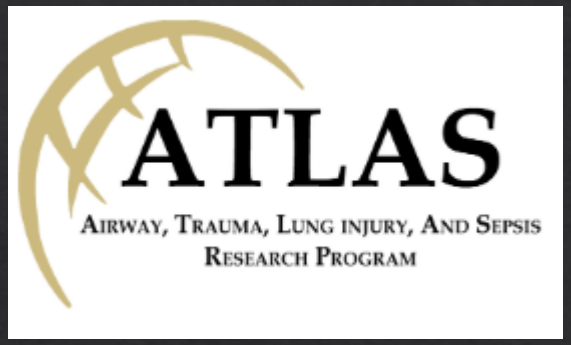

Strategy to Avoid Excessive Oxygen (SAVE-O2) Trials

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Trial PI: Dr. Adit Ginde, MD, MPH

Key DoD Collaborators: COL Dr. Vikhyat Bebarta, MD

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Disclosures

No conflicts of interest

Funding:

1) NIH, National Heart, Lung, and Blood Institute (NHLBI)
2) Joint Warfighter Medical Research Program (JWMRP)
3) Special Operations Medical Association (SOMA)

The views and conclusions contained herein are those of the authors and should not be interpreted as necessarily representing the official policies or endorsements, either expressed or implied, of the Department of Defense, the USAMRDC, or the U.S. Government.

The SAVE-O2 AI trial was investigator-initiated. PRO100 devices were rented from O2matic (Herlev, Denmark) for the trial. O2matic was not involved in the funding, design, data collection, analysis, or decision to publish.

Goals & Objectives

1) Clinical implications and practice guidelines from the SAVE-O2 Trial

2) Introduce *autonomous* solutions for oxygen titration via the SAVE-O2 AI Trial

3) Explore the role of skin pigmentation in pulse oximeter performance

ATLAS – Airway, Trauma, Lung injury, and Sepsis Research

Strategy to Avoid Excessive Oxygen in Critically Ill Trauma Patients

Trial Summary

SAVE-O_2
STRATEGY TO AVOID EXCESSIVE OXYGEN

Objective: determine feasibility, safety & effectiveness of targeted normoxemia to improve outcomes in critically injured patients

Design: Cluster Randomized, Stepped Wedge Implementation Trials

- Minimal Risk, Waiver of Informed Consent (efficient & saves costs)
- One-way crossover to normoxemia protocol (target SpO2 90-96%)

