, and hyperoxaemia, and the lowest measured values reflect the depth of hypoxaemia and bradycardia.

To improve the way in which ABC is handled in our NICU, we provided training and implemented an oxygen titration guideline. We observed that this approach resulted in a faster response by the nurses to hypoxaemia and improved titration of oxygen after ABC. Moreover, although the occurrence of hypoxaemia and hyperoxaemia did not decrease, the duration of both hypoxaemia and hyperoxaemia decreased significantly. When we included the initial first baseline measured in our analysis, we observed that although training decreased the median duration of hyperoxaemia by 50% (from 2 minutes values to 1 minute value), the largest decrease in hyperoxaemia duration (from 7 minutes values to 2 minutes values) occurred before training was given and before the guideline was implemented. Consistent with this finding, the duration of oxygen supplementation after ABC was greatly decreased (from 14 minute values to 3 minute values) even before training. One possible explanation for this finding is that the results of the first audit were already communicated to the nursing staff before the training session and guidelines were implemented. Indeed,

the team members who were responsible for quality improvement were also working daily in our NICU.

The following two items were not difficult to correct once the nurses become aware of them: *i*) setting the alarm, and *ii*) the use of the "increase FiO_2" button on the AVEA ventilator. The "increase FiO_2" button on the AVEA ventilator provides a controlled way to temporarily increase the oxygen being delivered. When this button is pressed, the ventilator increases the fraction of inspired oxygen (FiO_2) by 20% (relative increase) for two minutes, after which FiO_2 returns to the previous setting. In addition, we emphasised the proper use of alarm settings, particularly when the infant was breathing ambient air (SpO_2 alarm set to 100%) but received additional oxygen following ABC (the alarm should be set to 96%). Although these items were stressed both during the training sessions and in the guidelines, it is likely that the early communication of our findings already improved compliance among our nurses and they had already started using the "increase FiO_2" button more often and were more vigilant in adjusting the alarm settings. Nevertheless, the duration of hypoxaemia decreased only after training and guideline implementation, and the duration of hyperxaemia decreased further. Thus, it is likely that training and guideline implementation were successful in terms of creating additional awareness regarding the consequences of ABC and the need to titrate oxygen more diligently. When we consider the total effect of training and implementing the new guidelines, it becomes apparent that our nurses were strongly motivated to improve their responsiveness and intervention.

After we narrowed the TR from 85-95% to 90-95%, we also evaluated how ABC events were handled. Lower SpO_2 is associated with an increased prevalence of hypoxaemia.[79] However, this relationship could not be confirmed in our study, as we observed no decrease in the occurrence or duration of ABC events in cases in which oxygen was given when TR was set to avoid hypoxaemia. It is possible that a beneficial effect occurred in ABC cases in which additional oxygen was not needed; however, we did not measure this. The narrower (higher) TR led to a trend toward an increased prevalence of hyperoxaemia, which is consistent with our observation with respect to SpO_2 distribution. It is possible that the lack of effect was influenced by the higher tendency of nurses to maintain SpO_2 at the upper end of TR when the 85-95% range was used compared to the 90-95% range.

In addition, we examined the effect of using automated oxygen control on ABC outcome. Implementing automated oxygen control had no effect on the depth or duration of bradycardia, but it significantly shortened the duration of hypoxaemia. The need for oxygen prior to ABC was higher with automated oxygen control than with manual control, whereas the prevalence of ABC with hyperoxaemia decreased with the use of automated oxygen control. Furthermore, with automated oxygen control, the duration of hyperoxaemia was significantly shorter compared to manual control. Although the median number of ABC events per day did not change after automated oxygen control was implemented, the total

number of ABC events was higher with automated oxygen control compared to manual control. This unexpected finding may be explained by the fact that nurses intervene more frequently when performing manual control, and this increased diligence could have prevented and/or inhibited apnoea events, leading to less need for additional oxygen. Specifically, the nurse can reposition the CPAP prongs/mask, provide tactile stimulation, and/or perform suctioning; in contrast, an automatic oxygen controller can perform only one intervention (increasing the oxygen level) in response to only one input parameter (SpO_2). However, after this study we also evaluated ABC cases in which no additional oxygen was given, but we observed no differences between automated oxygen control and manual control. Nevertheless, it remains possible that some ABC events were prevented by the nurses' intervention.

