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# Changes in Attitudes and Actual Practice of Oxygen Therapy in ICUs after Implementation of a Conservative Oxygenation Guideline

Chloe CA Grim, Hendrik JF Helmerhorst, Marcus J Schultz, Tineke Winters, Peter HJ van der Voort, David J van Westerloo, and Evert de Jonge

**BACKGROUND:** Little is known to what extent attitudes of ICU clinicians are influenced by new insights and recommendations to be more conservative with oxygen therapy. Our aim was to investigate whether implementation of a conservative oxygenation guideline structurally changed self-reported attitudes and actual clinical practice. **METHODS:** After the implementation of a conservative oxygen therapy guideline in 3 teaching hospitals in the Netherlands, ICU clinicians were surveyed regarding their attitudes toward oxygen therapy. The survey results were compared with survey results taken before the introduction of the new guideline. Arterial blood gas analysis data and ventilator settings were retrieved from all patients admitted to the participating ICUs in the studied period, and changes after implementing the guideline were assessed. **RESULTS:** In total, 180 ICU clinicians returned the survey. Compared to before implementation of a conservative oxygen guideline, more clinicians chose a preferred  $P_{aO_2}$  and an oxygen saturation measured from an arterial sample ( $S_{aO_2}$ ) limit after implementation of the guideline. In general, clinicians reported a more conservative approach toward management of  $F_{IO_2}$  and less frequently increased the  $F_{IO_2}$ . In the period after the active implementation of the guideline, 5,840 subjects were admitted to the participating ICUs and 101,869 arterial blood gas analyses were retrieved. Actual practice changed with overall lower oxygenation levels (median  $P_{aO_2}$  77.93 mm Hg, compared to 86.93 mm Hg before implementation) of arterial blood and a decrease of PEEP and  $F_{IO_2}$ . **CONCLUSIONS:** Implementing a conservative oxygenation guideline was an effective method that changed self-reported attitudes and actual clinical practice and improved adherence to conservative oxygenation targets in a short period of time. *Key words:* guideline; oxygen; intensive care units; critical care; mechanical ventilators; surveys and questionnaires. [Respir Care 2020;65(10):1502–1510. © 2020 Daedalus Enterprises]

## Introduction

Despite accumulating evidence suggesting adverse effects of liberal oxygenation strategies in critical care, optimal targets of oxygenation remain a matter of debate.<sup>1-4</sup>

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A dose-response relationship has been shown between  $P_{aO_2}$  and mortality, yet arterial oxygen and saturation targets associated with optimal outcome in ICU patients vary across clinical studies and in different scenarios, and clinicians may consider several factors when determining which  $P_{aO_2}$  values should primarily be targeted.<sup>1,3,5-7</sup>

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Supplementary material related to this paper is available at <http://www.rcjournal.com>.

In 2012, we performed a survey of ICU personnel to elicit self-reported behavior with respect to oxygen therapy, and we retrieved arterial blood gas (ABG) data and ventilator settings to assess actual ventilatory practice.<sup>8</sup> Most clinicians acknowledged the potential adverse effects of prolonged exposure to hyperoxia. Nevertheless, extracted data exposed that this knowledge was not consistently reflected in clinical practice, showing a striking contrast between self-reported tolerance of low arterial oxygen levels on the one hand and actual treatment with frequent supraphysiologic oxygenation in ICU patients on the other hand.

Subsequently, we introduced a stepwise implementation of conservative oxygenation targets in the same participating ICUs and reported that this strategy was feasible, effective, and safe in the care of critically ill patients.<sup>9</sup> However, we did not know whether the implementation of this approach in an experimental setting structurally and persistently changed the views and actual practice of ICU clinicians with respect to oxygen therapy after the implementation period.

The aim of this study was to investigate whether self-reported attitudes and actual clinical practice were structurally changed after the active implementation of the conservative oxygenation targets. We hypothesized that, compared to before the implementation of conservative oxygenation targets, awareness and self-reported behavior of conservative oxygenation increased and ventilatory settings would more often be adjusted to achieve more conservative levels. Likewise, we postulated that arterial hyperoxia and hypoxia would occur less frequently due to increased awareness and stricter adherence to target guidelines.

## Methods

### Study Phases

We performed this project in 3 consecutive phases, of which the first 2 phases have been described previously.<sup>8,9</sup> The following oxygen therapy strategies were applicable. During the baseline period (June 2012 to August 2012),<sup>8</sup> standard treatment with local guidelines, recommended a  $P_{aO_2} > 75$  mm Hg as the lowest acceptable  $F_{IO_2}$ . During the implementation period (July 2012 to July 2014),<sup>9</sup> there were 2 phases. In phase 1, we implemented a written guideline as well as education and feedback on conservative oxygen therapy. Target values were  $P_{aO_2}$  55–86 mm Hg and

## QUICK LOOK

### Current knowledge

Accumulating evidence indicates harmful effects of liberal oxygen therapy. Self-reported tolerance of ICU clinicians toward conservative oxygen therapy showed a contrast with actual clinical practice in that supraphysiologic oxygenation was generally permitted. Implementing conservative oxygenation targets in an experimental setting can be effective and safe.

### What this paper contributes to our knowledge

Our results indicate that implementing a conservative oxygenation guideline improved adherence to conservative oxygenation targets, which may benefit outcomes of critically ill patients. After a stepwise implementation of a conservative oxygen therapy guideline, more clinicians were accepting of conservative oxygenation targets and indicated that they would decrease oxygen therapy sooner. Education, feedback, and temporary decision support in the ICU was a feasible implementation method that rapidly and structurally changed clinicians' attitudes and behavior.

