Automated titration of nasal high flow oxygen in the emergency department: a randomised controlled trial

Louis Kirton ,[1,2] Julie Cook,[1] Rowan Hamill,[1] Tanira Kingi,[1,3] Neakiry Kivi,[1,3] Allie Eathorne,[1] Alice Rogan ,[3] Mark Weatherall,[3] Richard Beasley [1]

Handling editor Jon Bailey

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/emermed-2024-214023).

[1]Medical Research Institute of New Zealand, Wellington, New Zealand
[2]Te Herenga Waka - Victoria University of Wellington, Wellington, New Zealand
[3]University of Otago Wellington, Wellington, New Zealand

Correspondence to
Dr Louis Kirton;
louis.kirton@mrinz.ac.nz

Received 24 February 2024
Accepted 29 December 2025
Published Online First
30 January 2026

To cite: Kirton L, Cook J, Hamill R, *et al*. *Emerg Med J* 2026;**43**:215–222.

ABSTRACT

Background When delivering nasal high flow (NHF) therapy in a medical ward, a high dependency unit or an intensive care unit, automated oxygen titration increases time spent within a target oxygen saturation (SpO_2) range compared with standard, manually titrated oxygen. This study explores whether this improvement is also seen when titrating oxygen with NHF in an emergency department (ED).

Method This open-label, parallel groups, randomised controlled trial compared automated to manual oxygen titration using NHF therapy in hypoxaemic adult patients in the Wellington Regional Hospital ED between October 2022 and December 2023. Participants with a prescribed target SpO_2 range who demonstrated a minimum oxygen requirement were eligible for inclusion. A rank-based comparison was used for the primary outcome, the proportion of time spent within the target SpO_2 range of 92%–96%, or 88%–92% if at risk of hypercapnia, among participants achieving ≥30 min of therapy. An interaction term was applied to assess whether the proportion of time spent within target SpO_2 range depended on the prescribed target range itself (SpO_2 92%–96% or 88%–92%).

Results 83 participants were screened, 52 were randomised and 49 had data for the primary endpoint. Median (IQR) proportion of time spent within the target SpO_2 range with automated oxygen (n=25) was 96.4% (92.5% to 99.4%) compared with 89.9% (69.8% to 97.2%) with manually adjusted oxygen (n=24); difference (95% CI) 8.0% (1.7% to 16.9%), p=0.01. There was no evidence that the proportion of time spent within target SpO_2 range depended on the selected target SpO_2 range, P-interaction 0.60.

Conclusion Automatically titrated oxygen therapy significantly increased time spent within a target SpO_2 range, compared with manual oxygen titration in adult patients receiving NHF therapy in the ED.

WHAT IS ALREADY KNOWN ABOUT THIS TOPIC

⇒ Compared with standard manual oxygen titration, automated oxygen titration systems increase time spent within a target oxygen saturation range when used with nasal high flow (NHF) therapy in adults in medical wards, high dependency units and intensive care units.
⇒ It is not known whether this improvement is also applicable to patients with hypoxaemia managed in emergency departments (EDs) who might obtain the greatest benefit from tight oxygen control.

WHAT THIS STUDY ADDS

⇒ When delivering NHF therapy to adult patients with hypoxaemia in the ED, automated oxygen titration increases time spent within a target oxygen saturation range compared with manual oxygen titration.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study demonstrates that an automated oxygen titration system used with NHF therapy in adults managed in the ED provides similar improvements in oxygen control to when used in other hospital locations.
⇒ These findings suggest that automated oxygen titration may represent the optimal oxygen delivery strategy for ED patients receiving NHF oxygen.

INTRODUCTION

Hypoxaemia is a commonly encountered clinical scenario in patients presenting to an emergency department (ED).[1] The risks of progressively severe hypoxaemia range from transient disruption of cellular function to severe tissue ischaemia and even death.[2 3] While correcting severe hypoxaemia with supplemental oxygen clearly has the potential to save lives, excessive oxygen therapy leading to hyperoxaemia can also be potentially harmful.[4–6] Providing sufficient oxygen to mitigate hypoxaemia, while avoiding overoxygenation to prevent hyperoxaemia, respects these competing risks and has become widely accepted as the safest approach to supplement oxygen.

Acute care guidelines recommend oxygen be delivered within a target oxygen saturation (SpO_2) range,[2 3 7] a process that requires manual adjustment of the fraction of inspired oxygen (FiO_2). This depends on pulse oximetry to estimate blood oxygen saturation and a clinician to intermittently adjust the delivered FiO_2 to achieve SpO_2 readings within the prespecified target range. Titrating oxygen in this way may not be ideal, as it has been shown to maintain medical inpatients within a prescribed target SpO_2 range approximately half the time.[8] For ED patients and those receiving prehospital care, time spent within the target SpO_2 range when manually adjusting oxygen may be even lower.[1 9 10]

Automated oxygen titration systems represent a novel strategy to deliver oxygen to achieve a

prespecified target SpO_2 range.[11] They consist of a sophisticated closed-loop control algorithm that adjusts the FiO_2 according to the current and predicted future SpO_2. In a previous ED-based trial using conventional low flow oxygen therapy, the effect of automating oxygen titration was to significantly increase time spent within a target SpO_2 range.[12] However, in many hospital settings, nasal high flow (NHF) oxygen has become the first-line therapy for hypoxaemic respiratory failure,[13–15] and it is yet to be determined whether similar effects will be observed in an ED with automated oxygen titration integrated into an NHF device.