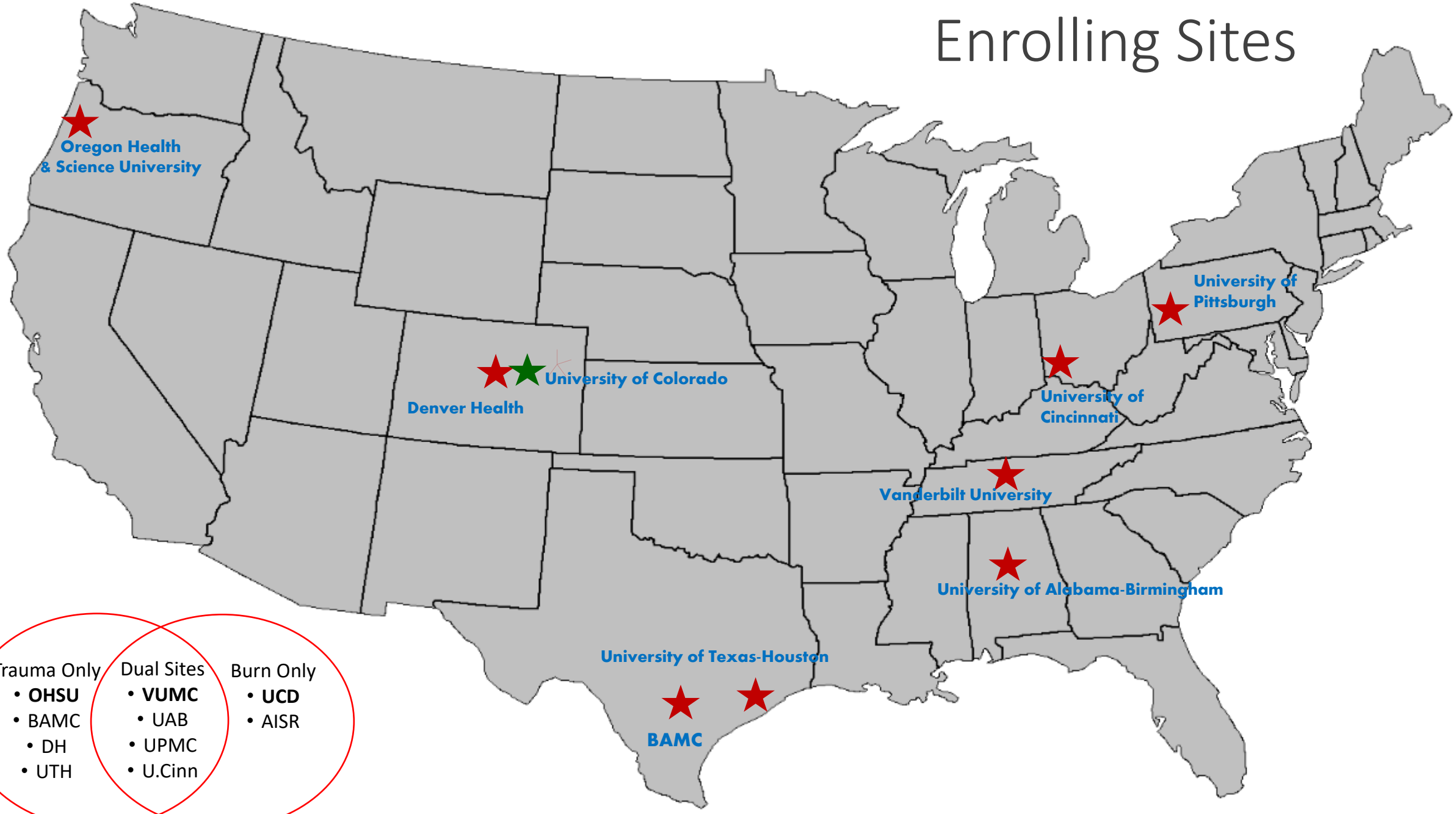
Population: Adult critically ill trauma pts hospitalized w/in 24h of injury at 8 US Level 1 Trauma Centers

Primary Endpoint: Supplemental Oxygen Free Days (SOFD) to day 28

- Defined as number of days alive and not on supplemental O_2

Hypothesis: Targeted normoxemia will limit exposure to hyperoxemia and safely reduce the use of concentrated oxygen

Enrolling Sites



Trauma Only	Dual Sites	Burn Only
• **OHSU**	• **VUMC**	• **UCD**
• BAMC	• UAB	• AISR
• DH	• UPMC	
• UTH	• U.Cinn	

SAVE-O_2
STRATEGY TO AVOID EXCESSIVE OXYGEN

Adult Trauma Patient admitted to ICU

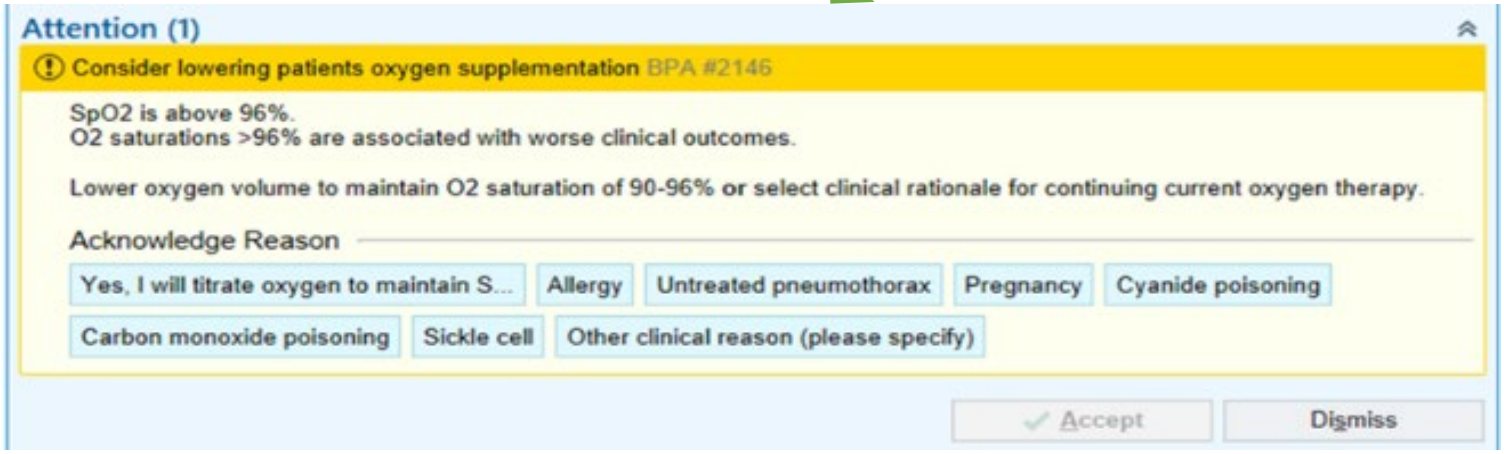
Engage and Educate Clinical Team Members RN, RT, MD, APP