$S_{pO_2}$  92–95%. In phase 2 (December 2013 to July 2014), we continued as in phase 1 with the addition of a computerized decision-support system. Target values were  $P_{aO_2}$  55–86 mm Hg and  $S_{pO_2}$  92–95%. During the follow-up phase (July 2014 to September 2015), target values of  $P_{aO_2}$  55–86 mm–Hg and  $S_{pO_2} > 92\%$  were adopted in the local guideline, and there was no more active feedback or computerized decision support. The importance of the follow-up phase lies in the absence of active implementation measures. Therefore it more closely represents normal clinical practice, without direct influence of research activities.

### Survey

The survey distributed at follow-up was identical to the survey used at baseline. The survey was designed to elicit self-reported behavior of ICU personnel with respect to oxygen therapy and was a modified version of surveys used previously in Canada, Australia, and New Zealand.<sup>8,10,11</sup> The survey consists of multiple-choice questions addressing specific clinical scenarios (see the supplementary materials at <http://www.rcjournal.com>). The target population consisted of physicians and nurses working in 3 participating tertiary-care, closed-format, mixed medical and surgical ICUs in Amsterdam (no. = 2) and Leiden (no. = 1) in the Netherlands. In these hospitals, all ICU clinicians (ie, ICU nurses and physicians) were allowed to autonomously

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modify ventilator settings. ICU clinicians were invited by email to complete the online survey. A reminder was sent once to all participants.

### Subject Data

The full study project included all patients admitted to the participating ICUs between June 2012 and September 2015, subdivided into cohorts from baseline (as previously published<sup>8</sup>), implementation (as previously published<sup>9</sup>), and follow-up (novel data in this paper). Anonymous encrypted data were automatically extracted from the patient data management system database (MetaVision, iMDsoft, Leiden, The Netherlands). The Dutch National Intensive Care Evaluation registry,<sup>12</sup> a high-quality database in which most Dutch ICUs participate, provided anonymous subject demographic data and data to quantify severity of illness. Arterial blood gas (ABG) analyses and concurrent ventilator settings with hourly pulse oximetry data were extracted from ICU admission to ICU discharge or death. Venous blood gas samples and patients on extracorporeal membrane oxygenation were excluded from the study. Informed consent or approval by an ethical committee was not needed according to the Dutch Medical Research Involving Human Subjects Act because only non-identifying registered data were used.

### Statistical Analysis

Survey data are presented as proportions of the total number of respondents, unless specified otherwise. Depending on data distribution, data are presented as mean  $\pm$  SD or median (interquartile range). Differences in survey responses over time were analyzed using the chi-square test or the Fisher exact test as appropriate.

For the ABG data, mean and median were calculated over all ABG analyses. In a subset of mechanically ventilated subjects with 2 or more ABG samples with concurrent ventilator settings recorded, clinicians' responses were examined by assessing the adjustments in  $F_{IO_2}$  and PEEP. Subsequently, successive  $P_{aO_2}$  values after  $F_{IO_2}$  or PEEP adjustment were analyzed. Differences in ABG data and mechanical ventilation settings between baseline and follow-up were analyzed using with the Mann-Whitney  $U$  test for numerical non-normally distributed data or with the chi-square test for categorical data. Differences between the 3 phases (ie, baseline, implementation, and follow-up) were analyzed with the Kruskal-Wallis or one-way analysis of variance test depending on distribution. Analyses were performed in subgroups of subjects resembling the case scenarios in the survey (ie, ARDS, cardiac ischemia, cerebral ischemia, sepsis, and untreatable anemia). The subgroups were based on admission diagnosis, except for ARDS and untreatable anemia. For the ARDS subgroup, we selected

data from subjects admitted with ARDS as APACHE-IV reason for admission or when the  $P_{aO_2}/F_{IO_2}$  ratio was  $< 100$  mm Hg without an admission diagnosis of heart failure. For the untreatable anemia case scenario in the survey, we selected data if hemoglobin was  $< 4$  mmol/L in 2 consecutive ABG results, where anemia appeared to be untreated. We also conducted linear regression models adjusting for study phase for these subgroups. A 2-sided  $P < .05$  was considered statistically significant. Statistical analyses were conducted using R i386 3.4.4 and SPSS 23 (IBM, Armonk, New York).

## Results

### Survey

The survey was sent to 500 ICU clinicians and returned by 180 respondents (response rate 36%; to view the complete survey, see the supplementary materials at <http://www.rcjournal.com>). Respondents consisted of 19 intensivists (10.6%), 6 fellows (3.3%), 8 residents (4.4%), 143 ICU nurses (79.4%), and 4 ICU nurses in training (2.2%). The 3 medical centers were equally represented in the group of respondents.

During follow-up, after implementation of the conservative oxygenation targets, more respondents considered oxygen-induced lung injury a major concern when placing a patient on mechanical ventilation in comparison to baseline (76% vs 59%;  $P < .001$ ). The number of respondents who considered high tidal volumes and high ventilator pressures a greater threat for lung injury for mechanically ventilated subjects than high  $F_{IO_2}$  did not change (81% vs 72%;  $P = .07$ ).

In total, 76% of respondents at follow-up chose  $P_{aO_2}$  52.5–75 mm Hg as the lowest acceptable  $P_{aO_2}$  range for 15 min, and 23% of respondents chose  $P_{aO_2}$  30–52.5 mm Hg (Figure 1). This was significantly different from baseline ( $P = .001$ ), where 81% of respondents chose  $P_{aO_2}$  52.5–75 mm Hg and 12% chose  $P_{aO_2}$  30–52.5 mm Hg. For the minimal acceptable  $P_{aO_2}$  for periods between 24 and 48 h, 92% of respondents at follow-up chose  $P_{aO_2}$  52.5–75 mm Hg, which was significantly more than at baseline (74%;  $P < .001$ ; Figure 1).