Accordingly, this study assesses the effect of automated oxygen titration using a novel NHF oxygen delivery device (Airvo-3 with $OptiO_2$, Fisher and Paykel Healthcare, Auckland, New Zealand) on time spent within a predefined target SpO_2 range, in patients with hypoxaemia presenting to an ED. We hypothesise that adherence to the target SpO_2 range will be improved with the use of this NHF device that can automate oxygen titration.

METHODS

Study design

This open-label, phase IIb, randomised, parallel groups, controlled trial evaluated the effect of the Airvo-3 device with automated oxygen titration ($OptiO_2$) in adults with hypoxaemia presenting to a single ED. The trial was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki. The trial was registered with the Australian and New Zealand Clinical Trials Registry: ACTRN12622000423718.

Patient and public involvement statement

There was no patient or public involvement in the design or conduct of this study.

Participants

Participants were adults presenting to the ED at Wellington Regional Hospital, Wellington, New Zealand, which receives approximately 175 patients per day. All participants provided written informed consent before the determination of eligibility. Inclusion criteria were patients expected to receive oxygen for at least 1 hour, with an appropriate target SpO_2 range of either 92%–96%, or 88%–92% when at risk of hypercapnia, and had received sufficient oxygen during a 10 min run-in period. During this period, participants were given NHF oxygen therapy with FiO_2 titrated automatically using the device in $OptiO_2$ mode. If the FiO_2 at the end of 10 min of therapy was at least 28% for those with a target SpO_2 range of 92%–96%, or at least 24% for those with an 88%–92% target range, participants could be included in the trial. If at the end of the 10 min eligibility assessment period, the FiO_2 was lower than these levels, or exceeded 50% and 40% for each SpO_2 target range, respectively, then participants were deemed ineligible. Other exclusion criteria were: age <18 years, haemodynamic instability (systolic blood pressure <90 mm Hg, or requiring vasopressor or inotropic support), documented respiratory acidosis at the time of enrolment (arterial blood gas with pH <7.35 and arterial partial pressure of carbon dioxide(PaCO2) >45 mm Hg), receiving end-of-life care, presence of a risk factor for barotrauma or a nasal/facial condition precluding NHF use, cognitive impairment or impaired consciousness precluding informed consent, or presence of any other condition believed to present a risk to participant safety.

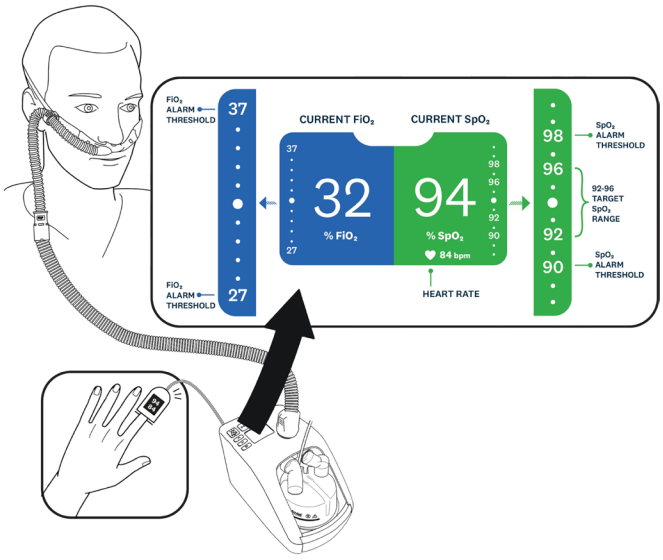

Figure 1 Schematic representation of the Airvo-3 NHF device with an automatic oxygen control system. While delivering NHF therapy, the Airvo-3 device continuously measures SpO_2 using an in-built pulse oximeter and displays current measurements on the device screen. The automated oxygen control function of the device ($OptiO_2$) operates a closed-loop control algorithm that titrates the FiO_2 to a prespecified target SpO_2 range. The device alarms when FiO_2 reaches the upper or lower FiO_2 limit, or if the SpO_2 alarm threshold values are breached. FiO_2, fraction of inspired oxygen; NHF, nasal high flow; SpO_2, peripheral oxygen saturation.

Randomisation

After completing the 10 min run-in period, eligible participants were block randomised, with a variable block size, in equal proportions (one to one) to receive the intervention: automated oxygen titration, or the control: manually titrated oxygen. All participants received the randomly allocated oxygen titration strategy via NHF therapy. The randomisation code was generated by the study statistician using a computer-generated sequence. Allocation was concealed by the Greenlight guru (Indianapolis, USA) electronic case report form and was released to investigators at the time of randomisation. The nature of the intervention meant that investigators and participants could not be blinded to the allocated intervention. The study statisticians were also unblinded due to the format of the data sheets used for the analysis.

Procedures

The configuration and operation of the Airvo-3 device are outlined in figure 1. Randomised participants remained on NHF oxygen therapy using the Airvo-3 device with Optiflow (Fisher and Paykel Healthcare) nasal cannula. The gas flow rate was titrated between 25 L/min and 70 L/min at the treating clinician's discretion. A finger probe pulse oximeter (Nonin 7000A, Minnesota, USA) remained attached to an appropriate finger. The pulse oximeter cable connected to the Airvo-3 device computer through a universal serial bus port, with the current measured SpO_2 value continuously displayed on the device screen and all the physiological and device variables recorded every 1 s onto the device computer.