The observed increase in the prevalence of ABC events in our study is in contrast with the findings of a previous study by Waitz *et al*. comparing manual and automated oxygen titration, which found a reduction in hypoxaemic episodes in the automated oxygen control group.[85] However, it is difficult to directly compare our results with the findings of Waitz *et al*. First, the TR used by Waitz *et al*. (88-96%) was wider than our TR (90-95%). Moreover, Waitz *et al*. defined hypoxaemia as SpO_2 <88%, whereas our definition was <80%. Finally, in contrast with our study, Waitz *et al*. did not combine hypoxaemia with bradycardia (defined as heart rate <80 bpm).

Strengths and limitations of the studies

The studies described in this thesis were performed in the form of audits after the introduction of various policy changes in our NICU. This study design was pragmatic and did not increase the workload of the medical or nursing staff. The benefit of defining outcome using the data collected from standard care is that the results can easily be translated when evaluating the patient during daily rounds. Moreover, the results reflect the actual clinical situation, as the data were collected for the entire time during which the infants required respiratory support in the NICU, in a setting in which the infants received care from the nursing staff and in which workload varied. Moreover, the data were collected for a relatively long period during routine care, thereby decreasing the risk of a Hawthorne (i.e. observer) effect.

The observed improvement in quality was achieved only because the nursing and medical staff embraced the policy changes and were motived to improve their outcome with respect to targeting SpO_2. We therefore ensured that the entire staff was updated regarding the results of each audit. Group meetings were held regularly, allowing the nursing staff to discuss any problems and/or concerns regarding the policy changes, and these meetings were generally well attended. In addition, it was important that the team members responsible for quality improvement were available for troubleshooting on a daily basis. Another strength of this thesis project lies in the fact that the nurse responsible for quality

improvement was also a working member of the NICU staff and was therefore familiar with all of the practical issues associated with targeting SpO$_2$ and handling ABC events.

Although this thesis project was comprised of prospective observational cohort studies, we used parameters that were collected during standard care in order to assess outcome. Therefore, the studies have the same limitations intrinsic to a retrospective study. We used data that were sampled at 1-minute intervals and stored in our Patient Data Management System (PDMS). In contrast with other studies,[14][85] we were unable to collect data more frequently. However, although our approach provided a slightly more crude reflection of the time course of SpO$_2$, the results are still comparable, as the studies used the same methodology. In addition, because the data were collected using standard methods, our medical and nursing staff were familiar with the values and could draw from these data when evaluating patients during daily rounds.

After the first audit, we changed the brand of pulse oximeters in our NICU from a Nellcor oximeter to a Masimo SET pulse oximeter. Then we became aware that the Masimo algorithm integrated into the Philips bedside monitor (Intellivue MP70, Tilburg, The Netherlands), still used the unrevised version, which is reflected by the well described dip in the frequencies of SpO$_2$ 87-90%, and higher frequencies of saturation between 91-96%.[75][94] In contrast, the Masimo integrated to the AVEA ventilator used a revised algorithm. It is therefore possible that this change in pulse oximeter could have influenced the effect of the policy changes. However, to ensure that our analyses of the data were not biased by the use of different pulse oximeters or algorithms, we re-analysed data collected from new cohorts in which the same pulse oximeter was used, and we obtained similar results.

Lastly, we did not adjust our analysis for the number of ABC events in each patient; rather, we considered each ABC to be an independent event, as all events are handled the same. Due to the retrospective nature of the analysis, it is possible that we may have missed any ABC events that were resolved within one minute. Given these limitations, the results presented in this thesis should be interpreted with caution. Moreover, this study was not designed to compare morbidity and mortality before and after policy changes; rather, it was designed to evaluate SpO$_2$ distribution and compliance with respect to targeting SpO$_2$.