SpO_2 90-96%
(or PaO_2 60-100mmHg)

SpO_2 >96%
(or PaO_2 >100mmHg)

Maintain Current O_2 Delivery

Down-Titrate O_2 within One Hour*



***Intervention non-binding & can be overridden by clinician when in best interest of patient**

Original Investigation | Surgery

March 31, 2025

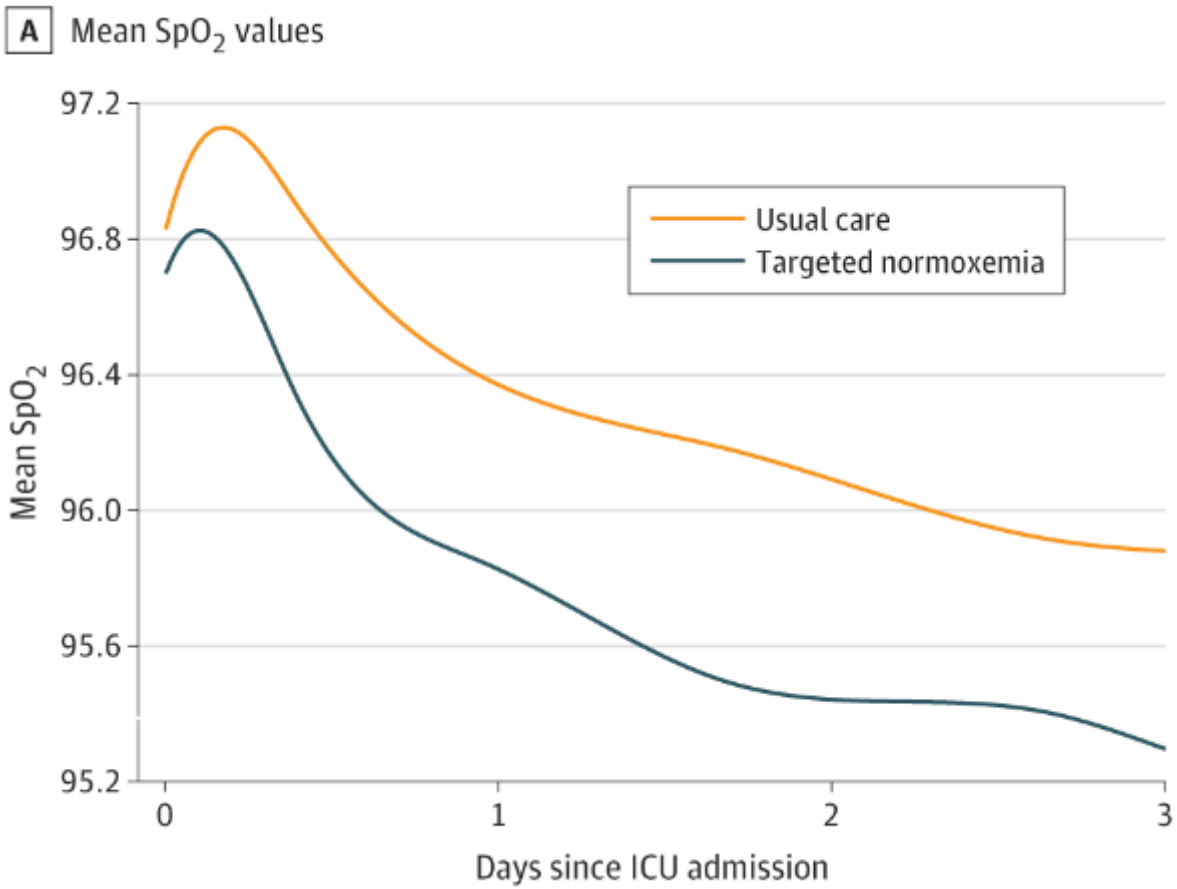
Targeted Normoxemia and Supplemental Oxygen-Free Days in Critically Injured Adults