The control of FiO_2 was set according to the randomised treatment allocation, either using the automated setting ($OptiO_2$) or manually at the discretion of the participant's primary nurse.

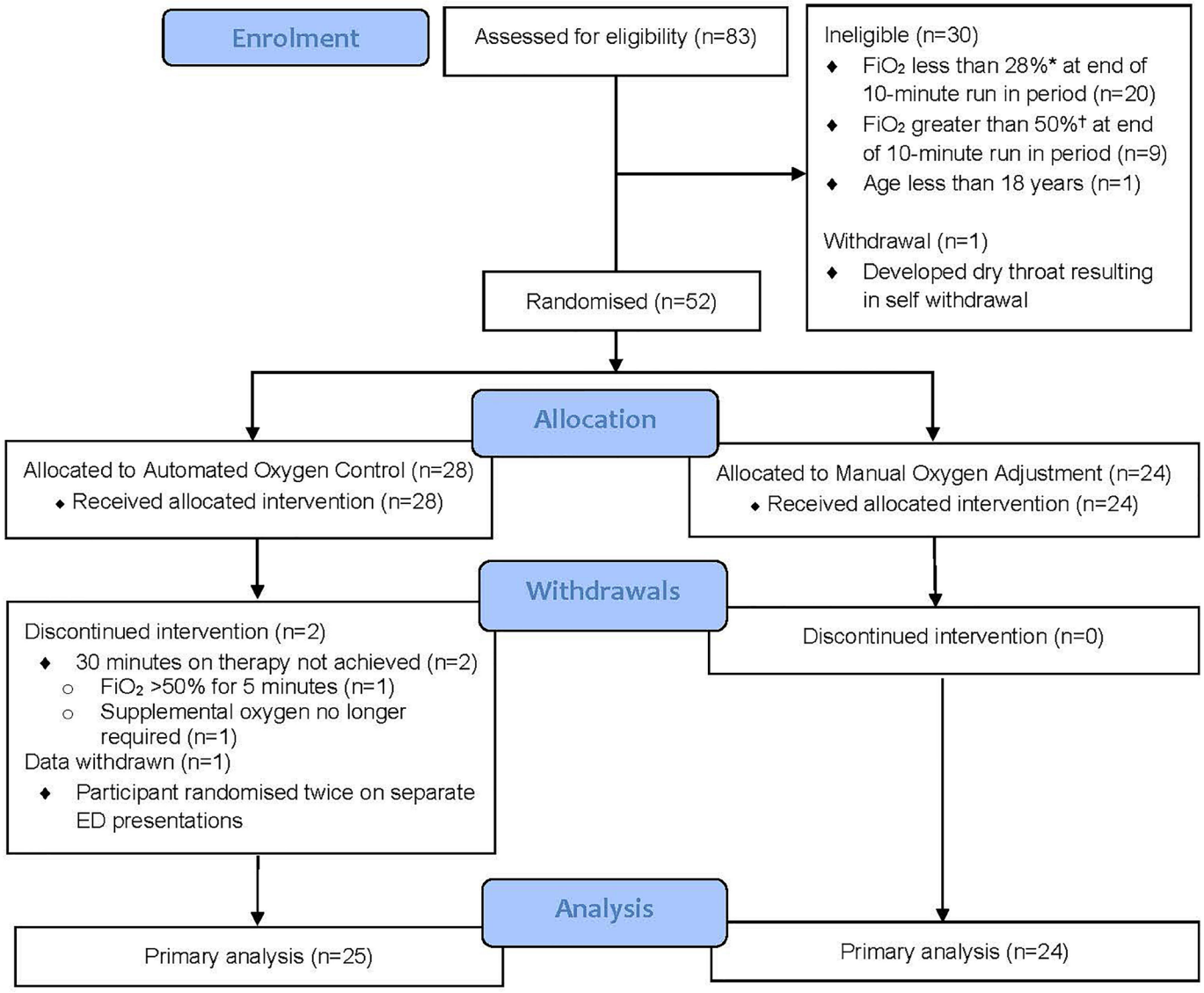

Figure 2 CONSORT diagram. *Or less than 24% for those with an 88%–92% target SpO_2 range; †Or greater than 40% for those with 88%–92% target SpO_2 range. CONSORT, Consolidated Standards of Reporting Trials, ED, emergency department; FiO_2, fraction of inspired oxygen; SpO_2, peripheral oxygen saturation.

Nurses were trained to use the Airvo-3 device and the $OptiO_2$ automated oxygen system. For participants randomised to automated oxygen control, nurses were instructed to adjust the FiO_2 settings if they had a clinical concern, or if prompted by device alarms that alerted them to a clinical deterioration as outlined in the online supplemental appendix S1. The nurses of participants randomised to manually adjusted oxygen were instructed to adjust the FiO_2 as they normally would as part of usual care. A study investigator was available throughout the entire study duration to assist nurses with troubleshooting device alarms and ensuring adherence to the study protocol. On completion of the study, the data were downloaded from the Airvo-3 device, uploaded onto a study computer and processed into spreadsheets for analysis.

Outcomes

The primary outcome was the proportion of time spent within the target SpO_2 range in those receiving at least 30 min of therapy. Secondary outcomes were the time spent within the target SpO_2 in each target SpO_2 subgroup (92%–96% or 88%–92%), as well as the time spent above and below the target SpO_2 range. Additional outcomes were the responses of physiological parameters (heart rate, respiratory rate, FiO_2) to randomised therapies.