Overall effect of the project

Compliance and SpO$_2$ distribution

Although each policy change had relatively little effect on hypoxaemia, we observed a small but steady decrease in hypoxaemia after each change, leading to 50% reduction over three years' time (from 1.9% to 0.9%;Table 1). The effect of quality improvement on hyperoxaemia was considerably larger – hyperoxaemia decreased from 44% to 19%. It is difficult to determine which quality improvement component contributed most to this improvement, as the change in the SpO$_2$ TR could have obscured the effects of training and/or guideline implementation.

Table 1. Percentage of time in different SpO_2 ranges measured at each audit

	Before training & guideline implementation (baseline)	After training & guideline implementation	After changing SpO_2 TR from 85-95% to 90-95%	Before autoFiO$_2$	During autoFiO$_2$
SpO_2 <80%	1.9 (1.0 - 3.0)	1.7 (0.8-2.6)	1.5 (0.8 - 2.1)	1.1 (0.4 - 1.7)	0.9 (0.5 - 2.1)
SpO_2 <85%	5.9 (2.8 - 7.9)	6.2 (2.5 - 8.0)	3.5 (2.6 - 5.3)	2.7 (1.4 - 4.0)	3.2 (1.8 - 5.1)
SpO_2 <90%	15.7 (7 - 21)	15.7 (7 - 21)	10.7 (8.4 - 13.7)	8.6 (7.2 - 11.7)	15.1 (14.0 - 21.1)
SpO_2 85-95%	48.0 (19.6 - 63.9)	61.9 (48.5 - 72.3)	56.5 (32.6 - 64.7)	48.4 (41.5 - 56.4)	62.0 (56.4 - 68.6)
SpO_2 90-95%	44.0 (27.8 - 66.2)	49.2 (39.6 - 59.7)	46.9 (27.1 - 57.9)	41.9 (30.6 - 49.4)	19.3 (11.5 - 24.5)
SpO_2 >95%	44.0 (27.8 - 66.2)	30.8 (22.6 - 44.5)	39.0 (28.8 - 59.2)	41.9 (30.6 - 49.4)	19.3 (11.5 - 24.5)
SpO_2 >98%	9.4 (4.2 - 26.8)	6.1 (2.3 - 12.1)	8.9 (3.3 - 17.9)	10.1 (3.7 - 14.4)	2.1 (0.7 - 3.1)

Notes: values are presented as the Median (IQR).

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Both training and the introduction of automated oxygen control led to increased compliance with respect to targeting SpO_2. Narrowing the SpO_2 TR toward the higher end led to fewer low SpO_2 values but did not decrease hypoxaemia; rather, we observed was a trend toward hyperoxaemia, indicating that the nurses found it difficult to comply with the more narrow TR. The quality improvement steps taken during this thesis project received considerable attention from the nurses and doctors, and it was clear that during the three years the staff became much more aware of the need to effectively target SpO_2 and to avoid both low and high SpO_2 levels during oxygen therapy. Although the introduction of automated oxygen control had relatively little effect on the ability to avoid low SpO_2 levels, it played a large role in decreasing hyperoxaemia.

Handling ABC events and oxygen titration
The quality improvement project in this thesis increased awareness of the need to promptly handle ABC events and titrate oxygen diligently. However, the beneficial effects of the policy changes with respect to *how* ABC events are handled and *how* oxygen is titrated are less clear. When we look at the effect over the three-year project (Table 2), it becomes clear that most of the reduction in hyperoxaemia occurred before the policy changes were implemented. This can likely be explained by the fact that the first audit results were communicated to the nurses even before training and before the guideline was developed.

After training and implementing the oxygen titration guideline, duration of both hypoxaemia and hyperoxaemia after ABC reduced further. We also observed an effect when the target SpO_2 range was narrowed from 85-95% to 90-95%. The effect of training apparently did not last, however, as the duration of both hypoxaemia and hyperoxaemia increased before the introduction of automated oxygen control, which again reduced the duration of both hypoxaemia and hyperoxaemia.