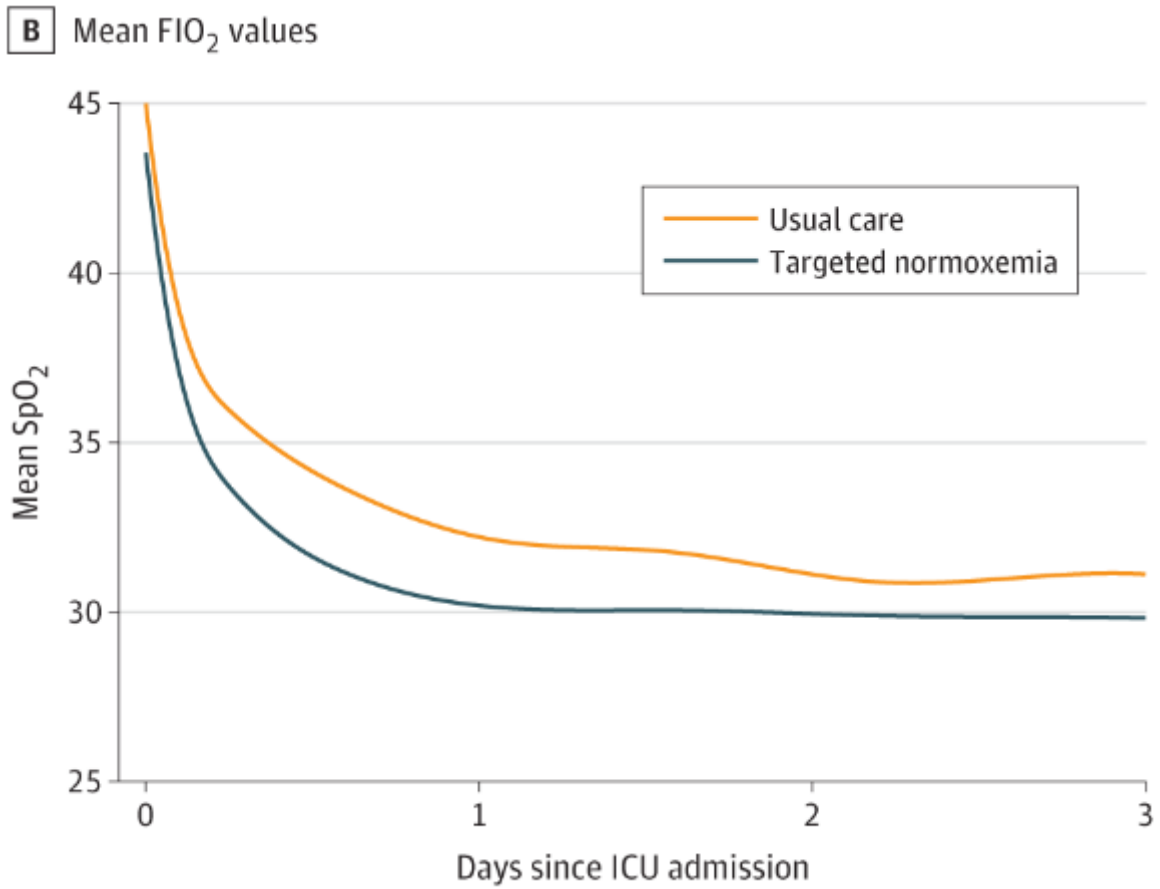
A Stepped-Wedge Cluster Randomized Clinical Trial

David J. Douin, MD[1]; John D. Rice, PhD[2]; Erin L. Anderson, RN[3]; et al

» A
JAM

SAVE-O_2
STRATEGY TO AVOID EXCESSIVE OXYGEN





Original Investigation | Surgery

March 31, 2025

Targeted Normoxer
Days in Critically Inj
A Stepped-Wedge C

David J. Douin, MD[1]; John D. Rice, PhD[2]; Erin L.