Sample size

Based on our previous study of medical inpatients,[16] we estimated that a total sample size of 50 participants would provide 90% power to detect a 15% difference in time spent in the target range between intervention and control, with an SD of 14. This sample size calculation was based on an unpaired t-test to compare groups, equal size numbers in intervention and control groups, and a two-sided type 1 error rate (alpha) of 5%.

Statistical methods

The primary analysis for the primary outcome, time to SpO_2 in the range, was by the Mann-Whitney U test with the Hodges-Lehmann estimator for location difference and appropriate CIs.

The following sensitivity analyses were also performed for the primary outcome: count of seconds in the range by Poisson

Table 1 Baseline participant characteristics

	All participants		Automated oxygen titration		Manual oxygen titration	
Continuous variables	**N**	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**Mean (SD)**
Age (years)	49	73.2 (13.1)	25	74.8 (12.3)	24	71.6 (14)
Systolic blood pressure (mm Hg)	49	133.7 (21.1)	25	137.1 (25.7)	24	130.1 (14.7)
Heart rate (beats/minute)	49	86.6 (17)	25	85.9 (20.3)	24	87.3 (13)
Respiratory rate (breaths/minute)	49	21.6 (5.1)	25	21.6 (4.3)	24	21.7 (6)
FiO_2 (%)	49	29.2 (4.4)	25	29.6 (4.8)	24	28.8 (4)
SpO_2 (%)	49	93.1 (2.4)	25	93.2 (2.5)	24	92.9 (2.3)
Categorical variables	**All participants N/49 (%)**		**Automated oxygen titration N/25 (%)**		**Manual oxygen titration N/24 (%)**	
Sex (female)	21 (42.9)		11 (44.0)		10 (41.7)	
Ethnicity						
Asian	3 (6.1)		1 (4.0)		2 (8.3)	
European	38 (77.6)		19 (76.0)		19 (79.2)	
MELAA	1 (2.0)		1 (4.0)		0 (0.0)	
Māori	5 (10.2)		4 (16.0)		1 (4.2)	
Pacific	2 (4.1)		0 (0.0)		2 (8.3)	
Smoking status						
Never	25 (51.0)		13 (52.0)		12 (50.0)	
Current	4 (8.2)		2 (8.0)		2 (8.3)	
Former	20 (40.8)		10 (40.0)		10 (41.7)	
Admitted to hospital	49 (100.0)		25 (100.0)		24 (100.0)	
Admitted to HDU directly from ED	5 (10.2)		4 (16.0)		1 (4.2)	
Admitted to ICU directly from ED	0 (0.0)		0 (0.0)		0 (0.0)	
Presentation diagnosis*						
Pneumonia	24 (49.0)		10 (40.0)		14 (58.3)	
COPD	6 (12.2)		4 (16.0)		2 (8.3)	
Pulmonary oedema/heart failure	8 (16.3)		5 (20.0)		3 (12.5)	
Pulmonary embolus	3 (6.1)		2 (8.0)		1 (4.2)	
Lower respiratory tract infection	2 (4.1)		0 (0.0)		2 (8.3)	
Diffuse parenchymal lung disease	2 (4.1)		2 (8.0)		0 (0.0)	
COVID-19	1 (2.0)		1 (4.0)		0 (0.0)	
Other	8 (16.3)		5 (20.0)		3 (12.5)	
Prestudy oxygen delivery method						
Nasal canula	44 (89.8)		22 (88.0)		22 (91.7)	
Simple face mask	1 (2.0)		0 (0.0)		1 (4.2)	
NHF	4 (8.2)		3 (12.0)		1 (4.2)	
At risk of hypercapnia (target SpO_2 88%–92%)	15 (30.6)		8 (32.0)		7 (29.2)	
Not at risk of hypercapnia (target SpO_2 range 92%–96%)	34 (69.4)		17 (68.0)		17 (70.8)	

*More than one response allowed.
COPD, chronic obstructive pulmonary disease; ED, emergency department; FiO_2, fraction of inspired oxygen; HDU, high dependency unit; ICU, intensive care unit; MELAA, Middle Eastern Latin American African; mm Hg, millimetres of mercury; NHF, nasal high flow therapy; SpO_2, peripheral oxygen saturation.

regression analysis with and without a treatment interaction by 92%–96% or 88 to 96% target SpO_2 range, each with baseline FiO_2 as a covariate, and the number of observations made (as a surrogate for time in the study) as an offset variable to take account of differential weighting based on time of observation and participant as a random effect to account for repeated measures. Note that for all Poisson models, overdispersion was present (checked by comparing mean and variance, plus Pearson and deviance statistics) and as such the Pearson statistic was used as a scale parameter for all models. Each of these analyses has also been performed using negative binomial models.

All other times, SpO_2 in/below/above range variables were analysed by a Mann-Whitney U test with the Hodges-Lehmann estimator for location difference and appropriate CIs.

Due to normality assumptions not being well met (checked by residual distributions and plots of residuals vs predicted values) the number of FiO_2 adjustments was analysed by a Mann-Whitney U test with the Hodges-Lehmann estimator for location difference and appropriate CIs.

For the density plot, non-parametrical kernel density estimates with a standardisation bandwidth of 3 were overlaid on transparent histograms. For the large data set, withone measurement per second per participant for the duration of the study, every fifth measurement was used to manage the algorithm to generate the plots.

SAS V.9.4 was used. A statistical analysis plan was followed.

Patient and public involvement statement

There was no patient or public involvement in the design or conduct of this study.