In most scenarios, a significant difference was found between survey responses between follow-up and baseline for  $F_{IO_2}$  adjustments after  $P_{aO_2}$  values of 68 and 90 mm Hg (Table 1). In the ARDS case, with a  $S_{aO_2}$  of 90–100%, more respondents would lower  $F_{IO_2}$  at follow-up compared to baseline. In the sepsis case, which involved a septic patient with  $S_{aO_2}$  85–100%, more respondents would lower  $F_{IO_2}$  at follow-up compared to baseline. For the cardiac ischemia, cerebral ischemia, or untreatable anemia scenario, self-reported adjustment of ventilator settings did not change over time. Overall, survey responses did not change

## OXYGEN THERAPY IMPLEMENTATION IN THE ICU

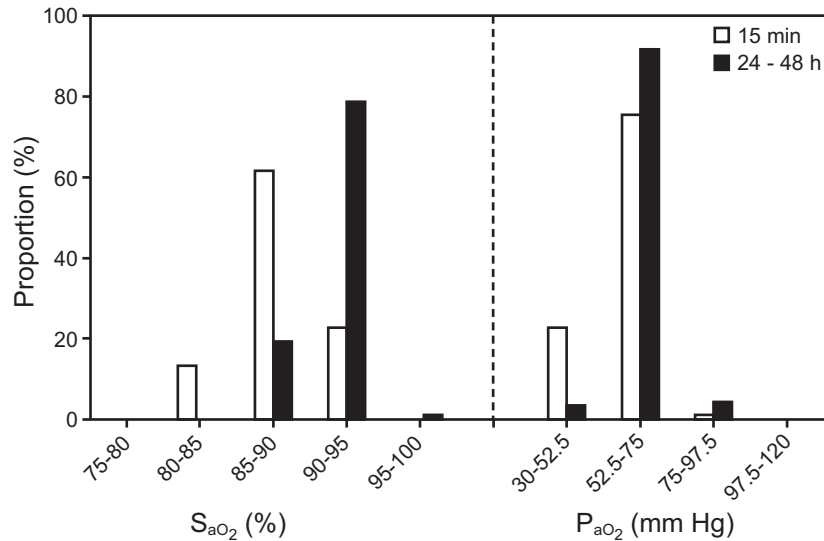


Fig. 1. Self-reported short-term and long-term tolerance limits for oxygenation. Bars represent percentages of respondents ( $n = 180$ , mixed nurses and physicians). The presented case is a young- to middle-aged subject with ARDS in the ICU who required mechanical ventilation. There are no signs of end-organ ischemia, and hemodynamics are stable. Ventilator settings are optimized with respect to the  $P_{aO_2}/F_{IO_2}$  ratio, hemodynamic indices, and risk for lung injury.

Table 1. Percentage of Respondents Adjusting  $F_{IO_2}$  Levels in Specified Clinical Scenarios

Scenario	Study Phase	$F_{IO_2}$ Response	$S_{aO_2}$ , %				$P_{aO_2}$ , mm Hg			
			80-85	85-90	90-95	95-100	45	67.5	90	120
ARDS	Baseline 2012	Higher	97	62	0*	0*	97	9*	0*	0
		Lower	0	0	18*	83*	0	6*	73*	100
	Follow-up 2014	Higher	95	56	0*	0*	98	2*	0*	0
		Lower	0	2	29*	97*	0	22*	94*	100
Cardiac ischemia	Baseline 2012	Higher	100	96	43	3	98	60	6*	2
		Lower	0	0	3	36	0	2	34*	88
	Follow-up 2014	Higher	100	95	41	3	99	49	3*	1
		Lower	0	0	2	43	0	2	50*	94
Cerebral ischemia	Baseline 2012	Higher	99	92	23	1	98	41*	2*	0
		Lower	0	0	5	58	0	1*	44*	95
	Follow-up 2014	Higher	99	90	20	1	99	31*	1*	0
		Lower	0	0	10	69	0	62*	63*	98
Sepsis	Baseline 2012	Higher	100	93*	19*	1*	98	38*	0*	0
		Lower	0	0*	48*	59*	0	2*	51*	100
	Follow-up 2014	Higher	99	85*	4*	1*	98	10*	0*	0
		Lower	0	0*	12*	88*	0	9*	81*	100
Untreatable anemia	Baseline 2012	Higher	93	85	58	33	97	67	22*	6*
		Lower	0	1	6	67	0	2	25*	68*
	Follow-up 2014	Higher	92	86	60	22	93	56	13*	5*
		Lower	0	1	11	0	1	2	42*	82*

All clinical scenarios represent subjects in the ICU who had been invasively mechanically ventilated for at least 5 d with  $F_{IO_2}$  set at 0.50.

\* Baseline versus follow-up:  $P < .05$ .

$S_{aO_2}$  = oxygen saturation measured from an arterial sample

ARDS = subjects with ARDS and pneumonia

Cardiac ischemia = subjects with signs of cardiac ischemia (ST-depressions in het anterior leads, max 3 mm) and pneumonia

Cerebral ischemia = subjects with recent cerebral ischemia and one-sided hemiplegia

Sepsis = subjects with liver abscess and sepsis

Untreatable anemia = a Jehovah's Witness with stable hemoglobin of 1.8 mmol/L after gastric bleeding