» Author Affiliations | Article Information

JAMA Netw Open. 2025;8(3):e252093. doi:10.1

Table 1. Patient Demographics and Injury Characteristics at Baseline

Characteristic	Patients, No. (%)	
	Targeted normoxemia group (n = 5661)	Usual care group (n = 6826)
Age, mean (SD), y	53.2 (21.3)	50.4 (20.9)
Sex		
Female	1655 (29.2)	2033 (29.8)
Male	4006 (70.8)	4793 (70.2)
Race and ethnicity[a]		
Hispanic	642 (11.3)	483 (7.1)
Non-Hispanic Black	599 (10.6)	1372 (20.1)
Non-Hispanic White	2930 (51.8)	4088 (59.9)
Other[b]	376 (6.6)	513 (7.5)
Unknown	1114 (19.7)	370 (5.4)
BMI, mean (SD)	27.9 (6.6)	28.2 (6.9)
Current or former smoker	1212 (21.4)	1305 (19.1)
Supplemental oxygen use at baseline	76 (1.3)	127 (1.9)
No. of Elixhauser comorbidities, mean (SD)	2.9 (2.3)	2.4 (2.2)
Cardiac comorbidities	882 (15.6)	1130 (16.6)
Pulmonary comorbidities	494 (8.7)	720 (10.5)
Penetrating mechanism of injury[c]	699 (12.3)	1161 (17.0)
EMS mode of arrival	5391 (95.2)	6616 (96.9)
Initial GCS score, mean (SD)	12.1 (4.3)	11.7 (4.5)
ISS, mean (SD)	19.3 (11.7)	19.9 (12.2)
TBI	2616 (46.2)	1879 (27.5)
Mechanical ventilation before ICU	1846 (32.6)	2826 (41.4)
Proportion of time receiving invasive mechanical ventilation, mean (SD), %	22.3 (34.2)	26.2 (34.5)
Mechanical ventilation at any time during ICU admission	2321 (41.0)	3388 (49.6)

VE-O_2

GY TO AVOID EXCESSIVE OXYGEN

Original Investigation | Surgery

March 31, 2025

Targeted Normoxemia and Supplemental Oxygen-Free Days in Critically Injured Adults

A Stepped-Wedge Cluster Randomized Clinical Trial

David J. Douin, MD[1]; John D. Rice, PhD[2];