RESULTS

Between 11 October 2022 and 12 December 2023, 85 participants were screened, 52 were randomised to receive the study

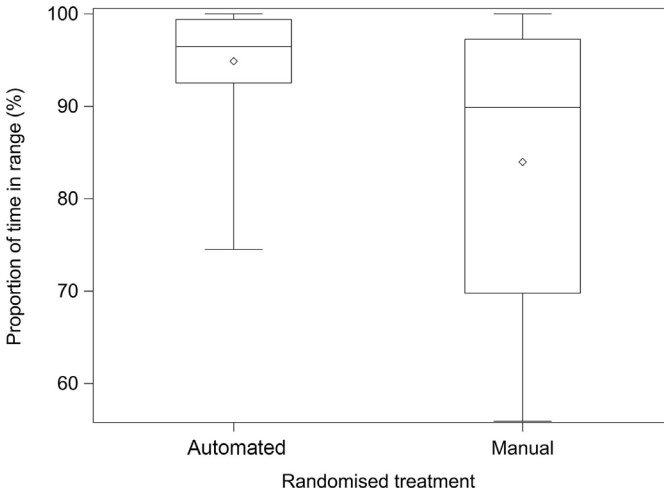

Figure 3 Box plot of proportion of time within the target SpO_2 range in all study participants between the intervention and control groups. On the box plots, the horizontal lines are the 25th, 50th (median) and 75th percentiles, the symbol is the mean and the whiskers extend from the minimum to maximum values. Automated, automated oxygen titration; Manual, manual oxygen titration; SpO_2, peripheral oxygen saturation.

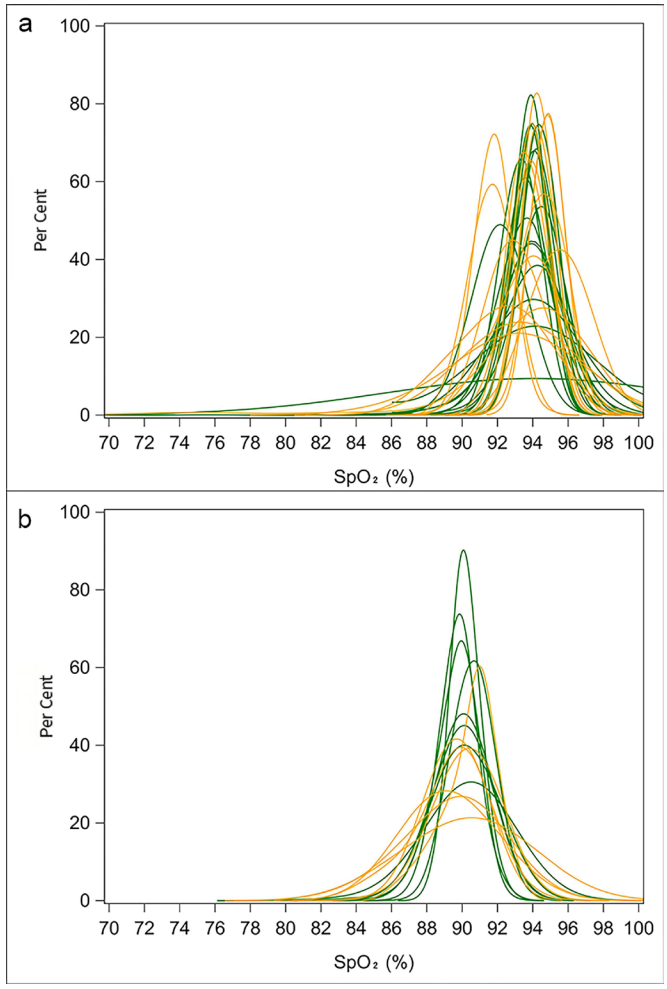

Figure 4 Distribution of SpO_2 values between automated (green) and manual (orange) oxygen titration strategies, by target SpO_2 range ((a) 92%–96%, (b) 88%–92%). SpO_2, peripheral oxygen saturation.

intervention, 2 withdrew before 30 min of therapy was complete, and 1 participant who was inadvertently enrolled twice during separate ED presentations had their second set of data excluded from the final analyses (figure 2). Baseline participant characteristics are summarised in table 1. The baseline FiO_2 and SpO_2 were similar in the automated and manual groups; the numbers of patients admitted to the high dependency unit (HDU) directly from the ED were 4 and 1, respectively (table 1). Participant characteristics and results for the primary outcome categorised by sex are presented in online supplemental tables S1 and S2.

In the 49 participants analysed for the primary outcome, time spent on the study interventions was similar between groups. The median (IQR) proportion of time spent within the target SpO_2 range was 96.4% (92.5% to 99.4%) in the automated oxygen titration group (n=25) and 89.9% (69.8% to 97.2%) in the manual oxygen titration group (n=24); a difference of 8.0% (1.7% to 16.9%), p=0.01 (figures 3 and 4, table 2).

A reduction in the proportion of time spent below the target SpO_2 range was seen with automated oxygen titration compared with manual oxygen titration, that was of borderline statistical significance (p=0.054). Between the automated and manual oxygenation strategies, there was no significant difference in time spent with SpO_2: above the target range, below 85%, below 90% (for those with a 92%–96% target range) or below 86% (for those with an 88%–92% target range) (table 3 and online supplemental table S3).