Higher = increase in  $F_{IO_2}$ , higher than current 0.50

Lower = decrease in  $F_{IO_2}$ , lower than current 0.50

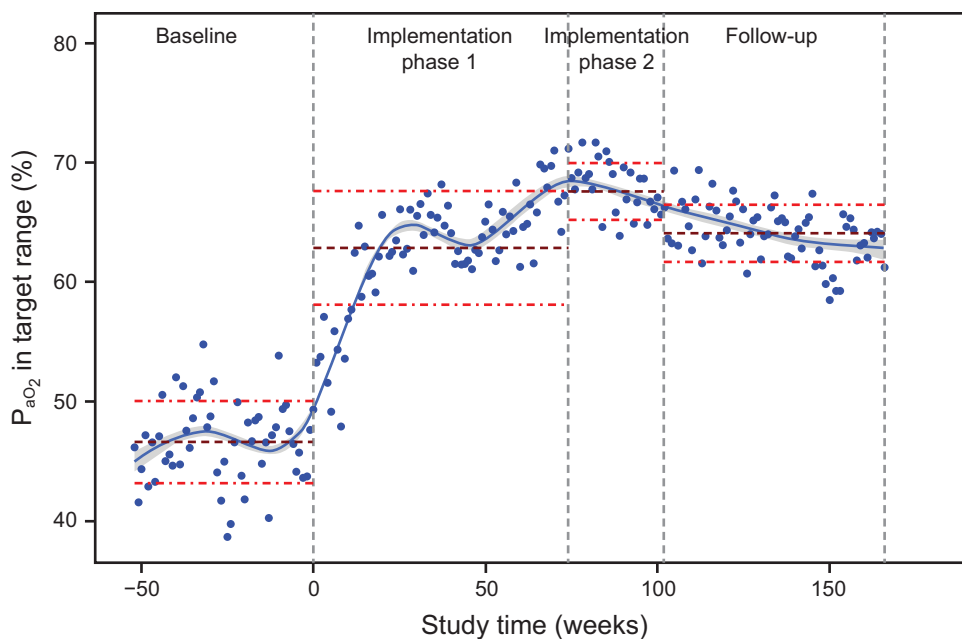


Fig. 2. Percentage of arterial blood gas analyses in the targeted oxygenation range ( $P_{aO_2}$  55–86 mm Hg) before, during, and after implementation of the conservative oxygenation guideline. Blue line and scatters are weekly means with 95% CI per study phase. Red horizontal lines are study phase means with SD. Part of this data has been published previously in Ref. 9.

with regard to increasing  $F_{IO_2}$  levels when  $S_{aO_2}$  or  $P_{aO_2}$  were very low (ie, 80–85%; 45 mm Hg) and decreasing  $F_{IO_2}$  levels when  $P_{aO_2}$  was 120 mm Hg except for the case featuring untreatable anemia.

### Data Derived from ABG Measurements and Ventilator Settings

During follow-up (July 2014 to September 2015), 5,840 subjects were admitted to the participating ICUs, and a total of 101,964 ABG results with concurrent ventilator settings were recorded.

Mean  $P_{aO_2}$  was 87 mm Hg and median  $P_{aO_2}$  was 78 mm Hg, which was lower compared to baseline ( $P < .001$ ) (see the supplementary materials at <http://www.rcjournal.com>). The proportion of ABG samples with  $P_{aO_2}$  in the range of 52.5–75 mm Hg, which was the self-reported target range from the survey, increased from baseline to the active implementation phase and remained stable at follow-up (Figure 2). Correspondingly, mean  $S_{pO_2}$  decreased from 97% at baseline to 96% at follow-up ( $P < .001$ ).

Hypoxic episodes ( $P_{aO_2} < 45$  mm Hg) occurred in 0.70% of ABG samples, which was slightly more compared to baseline (0.46%;  $P < .001$ ) (see the supplementary materials at <http://www.rcjournal.com>). The incidence of episodes with  $P_{aO_2} \geq 120$  mm Hg decreased significantly during follow-up from 15.3% to 8.4%. At the same time, ventilator settings (PEEP and  $F_{IO_2}$ ) were significantly lower during follow-up compared to baseline ( $P < .001$ ).

During follow-up, if  $P_{aO_2}$  was at or above the preferred self-reported range ( $P_{aO_2}$  52.5–75 mm Hg),  $F_{IO_2}$  was subsequently decreased more often compared to baseline ( $P < .001$ ) (Table 2; see the supplementary materials at <http://www.rcjournal.com>). If  $F_{IO_2}$  was  $> 80\%$  and  $P_{aO_2}$  was  $> 75$  mm Hg, the following decrease in  $F_{IO_2}$  and PEEP was larger in the follow-up period compared to baseline ( $P = .01$ ) (Table 3).

In linear regression models for the subgroups of cardiac ischemia, sepsis, and cerebral ischemia, the overall decrease in  $F_{IO_2}$  was significantly greater at follow-up compared to baseline, but this did not occur for ARDS and untreated anemia (data not shown). In subjects with ARDS, cardiac ischemia, and sepsis, when  $P_{aO_2}$  was 67.5–90 mm Hg,  $F_{IO_2}$  was lowered more often at follow-up compared to baseline (see the supplementary materials at <http://www.rcjournal.com>).

### Discussion

Our results indicate that ICU clinicians were more often concerned about oxygen-induced lung injury and that more clinicians preferred conservative  $P_{aO_2}$  and  $S_{aO_2}$  limits in the period after implementation of a conservative oxygenation guideline compared to before that implementation. Accordingly, actual practices regarding oxygen therapy and adjustment of mechanical ventilation in ICU subjects permanently changed, resulting in overall lower oxygenation levels of arterial blood, fewer

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Table 2. Arterial Blood Gas Analysis With the Following F<sub>IO<sub>2</sub></sub> Adjustment and Its Effect on Successive P<sub>aO<sub>2</sub></sub> in Real Subject Data