» Author Affiliations | Article Informa

JAMA Netw Open. 2025;8(3):e252093. d

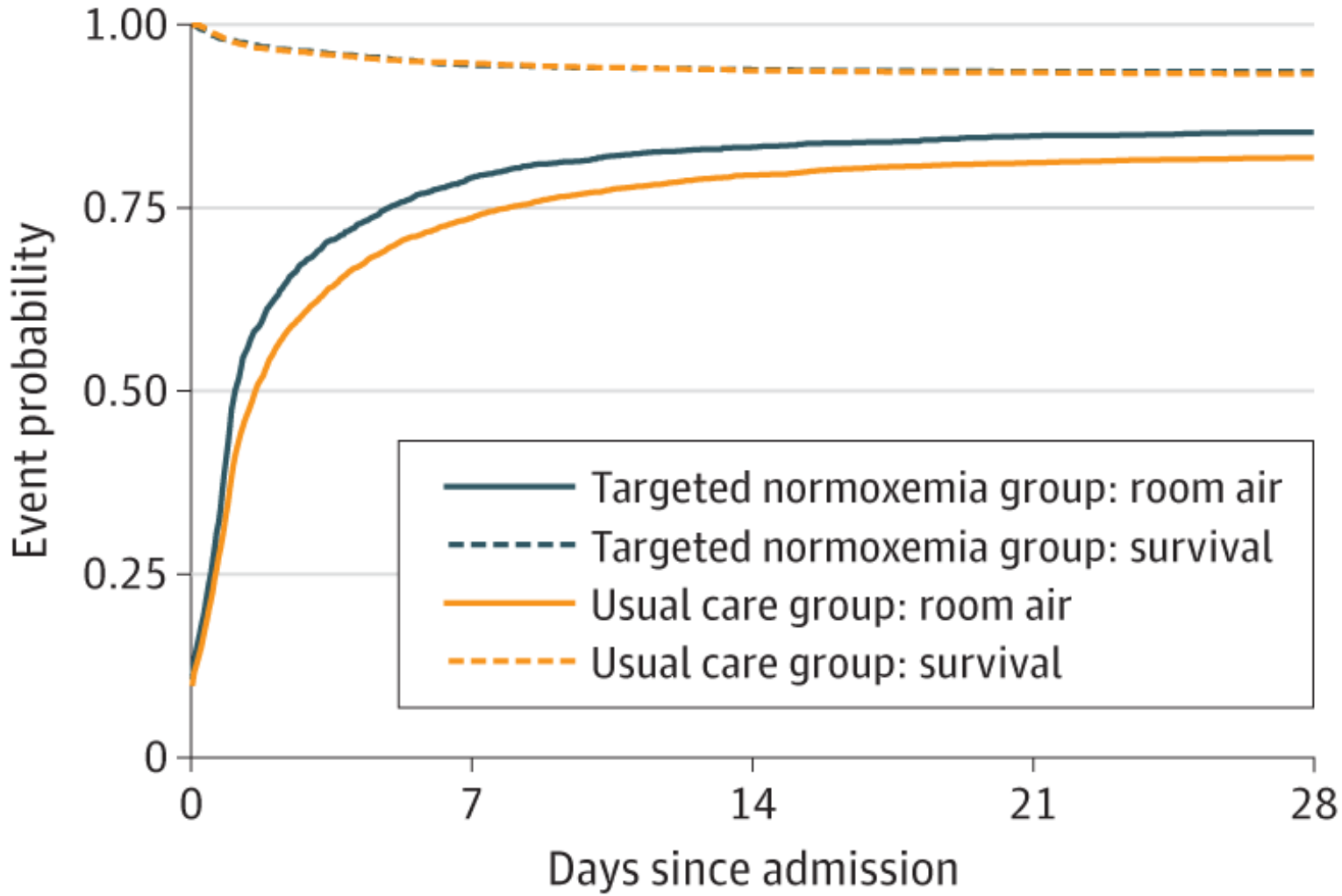
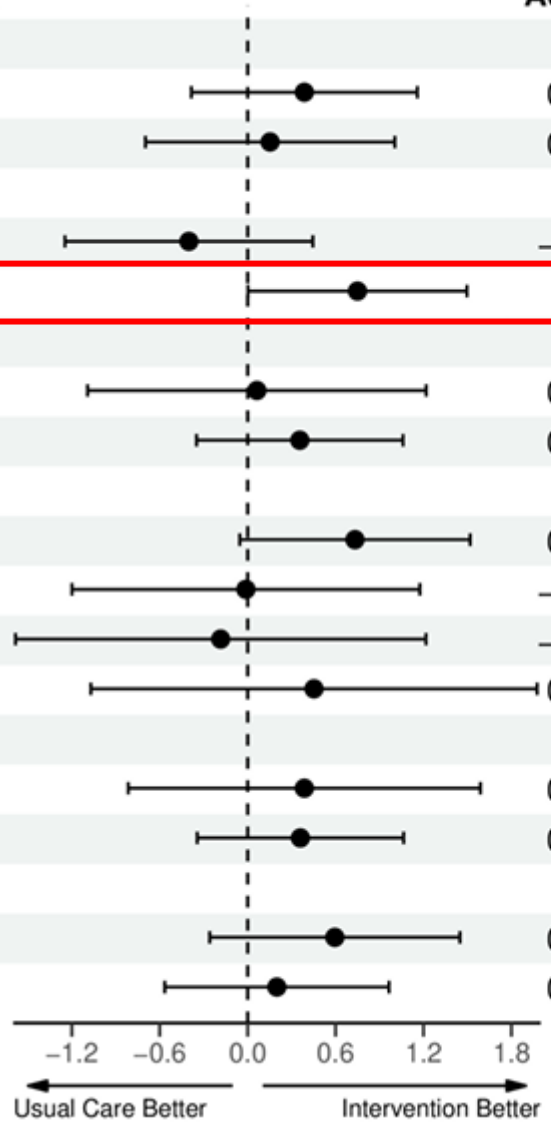