The Poisson regression and negative binomial sensitivity analyses showed no evidence for a difference in treatment effect depending on the target SpO_2 range (P-interaction=0.60) (online supplemental table S5). For the target SpO_2 range of 88%–92%, the automated oxygen titration group resulted in a significantly greater proportion of time within the range than the manual oxygen titration group; the difference was not significant in the 92%–96% target range subgroup (figure 4, table 3).

The mean (SD) number of occasions when a clinician manually adjusted the device FiO_2 settings per participant was 0.2 (0.5) in the automated oxygen group and 0.8 (1.4) in the manual oxygen group. The responses of other physiological and device-related variables between automated and manual oxygen titration groups are outlined in online supplemental table S4.

There were no serious adverse events.

DISCUSSION

In ED patients with hypoxaemia, NHF therapy with automated oxygen titration significantly increased the proportion of time within a target SpO_2 range compared with manual oxygen titration. This extends the evidence of tighter delivery of oxygen therapy within prespecified SpO_2 ranges with the automated oxygen titration system in medical wards,[16 17] HDUs[17] and intensive care units (ICUs).[18 19] In each of these trials, the proportion of time spent within a target SpO_2 range using automated oxygen titration was greater than 90%, suggesting that when used with NHF, automated oxygen provides similarly effective titration across a range of patient acuities and care settings. In contrast, manual oxygen titration led to variable accuracy across these locations, likely depending on the intensity of nursing care and SpO_2 monitoring, with the median times spent within the range of 71% in a medical ward and 89% in an ICU. In the ED where the present study was conducted, participants receiving manual oxygen titration spent a median 90% of the time within the prespecified target range, suggesting that the accuracy of manual oxygen titration was similar to that observed in ICUs,

Table 2 Time receiving study intervention, and the proportion of time spent within, above and below the target SpO_2 range between automated oxygen titration and manual oxygen titration

Time spent on intervention (minutes)	N	Mean (SD)	Median (IQR)	Min to Max
Automated	25	149.3 (54.2)	181.1 (118.7 to 182.9)	43.0 to 194.3
Manual	24	156.5 (40.4)	180.2 (136.9 to 182.9)	55.3 to 193.7
Time SpO_2 in range (%)	N	**Mean (SD)**	**Median (IQR)**	**Min to Max**
Automated	25	94.9 (6.2)	96.4 (92.5 to 99.4)	74.5 to 100
Manual	24	84.0 (14.5)	89.9 (69.8 to 97.2)	55.9 to 100
Comparison	**Hodges Lehmann estimator (95% CI)**			**P value**
Automated minus manual	8.0 (1.7 to 16.9)			0.01
Time SpO_2 below range (%)	**N**	**Mean (SD)**	**Median (IQR)**	**Min to Max**
Automated	25	3.2 (5.2)	1.2 (0.2 to 4)	0 to 25.5
Manual	24	11.7 (13.3)	6.8 (0.1 to 19.4)	0 to 44.1
Comparison	**Hodges Lehmann estimator (95% CI)**			**P value**
Automated minus manual	−4.3 (−11.7 to 0.0)			0.054
Time SpO_2 above range (%)	**N**	**Mean (SD)**	**Median (IQR)**	**Min to Max**
Automated	25	1.9 (2.8)	0.4 (0 to 3.1)	0 to 10.8
Manual	24	4.3 (6.2)	2.6 (0.1 to 5.5)	0 to 23.3
Comparison	**Hodges Lehmann estimator (95% CI)**			**P value**
Automated minus manual	−0.4 (−3.1 to 0.1)			0.18

Max, maximum; Min, minimum; SpO_2, peripheral oxygen saturation.

likely reflecting the high nurse to patient ratio and routine use of continuous pulse oximetry.[18]

The interaction term for SpO_2 target range (88%–92% versus 92%–96%) was non-significant, implying that the proportion of time spent within the target range did not depend on the target SpO_2 range itself and automated oxygen control likely results in similar improvements in oxygen titration across both the target range groups.

The reported increase in time spent within the target SpO_2 range achieved with automated oxygen titration may be clinically advantageous for ED patients. Both underoxygenation and overoxygenation have been associated with an increased risk of morbidity and mortality, although the severity of illness likely confounds these associations.[2 20–24] While currently published studies comparing automated and manual oxygen titration are underpowered to detect differences in many clinically meaningful morbidity and mortality outcomes, some studies have reported a reduction in the frequency of device setting adjustments with automated oxygen titration, suggesting less clinician time is necessary to titrate oxygen.[17 19] Additionally, in the largest study to date (n=187), a reduction in hospital length of stay with automated versus manual oxygen titration was observed.[12]

Automation of oxygen delivery represents a technological solution that improves the quality of patient care. Similarities can be drawn with automated closed-loop insulin pumps, which are increasingly used in the care of patients with type 1 diabetes as they have been demonstrated to improve maintenance of euglycaemia, glycated haemoglobin levels and quality of life.[25 26]

NHF therapy with automated oxygen titration may also have a role as an oxygen weaning tool, as the FiO_2 automatically reduces as the requirement to maintain SpO_2 within the target range decreases. Such partial or full weaning from oxygen potentially reduces the ED patients' exposure to the harms of hyperoxaemia and may liberate patients from supplemental oxygen, influencing their post-ED disposition.