P <sub>aO<sub>2</sub></sub> , mm Hg	F <sub>IO<sub>2</sub></sub> Adjustment, %	Successive P <sub>aO<sub>2</sub></sub> , %							
		Baseline	Follow-up	Baseline			Follow-up		
				Higher	Unchanged	Lower	Higher	Unchanged	Lower
< 52.5	Higher	36	42	95	1	4	96	2	2
	Unchanged	48	40	87	4	9	90	3	7
	Lower	17	18	95	2	3	90	2	9
> 52.5–75	Higher	27*	24*	76	3	21	73	4	24
	Unchanged	58*	59*	65*	4*	30*	61*	5*	34*
	Lower	16*	18*	61	4	35	50	4	46
> 75–120	Higher	12*	9*	51	2	47	49	3	48
	Unchanged	65*	58*	47	3	50	41	4	56
	Lower	23*	33*	31	2	67	19	2	79
> 120	Higher	9*	7*	36	2	63	31	1	67
	Unchanged	46*	29*	30	3	68	26	2	72
	Lower	45*	64*	10	1	90	4	1	95

Adjustment of F<sub>IO<sub>2</sub></sub> (shown as proportions) was categorized as higher, unchanged, or lower. Successive P<sub>aO<sub>2</sub></sub> after F<sub>IO<sub>2</sub></sub> adjustment (shown as proportions) were categorized as higher, unchanged, or lower.  
\* Baseline versus follow-up: *P* < .05.

Table 3. Adjustment of F<sub>IO<sub>2</sub></sub> and PEEP After Arterial Blood Gas Analysis

F <sub>IO<sub>2</sub></sub> Setting	Study Phase	Adjustment	P <sub>aO<sub>2</sub></sub> , mm Hg						
			<52.5	>52.5–75	75–112.5	>112.5–150	>150–187.5	>187.5–225	>225
0.21–0.40%	Baseline 2012	ΔF <sub>IO<sub>2</sub></sub>	8.3 ± 11.3	6.1 ± 9.0*	2.8 ± 9.8*	0.7 ± 9.2	-0.3 ± 9.1	0.04 ± 7.6	12.5 ± 20.2*
		Δ PEEP	1.4 ± 3.0	0.2 ± 2.9*	-0.4 ± 2.7*	-0.5 ± 2.6	-0.4 ± 3.1*	-0.4 ± 4.1	2.1 ± 4.5
	Follow-up 2014	ΔF <sub>IO<sub>2</sub></sub>	10.2 ± 13.5	4.6 ± 11.4*	-0.01 ± 10.5*	-2.6 ± 11.3	-3.2 ± 14.0	2.0 ± 16.6	14.2 ± 19.6*
		Δ PEEP	2.4 ± 3.6	-0.3 ± 2.4*	-0.7 ± 2.3*	-1.1 ± 2.6	-1.5 ± 2.9*	-0.5 ± 1.8	1.1 ± 3.2
0.41–0.60%	Baseline 2012	ΔF <sub>IO<sub>2</sub></sub>	12.5 ± 16.9	4.5 ± 10.0*	-1.3 ± 10.1*	-4.8 ± 8.6*	-6.2 ± 9.7*	-7.4 ± 9.1*	-4.6 ± 14.5*
		Δ PEEP	1.9 ± 3.5	0.4 ± 2.9*	-0.7 ± 2.5	-1.3 ± 2.5*	-1.4 ± 2.7	-1.6 ± 2.6	0.2 ± 3.6*
	Follow-up 2014	ΔF <sub>IO<sub>2</sub></sub>	8.5 ± 15.2	1.7 ± 12.0*	-5.4 ± 10.2*	-9.8 ± 9.6*	-11.7 ± 10.3*	-13.0 ± 11.6*	-11.5 ± 13.7*
		Δ PEEP	2.4 ± 3.0	0.3 ± 2.9*	-0.7 ± 2.8	-1.2 ± 2.6*	-1.6 ± 2.3	-1.6 ± 2.6	-1.2 ± 3.1*
0.61–0.80%	Baseline 2012	ΔF <sub>IO<sub>2</sub></sub>	7.5 ± 17.3	0.7 ± 13.2*	-7.7 ± 9.6*	-12.1 ± 9.4*	-14.3 ± 11.2	-17.0 ± 9.0	-16.6 ± 13.7*
		Δ PEEP	1.8 ± 3.0	0.7 ± 3.1	-0.0 ± 2.9	-0.5 ± 2.7	-1.4 ± 2.2	-1.1 ± 3.3	-1.8 ± 3.8
	Follow-up 2014	ΔF <sub>IO<sub>2</sub></sub>	5.6 ± 14.3	-0.9 ± 14.3*	-10.1 ± 10.8*	-13.9 ± 13.8*	-18.5 ± 12.8	-20.5 ± 15.1	-23.8 ± 13.8*
		Δ PEEP	1.1 ± 3.7	0.9 ± 3.3	-0.5 ± 2.9*	-0.2 ± 3.1	-1.6 ± 3.0	-1.7 ± 2.2	-1.7 ± 2.9
0.81–1.0%	Baseline 2012	ΔF <sub>IO<sub>2</sub></sub>	-13.3 ± 23.7*	-10.4 ± 18.2*	-19.1 ± 18.5*	-22.8 ± 18.5	-28.0 ± 17.5	-29.4 ± 16.3	-37.4 ± 20.1*
		Δ PEEP	2 ± 6.6	0.9 ± 4.2	0.9 ± 4.4	0.1 ± 4.2	0.1 ± 3.7	-0.4 ± 3.8	-0.7 ± 4.2
	Follow-up 2014	ΔF <sub>IO<sub>2</sub></sub>	-16.0 ± 23.9*	-16.7 ± 23.0*	-19.7 ± 18.5*	-26.2 ± 21.8	-29.0 ± 20.9	-33.5 ± 15.9	-45.1 ± 20.1*
		Δ PEEP	2.4 ± 4.5	1.5 ± 4.1	0.5 ± 4.4	0.8 ± 3.7	-1.7 ± 3.0	0.2 ± 6.8	0.1 ± 3.5

Data are presented as mean ± SD.  
\* Baseline versus follow-up: *P* < .05.

hyperoxic episodes, and a decrease of PEEP and F<sub>IO<sub>2</sub></sub> levels.