Table 2. Clinical features of the ABC events measured at each audit

	Baseline assessment[a]	Before training & guideline implementation	After training & guideline implementation	After changing SpO$_2$, TR from 85-95% to 90-95%	Before AutoFiO$_2$	During AutoFiO$_2$
Number of independent ABC event, N	257[a]	186[b]	168[b]	204[b]	61[c]	254[c]
ABC with SpO$_2$ >95%	79%	73%	64%	73%	84%	67%
Depth of bradycardia, bpm	70 (63-76)	70 (60-75)	69 (61-75)	70 (62-75)	67 (61-72)	69 (60-74)
Duration of bradycardia, min	1 (1-1)	1 (1-1)	1 (1-1)	1 (1-1)	1 (1-1)	1 (1-1)
Depth of SpO$_2$ <80%, min	68 (61-73)	70 (62-76)	72 (61-77)	73 (63-77)	68 (50-73)	68 (56-75)
Duration SpO$_2$ <80%, min	2 (1-2)	2 (1-2)	1 (1-2)	1 (1-2)	2 (1-3)	1 (1-2)
Baseline FiO$_2$,	0.23 (0.21-0.28)	0.25 (0.21-0.31)	0.25 (0.21-0.30)	0.22 (0.21-0.25)	0.24 (0.21-0.27)	0.27 (0.25-0.31)
Max increase FiO$_2$	0.39 (0.30-0.67)	0.44 (0.39-0.52)	0.43 (0.37-0.51)	0.41 (0.31-0.45)	0.20 (0.19-0.47)	0.30 (0.18-0.50)
Duration of titration to baseline oxygen concentration, min	14 (4-52)	3 (2-16)	3 (2-7)	2 (2-6)	3 (2-6)	3 (2-4)
Duration SpO$_2$ >95%, min	7 (1-25)	2 (0-7)	1 (1-3)	1 (0-2)	5 (3-11)	2 (1-4)

Notes: Values are presented as percentages and median (IQR).
[a] Nellcor oximeter
[b] Masimo oximeter with the unrevised algorithm
[c] Masimo oximeter with the revised algorithm

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GENERAL CONCLUSIONS

The stepwise quality improvement project implemented in this thesis project improved compliance with respect to both targeting SpO_2 and improving oxygen titration. This led to improved SpO_2 distribution and decreases in both hypoxaemia and hyperoxaemia, as well as slight improvements in the handling of ABC events and oxygen titration following ABC. The introduction of training sessions, guidelines, and automated oxygen control increased awareness regarding the consequences of hypoxaemia and hyperoxaemia and led to increased efforts to prevent these complications. The beneficial effects culminating from three years of quality improvement will likely continue to improve outcome among preterm infants admitted to our NICU.

FUTURE PERSPECTIVES

Although we made clear progress with respect to targeting SpO_2 by reducing both hypoxaemia and hyperoxaemia, further studies are needed in order to determine whether these beneficial effects improve the long-term outcome of preterm infants in our NICU. Given that the beneficial effects of training tend to fade with time, the use of repetitive training should be integrated into daily care and should be adjusted as needed. Automated oxygen control systems are used increasingly in neonatal intensive care units, and trials are currently being performed to test its effect on long-term outcome. Although the use of automated oxygen control reduces hyperoxaemia, it appears to have little effect on hypoxaemia, although it is possible that changes in the system's algorithm could improve further. Several automated oxygen control devices are now available, and studies are needed in order to compare their effectiveness. Regardless, increasing oxygen using an automated system has no effect in cases of apnoea-induced oxygen desaturation. Future developments in technology should focus on the early detection and/or prevention of apnoea, as well as an integrated automated response in both oxygen levels and non-invasive ventilation. Additional studies are also needed in order to determine the ideal SpO_2 TR when using automated oxygen control. With respect to policy changes, collecting data at a higher rate (for example, at 1-second intervals instead of 1-minute intervals) may provide a more precise measure of the beneficial effect of specific interventions. This approach will also provide important information regarding fluctuations in SpO_2 in preterm infants and may even serve to indicate that an ABC is imminent, thereby decreasing the incidence of hypoxaemia and bradycardia.