We are aware of only one other ED-based trial comparing automated to manual oxygen titration.[12] In this trial, participants received conventional low flow oxygen, which resulted in a median time spent within the target SpO_2 range of 81% with automated oxygen and 52% with manual oxygen. This compares

Table 3 The proportion of time spent within the target SpO_2 range between automated and manual oxygen titration by target SpO_2 range (92%–96% and 88%–92%)

Time SpO_2 in range (%)				
Target SpO_2 range = 92%–96%	**N**	**Mean (SD)**	**Median (IQR)**	**Min to Max**
Automated	17	94.9 (6.7)	96.9 (92.5 to 99.7)	74.5 to 100
Manual	17	85.0 (15.8)	91.2 (68.4 to 97.8)	55.9 to 100
Comparison	**Hodges Lehmann estimator (95% CI)**			**P value**
Automated minus manual	3.2 (−0.3 to 20.3)			0.12
Time SpO_2 in range (%)	**N**	**Mean (SD)**	**Median (IQR)**	**Min to Max**
Target SpO_2 range = 88%–92%				
Automated	8	94.8 (5.3)	96 (92.8 to 98.7)	83.8 to 99.8
Manual	7	81.4 (11.5)	84 (71.1 to 90.2)	60.9 to 91.8
Comparison	**Hodges Lehmann estimator (95% CI)**			**P value**
Automated minus manual	10.7 (4.5 to 25.3)			0.02

Max, maximum; Min, minimum; SpO_2, peripheral oxygen saturation.

to 96% and 90%, respectively, for the present study, with key differences between these studies being that our study used NHF therapy, was a single-centre study, enrolled participants with lower baseline oxygen requirements and used a different automated oxygen titration device. It is also notable that in participants who completed our trial, the number of FiO_2 setting adjustments was infrequent in both the automated and manual oxygen titration groups. The 10 min period of automated oxygen titration received prior to the trial commencing may have set a new, more appropriate baseline FiO_2 for those randomised to manual titration to subsequently achieve better adherence to their target SpO_2 range over the remainder of the trial.

The integration of automated oxygen titration into NHF devices is particularly relevant as NHF therapy is increasingly used in ED patients with hypoxaemia. It can improve important clinical outcomes, including rates of escalation to higher levels of respiratory support, work of breathing and breathlessness.[13] As such, automated oxygen titration used with NHF in ED patients represents an advance in care over more commonly used conventional forms of manually titrated oxygen and may have dual benefits due to the flow-specific effects of NHF use, as well as more precise oxygen titration.

Strengths of this trial are that it is the first to characterise the effects of automated oxygen titration with NHF in an ED setting, where patients are often at the most severe stage of their illness, and the risks of respiratory acidosis, ventilatory support and mortality, associated with excessive or inadequate oxygen, are potentially the greatest.[1 10 21–23 27 28]

Limitations were that participants required relatively low FiO_2 throughout the trial, which may reduce the generalisability of the study findings; however, other studies have shown automated oxygen titration is similarly effective across a range of respiratory failure severities.[18] The automated oxygen titration group had numerically more patients admitted to the HDU (n=4) compared with the manual oxygen titration group (n=1), raising the possibility of more severe disease in the automatic group. However, this interpretation was not supported by the observation that the baseline characteristics were similar, in particular the FiO_2 and SpO_2, with mean values of 29.6% vs 28.8% and 93.2% vs 92.9%. The sickest patients presenting to ED were excluded from this trial and the study period was only 3 hours, so periods of particularly unstable SpO_2, for example, in those with haemodynamic instability, those who were being considered for ventilatory support and those who were asleep, were not represented in this study's findings. Our inability to blind clinicians, investigators and study statisticians to the study therapies may also have influenced the care that study participants received and the study outcomes.

In summary, automated oxygen titration increased the proportion of time spent within a target SpO_2 range compared with manual titration in patients using NHF in an ED. The consistently high level of time spent in the target SpO_2 range, being greater than 90% across the ED, ward, HDU and ICU settings, indicates that the efficacy of an automated oxygen titration system using NHF is generalisable to patients of varying severity and clinical situations requiring oxygen therapy.

Acknowledgements We acknowledge Ms Jenny Sparks for her contribution to adminstration and monitoring for this study

Contributors LK takes responsibility for the content of the manuscript. LK had full access to all the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis including and especially any adverse effects. JC, RH, TK, NK, AR, MW and RB contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript.

Funding Fisher and Paykel Healthcare awarded a research grant to fund this study, were involved in the study design, but were not involved in data collection, data analysis, data interpretation, manuscript preparation or the decision to submit for publication.

Competing interests LK, JC, RH, TK, NK and RB report financial support was provided by Fisher & Paykel Healthcare Limited to conduct this study. RB reports that the Institute responsible for this study manuscript has received research funding from Fisher and Paykel for other studies. LK and JC report a relationship with Fisher & Paykel Healthcare Limited that includes travel reimbursement. RB declares that he is a member of the Thoracic Society of Australasia and New Zealand (TSANZ) Oxygen Guidelines Group.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the New Zealand Central Health and Disability Ethics Committee (HDEC) (2022 FULL 11727). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data are available on reasonable request. Anonymised data sets are available on reasonable request, until a minimum of 10 years after publication to researchers who provide a methodologically sound proposal that has been approved by the study investigators. This is possible through a signed data access agreement and subject to approval by the principal investigator LK (Louis.Kirton@mrinz.ac.nz) and the study sponsor James Revie (James.Revie@fphcare.co.nz)

ORCID iDs
Louis Kirton https://orcid.org/0000-0001-6941-1615
Alice Rogan https://orcid.org/0000-0003-1305-0325
Richard Beasley https://orcid.org/0000-0003-0337-406X