Earlier studies on the opinion of nurses and physicians about oxygen toxicity in critically ill patients reported different results. Oxygen toxicity was considered a major threat to lung injury by only 26% of respondents from Australia in 2011<sup>10</sup> and by 51% of respondents in a Canadian study performed in 1996.<sup>11</sup> Opinions about oxygenation after implementation of a conservative oxygenation protocol were also studied in a recent Australian study.<sup>13</sup> After introduction of conservative oxygenation, 61% of respondents considered oxygen-related lung injury

to be of concern for mechanically ventilated patients; in that study, no baseline data before introducing the conservative oxygenation protocol were available.<sup>13</sup> While 72% of doctors and 60% of nurses in Australia tolerated S<sub>pO<sub>2</sub></sub> 90% for > 24 h,<sup>10,14</sup> this was almost 100% in our study. This difference in opinion may be related to different attitudes in different countries, but it may also be a trend in time due to increasing evidence that hyperoxia may be harmful. The first study showing an association between high P<sub>aO<sub>2</sub></sub> levels and mortality in ICU subjects was published in 2008,<sup>6</sup> and since then studies on the risks of hyperoxia have been accumulating.<sup>3</sup> In a Northern European survey, ICU physicians'

preferences for adjusting  $F_{IO_2}$  according to measured  $P_{aO_2}$  in different settings was explored.<sup>15</sup> In this study, decisions to decrease or increase  $F_{IO_2}$  in patients with ARDS, sepsis, or cardiac ischemia were very similar to the responses given in the baseline period in our present study.

In this study, we have documented that self-reported attitudes changed toward conservative oxygen therapy within a relatively short time period. Compared to 2012, more clinicians reported they would lower  $F_{IO_2}$  and fewer would increase  $F_{IO_2}$  in several patient scenarios in the ICU. It is likely that this change in self-reported attitude was a direct result of the implementation of conservative oxygen therapy in these ICUs. The fact that the presented change in attitude took place over just 2 y suggests that it was not only a general trend in time but was likely related to an intervention (ie, the active implementation strategy). Regular barriers experienced by physicians affecting knowledge, attitudes, and external behavior undermine the process of adherence to clinical practice guidelines.<sup>16</sup> Apparently, few barriers were experienced by our group of ICU clinicians, which ensured adherence to the new conservative oxygenation targets. However, a ceiling effect in adherence to our guideline was also evident and may be explained by barriers,<sup>17</sup> such as clinician reluctance to adhere to new guidelines, resistance to change, and reluctance to replace preexisting guidelines, but also the perception of oxygen as a universal remedy.<sup>17-20</sup> It has previously been noted that guideline implementation strategies are effective when strategies are multifaceted and actively engage clinicians throughout the process.<sup>21</sup>

Furthermore, it should be noted that the difference between baseline in 2012 and follow-up in 2014 in the proportion of respondents stating that they would lower  $F_{IO_2}$  or PEEP, if  $S_{pO_2}$  were sufficient, was present for patients with ARDS or sepsis, but not for subjects with cardiac ischemia, cerebral ischemia, or untreatable anemia. Accordingly, this trend to lower oxygenation targets was also found in the actual subject data for ARDS, cardiac ischemia, and sepsis, but not for cases of cerebral ischemia and untreated anemia, even though the amount of ABG data for these specific subject categories was relatively small. Interestingly, the 3 scenarios in which no difference in self-reported attitudes toward oxygenation was found were explicitly excluded from the implementation of low  $P_{aO_2}$  and  $S_{pO_2}$  targets.<sup>9</sup> This also suggests that the effects found in this study are directly related to the implementation of the conservative oxygenation guideline.

We cannot rule out that the different attitudes regarding oxygenation targets expressed by respondents in our survey may be partly explained by giving “socially acceptable” answers according to the new guideline for conservative oxygenation (ie, awareness bias). If so, attitudes expressed in the survey could differ from real behavior in clinical practice. To explore real behavior, we analyzed all ABG

analysis samples and concurrent ventilator settings. After the implementation phase, overall mean  $P_{aO_2}$  was lower than at baseline and very similar to the active implementation period, although it was still slightly higher than the target range in the protocol. Likewise, the proportion of  $P_{aO_2}$  measurements within the conservative oxygenation range was higher than at baseline and the same as during the implementation phase. Whereas the incidence of hyperoxia decreased by 6.9% from baseline to follow-up, the incidence of hypoxemia increased, although this remained rare.

ICU nurses and physicians did not merely express a more conservative attitude regarding oxygenation; this was reflected in different treatment of their ICU patients with lower  $P_{aO_2}$  values noted in the adjustment of mechanical ventilation. Remarkably, adjustments in PEEP changed less over time than adjustments in  $F_{IO_2}$ . This may be explained by nurses being allowed to independently adjust  $F_{IO_2}$ , whereas adjustments in PEEP are usually made by physicians. Another explanation could be that PEEP is not only titrated on  $P_{aO_2}$  values, but also on measured lung mechanics and clinical signs of atelectasis. The mean  $P_{aCO_2}$  during the follow-up phase was 45 mm Hg compared with 42 mm Hg at baseline and in the implementation phase, whereas median and mean  $P_{aO_2}$  were unchanged from the implementation phase to the follow-up phase. Although the protocols on mechanical ventilation were not different in the subsequent study phases, it is possible that this represents advanced insight to protective ventilation.<sup>22</sup> Alternatively, the higher  $P_{aCO_2}$  may be a result of the interaction of ventilation and oxygenation being influenced by better adherence to the lower  $P_{aO_2}$  targets.