REFERENCES

1 Hale KE, Gavin C, O'Driscoll BR. Audit of oxygen use in emergency ambulances and in a hospital emergency department. *Emerg Med J* 2008;25:773–6.
2 O'Driscoll BR, Howard LS, Earis J, *et al*. BTS guideline for oxygen use in adults in healthcare and emergency settings. *Thorax* 2017;72:ii1–90.
3 Beasley R, Chien J, Douglas J, *et al*. Thoracic Society of Australia and New Zealand oxygen guidelines for acute oxygen use in adults: "Swimming between the flags". *Respirology* 2015;20:1182–91.
4 Chu DK, Kim L-Y, Young PJ, *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;391:1693–705.
5 Robinson TD, Freiberg DB, Regnis JA, *et al*. The role of hypoventilation and ventilation-perfusion redistribution in oxygen-induced hypercapnia during acute exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000;161:1524–9.
6 Hafner S, Beloncle F, Koch A, *et al*. Hyperoxia in intensive care, emergency, and peri-operative medicine: Dr. Jekyll or Mr. Hyde? A 2015 update. *Ann Intensive Care* 2015;5:42.
7 Piraino T, Madden M, Roberts KJ, *et al*. AARC Clinical Practice Guideline: Management of Adult Patients With Oxygen in the Acute Care Setting. *Respir Care* 2022;67:115–28.
8 Harper JCP, Semprini R, Kearns NA, *et al*. Determination of oxygen saturation compared to a prescribed target range using continuous pulse oximetry in acutely unwell medical patients. *BMC Pulm Med* 2021;21:332.
9 Wijesinghe M, Perrin K, Healy B, *et al*. Pre-hospital oxygen therapy in acute exacerbations of chronic obstructive pulmonary disease. *Intern Med J* 2011;41:618–22.
10 O'Driscoll BR, Rudenski A, Turkington PM, *et al*. An audit of hypoxaemia, hyperoxaemia, hypercapnia and acidosis in blood gas specimens. *Eur Respir J* 2012;39:219–21.
11 Beasley R. "Swimming between the flags" with oxygen therapy is getting closer to reality. *Respirology* 2023;28:960–1.
12 L'Her E, Dias P, Gouillou M, *et al*. Automatic *versus* manual oxygen administration in the emergency department. *Eur Respir J* 2017;50:1602552.

13 Huang C-C, Lan H-M, Li C-J, *et al*. Use High-Flow Nasal Cannula for Acute Respiratory Failure Patients in the Emergency Department: A Meta-Analysis Study. *Emerg Med Int* 2019;2019:1–10.
14 Rochwerg B, Einav S, Chaudhuri D, *et al*. The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline. *Intensive Care Med* 2020;46:2226–37.
15 Oczkowski S, Ergan B, Bos L, *et al*. ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure. *Eur Respir J* 2022;59:2101574.
16 Harper J, Kearns N, Bird G, *et al*. Automatic versus manual oxygen titration using a novel nasal high-flow device in medical inpatients with an acute illness: a randomised controlled trial. *BMJ Open Respir Res* 2021;8:e000843.
17 Kirton LW, Eathorne AL, Cook JK, *et al*. Automated Oxygen Titration With Noninvasive Respiratory Support in Acute In-Patient Care. *Respir Care* 2025;70:1405–14.
18 Roca O, Caritg O, Santafé M, *et al*. Closed-loop oxygen control improves oxygen therapy in acute hypoxemic respiratory failure patients under high flow nasal oxygen: a randomized cross-over study (the HILOOP study). *Crit Care* 2022;26:108.
19 Kirton LW, Cruz RS, Navarra L, *et al*. Effect of automated titration of oxygen on time spent in a prescribed oxygen saturation range in adults in the ICU after cardiac surgery. *Crit Care Resusc* 2024;26:64–70.
20 Beasley R, Mackle D, Young P. Oxygen: a new look at an old therapy. *Journal of the Royal Society of New Zealand* 2019;49:126–42.
21 Goodacre S, Turner J, Nicholl J. Prediction of mortality among emergency medical admissions. *Emerg Med J* 2006;23:372–5.
22 Echevarria C, Steer J, Wason J, *et al*. Oxygen therapy and inpatient mortality in COPD exacerbation. *Emerg Med J* 2021;38:170–7.
23 Cameron L, Pilcher J, Weatherall M, *et al*. The risk of serious adverse outcomes associated with hypoxaemia and hyperoxaemia in acute exacerbations of COPD. *Postgrad Med J* 2012;88:684–9.
24 Austin MA, Wills KE, Blizzard L, *et al*. Effect of high flow oxygen on mortality in chronic obstructive pulmonary disease patients in prehospital setting: randomised controlled trial. *BMJ* 2010;341:c5462.
25 Brown SA, Kovatchev BP, Raghinaru D, *et al*. Six-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes. *N Engl J Med* 2019;381:1707–17.
26 Lee TTM, Collett C, Bergford S, *et al*. Automated Insulin Delivery in Women with Pregnancy Complicated by Type 1 Diabetes. *N Engl J Med* 2023;389:1566–78.
27 Wedzicha W, Brill S. Oxygen therapy in acute exacerbations of chronic obstructive pulmonary disease. *COPD* 2014;1241.
28 Beasley R, Patel M, Perrin K, *et al*. High-concentration oxygen therapy in COPD. *The Lancet* 2011;378:969–70.