The lower mean  $P_{aO_2}$  in ICU patients differs markedly from clinical practice earlier this century. In a previous study from the Netherlands, 22% of  $P_{aO_2}$  values were  $> 120$  mm Hg, and in 78% of these cases with very high  $P_{aO_2}$ , no adjustment of either  $F_{IO_2}$  or PEEP was made if  $F_{IO_2}$  was not  $> 40\%$ .<sup>23</sup> Likewise, in a single-center study from Australia, mean  $P_{aO_2}$  in mechanically ventilated subjects was 114 mm Hg and subjects were never ventilated without supplemental oxygen.<sup>24</sup> In another Australian ICU, subjects spent 50% of time in hyperoxia ( $S_{pO_2} > 98\%$ ).<sup>25</sup>

The difference in behavior and opinions toward acceptable  $P_{aO_2}$  levels between countries and over time may not be surprising, considering the varying guidelines and evidence specifically for ICU patients. The British Thoracic Society guideline recommended a target  $S_{pO_2}$  of 94–98% for most acutely ill patients.<sup>26</sup> Yet it has been suggested that aiming for this target may result in a substantial amount of hyperoxic blood samples ( $P_{aO_2} > 97.5$  mm Hg).<sup>27</sup> Furthermore, a clinical practice guideline was published for acutely ill patients recommending an  $S_{pO_2}$  not  $> 96\%$  in patients receiving oxygen therapy.<sup>28</sup> Three randomized controlled trials of conservative versus liberal oxygenation targets in ICU patients have been conducted with varying results.



Recently, the ICU-ROX investigators ( $S_{pO_2}$  91–96% versus no upper  $S_{pO_2}$  limit) found no significant difference in ventilator-free days and mortality,<sup>29</sup> which confirmed findings from Panwar et al ( $S_{pO_2}$  88–92% versus  $\geq 96\%$ ).<sup>7</sup> In contrast, a randomized controlled trial conducted in Italy ( $P_{aO_2}$  70–100 mm Hg or  $S_{pO_2}$  94–98% versus  $P_{aO_2}$  up to 150 mm Hg or  $S_{pO_2}$  97–100%) reported lower ICU mortality, shock, liver failure, and bacteremia favoring conservative oxygenation targets.<sup>1</sup> Results of these trials should, however, be compared with caution because the strategies used were very different. More robust trials are needed to confirm the changing beliefs and behavior we found in our cohort of ICU clinicians.

The following study strengths and limitations should be considered. The cases included in the survey do not represent the full complexity of patients in daily practice. Additionally,  $S_{aO_2}$  and  $P_{aO_2}$  ranges in the survey were chosen arbitrarily. Furthermore, in the analysis of actual daily practice, we generalized the surveyed tolerance limits of  $S_{aO_2}$  and  $P_{aO_2}$  to all patients independent of admission diagnosis, although the surveyed tolerance limits were asked in an ARDS case vignette. Moreover, response rates were modest. Strengths of this study are the survey responses combined with the large set of ABG and ventilatory patient data, derived from the same 3 ICUs where previous studies were conducted.<sup>8,9</sup> This allowed an extensive and detailed comparison across time, centers, and professions, between attitudes and actual practice. Furthermore, it allowed further insight into attitudes and possible barriers when implementing new guidelines, which will be useful for the effective execution of oxygenation targets in future guidelines and protocols. Finally, the survey used in the baseline and follow-up phase is very similar to one previously used in Canada and Australia, thereby allowing for extensive geographical and chronological comparisons.

### Conclusions

In this multi-center survey and follow-up of an implementation study, we noted that self-reported attitudes and behavior changed considerably in the period after a step-wise implementation of conservative oxygenation targets in critically ill patients in 3 ICUs in the Netherlands. Actual treatment of ICU patients permanently changed, resulting in consistently lower oxygenation levels and lower ventilator settings in the period after implementing the new guideline. The previously reported contrast between self-reported attitudes toward oxygen therapy and actual treatment by the same clinicians was reduced after implementation, which suggests that attitudes toward oxygen therapy changed and more accurately reflect actual practice. We confirmed that implementing a conservative oxygenation guideline was an effective and structural method that

changed clinical practice and improved long-term adherence to conservative oxygenation targets.

### REFERENCES

- Girardis M, Busani S, Damiani E, Donati A, Rinaldi L, Marudi A, et al. Effect of conservative vs conventional oxygen therapy on mortality among patients in an intensive care unit: the oxygen-ICU randomized clinical trial. *JAMA* 2016;316(15):1583-1589.
- Wepler M, Demiselle J, Radermacher P, Asfar P, Calzia E. Before the ICU: does emergency room hyperoxia affect outcome? *Crit Care* 2018;22(1):59.
- Chu DK, Kim LH, Young PJ, Zamiri N, Almenawer SA, Jaeschke R, et al. Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy (IOTA): a systematic review and meta-analysis. *Lancet* 2018;391(10131):1693-1705.
- Page D, Ablordepey E, Wessman BT, Mohr NM, Trzeciak S, Kollef MH, et al. Emergency department hyperoxia is associated with increased mortality in mechanically ventilated patients: a cohort study. *Crit Care* 2018;22(1):9.
- Helmerhorst HJ, Arts DL, Schultz MJ, van der Voort PH, Abu-Hanna A, de Jonge E, et al. Metrics of arterial hyperoxia and associated outcomes in critical care. *Crit Care Med* 2017;45(2):187-195.
- de Jonge E, Peelen L, Keijzers PJ, Joore H, de Lange D, van der Voort PH, et al. Association between administered oxygen, arterial partial oxygen pressure and mortality in mechanically ventilated intensive care unit patients. *Crit Care* 2008;12(6):R156.
- Panwar R, Hardie M, Bellomo R, Barrot L, Eastwood GM, Young PJ, et al. Conservative versus liberal oxygenation targets for mechanically ventilated patients: a pilot multicenter randomized controlled trial. *Am J Respir Crit Care Med* 2016;193(1):43-51.
- Helmerhorst HJ, Schultz MJ, van der Voort PH, Bosman RJ, Juffermans NP, de Jonge E, et al. Self-reported attitudes versus actual practice of oxygen therapy by ICU physicians and nurses. *Ann Intensive Care* 2014;4:23.
- Helmerhorst HJ, Schultz MJ, van der Voort PH, Bosman RJ, Juffermans NP, de Wilde RB, et al. Effectiveness and clinical outcomes of a two-step implementation of conservative oxygenation targets in critically ill patients: a before and after trial. *Crit Care Med* 2016;44(3):554-563.
- Eastwood GM, Reade MC, Peck L, Jones D, Bellomo R. Intensivists' opinion and self-reported practice of oxygen therapy. *Anaesth Intensive Care* 2011;39(1):122-126.
- Mao C, Wong DT, Slutsky AS, Kavanagh BP. A quantitative assessment of how Canadian intensivists believe they utilize oxygen in the intensive care unit. *Crit Care Med* 1999;27(12):2806-2811.
- Arts D, de Keizer N, Scheffer GJ, de Jonge E. Quality of data collected for severity of illness scores in the Dutch National Intensive Care Evaluation (NICE) registry. *Intensive Care Med* 2002;28(5):656-659.
- Eastwood GM, Peck L, Young H, Suzuki S, Garcia M, Bellomo R. Intensive care clinicians' opinion of conservative oxygen therapy ( $SpO_2$  90–92%) for mechanically ventilated patients. *Aust Crit Care* 2014;27(3):120-125.
- Eastwood GM, Reade MC, Peck L, Baldwin I, Considine J, Bellomo R. Critical care nurses' opinion and self-reported practice of oxygen therapy: a survey. *Aust Crit Care* 2012;25(1):23-30.
- Schjorring OL, Toft-Petersen AP, Kusk KH, Mouncey P, Sorensen EE, Berezowicz P, et al. Intensive care doctors' preferences for arterial oxygen tension levels in mechanically ventilated patients. *Acta Anaesthesiol Scand* 2018;62(10):1443-1451.
- Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud P-A, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999;282(15):1458-1465.

17. Rubenfeld GD. Translating clinical research into clinical practice in the intensive care unit: the central role of respiratory care. *Respir Care* 2004;49(7):837-843.
18. Jones NE, Suurdt J, Ouellette-Kuntz H, Heyland DK. Implementation of the Canadian clinical practice guidelines for nutrition support: a multiple case study of barriers and enablers. *Nutr Clin Pract* 2007;22(4):449-457.
19. Simpson F, Doig GS. The relative effectiveness of practice change interventions in overcoming common barriers to change: a survey of 14 hospitals with experience implementing evidence-based guidelines. *J Eval Clin Pract* 2007;13(5):709-715.
20. Kelly CA, Lynes D, O'Brien MR, Shaw B. A wolf in sheep's clothing? Patients' and healthcare professionals' perceptions of oxygen therapy: an interpretative phenomenological analysis. *Clin Respir J* 2018;12(2):616-632.
21. Prior M, Guerin M, Grimmer-Somers K. The effectiveness of clinical guideline implementation strategies—a synthesis of systematic review findings. *J Eval Clin Pract* 2008;14(5):888-897.
22. Neto AS, Simonis FD, Barbas CSV, Biehl M, Determann RM, Elmer J, et al. Lung-protective ventilation with low tidal volumes and the occurrence of pulmonary complications in patients without acute respiratory distress syndrome: a systematic review and individual patient data analysis. *Crit Care Med* 2015;43(10):2155-2163.
23. de Graaff AE, Dongelmans DA, Binnekade JM, de Jonge E. Clinicians' response to hyperoxia in ventilated patients in a Dutch ICU depends on the level of FiO<sub>2</sub>. *Intensive Care Med* 2011;37(1):46-51.
24. Dennis D, Torre L, Baker S, Hebden-Todd T. A snapshot of the oxygenation of mechanically ventilated patients in one Australian intensive care unit. *Anaesth Intensive Care* 2017;45(3):359-364.
25. Suzuki S, Eastwood GM, Peck L, Glassford NJ, Bellomo R. Current oxygen management in mechanically ventilated patients: a prospective observational cohort study. *J Crit Care* 2013;28(5):647-654.
26. O'Driscoll BR, Howard LS, Earis J, Mak V, British Thoracic Society Emergency Oxygen Guideline Development Group. BTS guideline for oxygen use in adults in healthcare and emergency settings. *Thorax* 2017;72(Suppl 1):ii1-ii90.
27. Durlinger EMJ, Spoelstra-de Man AME, Smit B, de Grooth HJ, Girbes ARJ, Oudemans-van Straaten HM, Smulders YM. Hyperoxia: at what level of SpO<sub>2</sub> is a patient safe? A study in mechanically ventilated ICU patients. *J Crit Care* 2017;39:199-204.
28. Siemieniuk RAC, Chu DK, Kim LH-Y, Güell-Rous M-R, Alhazzani W, Soccia PM, et al. Oxygen therapy for acutely ill medical patients: a clinical practice guideline. *BMJ* 2018;363:k4169.
29. ICU-ROX Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group, Mackle D, Bellomo R, Bailey M, Beasley R, Deane A, et al. Conservative oxygen therapy during mechanical ventilation in the ICU. *N Engl J Med* 2019;382(11):989-998.