Table 2. Primary and Main Secondary Outcomes

Outcome	Mean (SD)		
	Targeted normoxemia group (n = 5661)	Usual care group (n = 6826)	Adjusted mean difference (95% CI)
Primary outcome: SOFDs through day 28	19.6 (10.3)	17.5 (10.4)	0.32 (−0.37 to 1.00)
P value	NA	NA	.30
In-hospital mortality to day 90, No. (%)	563 (9.9)	732 (10.7)	AHR: 1.05 (0.83 to 1.33)[a]
HFDs through day 90	69.8 (27.4)	69.0 (27.5)	1.16 (−0.35 to 2.68)
Hospital LOS, d	13.1 (17.4)	13.2 (16.1)	AHR: 1.08 (0.99 to 1.18)[a]
ICU LOS, d	5.7 (7.7)	6.3 (10.3)	−0.03 (−0.09 to 0.03)
VFDs through day 28[b]	23.3 (9.2)	22.4 (9.7)	0.55 (0.03 to 1.08)
Time to room air, d	1.6 (3.2)	2.7 (4.0)	AHR: 1.23 (1.13 to 1.33)[a]
Total volume of oxygen administered per patient, L	18 862 (43 097)	32 565 (62 793)	−5500 (−8720 to −2280)
Total volume of oxygen administered per patient, L/min	2.2 (3.3)	3.3 (3.7)	−0.54 (−0.72 to −0.35)
Proportion of time spent in normoxemia (Spo_2 90%-96%) in ICU, %	0.72 (0.29)	0.56 (0.32)	0.07 (0.06 to 0.09)
Proportion of time spent in hyperoxemia (Spo_2 >96%) in ICU, %	0.27 (0.29)	0.42 (0.31)	−0.07 (−0.09 to −0.06)
Proportion of time spent in hypoxemia (Spo_2 <88%) in ICU, %	0.011 (0.06)	0.011 (0.06)	0.0001 (−0.004 to 0.004)

Subgroup	Usual Care	Intervention	Adjusted MD (95% CI)
Injury Severity Score			
>/= 16	15 (10.7)	17 (11)	0.39 (−0.38 to 1.16)
< 16	21 (8.67)	23.1 (7.96)	0.15 (−0.70 to 1.00)
Mechanical Ventilation			
Ventilated Before ICU Arrival	13.1 (10.7)	13.4 (11.2)	−0.40 (−1.25 to 0.44)
Not Ventilated Before ICU Arrival	20.6 (8.86)	22.6 (8.3)	0.75 (0.00 to 1.50)
Penetrating Mechanism of Injury			
Yes	17.7 (10)	18.8 (10.1)	0.06 (−1.09 to 1.22)
No	17.5 (10.4)	19.7 (10.3)	0.36 (−0.35 to 1.06)
Race and Ethnicity			
Non−Hispanic White	17.1 (10.5)	19.9 (10.2)	0.73 (−0.05 to 1.52)
Non−Hispanic Black	18.2 (9.72)	18.7 (9.88)	−0.01 (−1.20 to 1.17)
Hispanic	17.4 (10.1)	18.8 (10.1)	−0.18 (−1.58 to 1.22)
Other	16.6 (11)	18.5 (10.9)	0.45 (−1.07 to 1.98)
Shock Index >/= 1.0			
Yes	18.3 (10.1)	19.3 (10)	0.39 (−0.81 to 1.59)
No			0.36 (−0.34 to 1.06)
Traumatic Brain Injury	15.9 (11.6)	18.6 (11.2)	
Yes	18.3 (9.69)	20.4 (9.27)	0.59 (−0.26 to 1.45)
No			0.20 (−0.57 to 0.96)



Conclusions of SAVE-O2 Trial

A targeted normoxemia approach:

- Is safe (no increased hypoxemia)
- Effectively reduced need for supplemental oxygen
  - Most (95%) patients needed little or no supplemental oxygen
- Maintained/improved patient outcomes
- Increased SOFD among patients not receiving mechanical ventilation

Open questions:

- **Autonomous solutions**

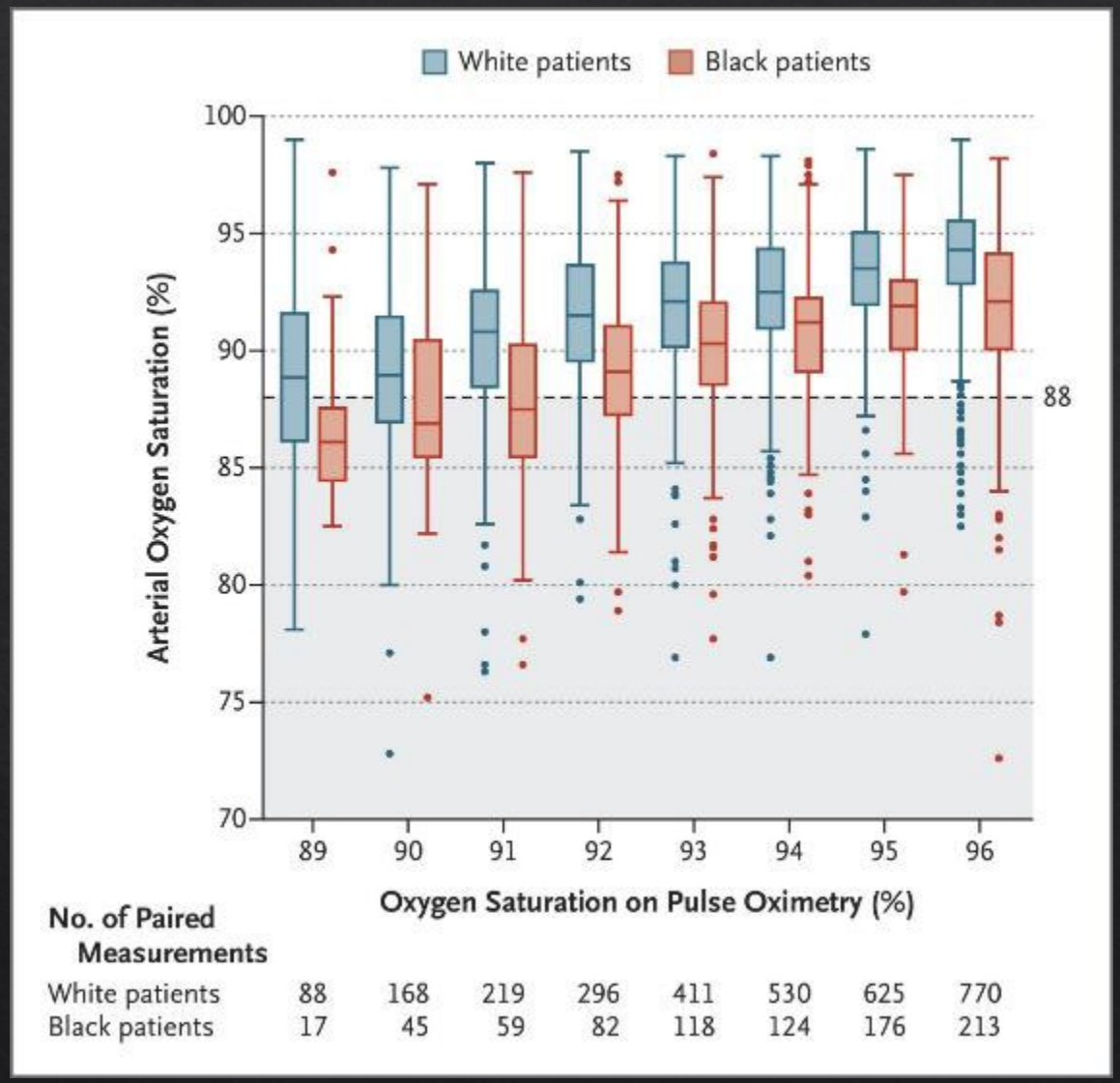
Skin Pigmentation and Unrecognized Hypoxemia

Pulse-Ox measurement error is common, & more frequent at lower pulse oximetry levels

Unrecognized hypoxemia ($SaO_2 < 88\%$ when $SpO_2 \geq 92\%$) is more common among patients with darker skin pigmentation

…Independent of clinical factors or pulse oximeter

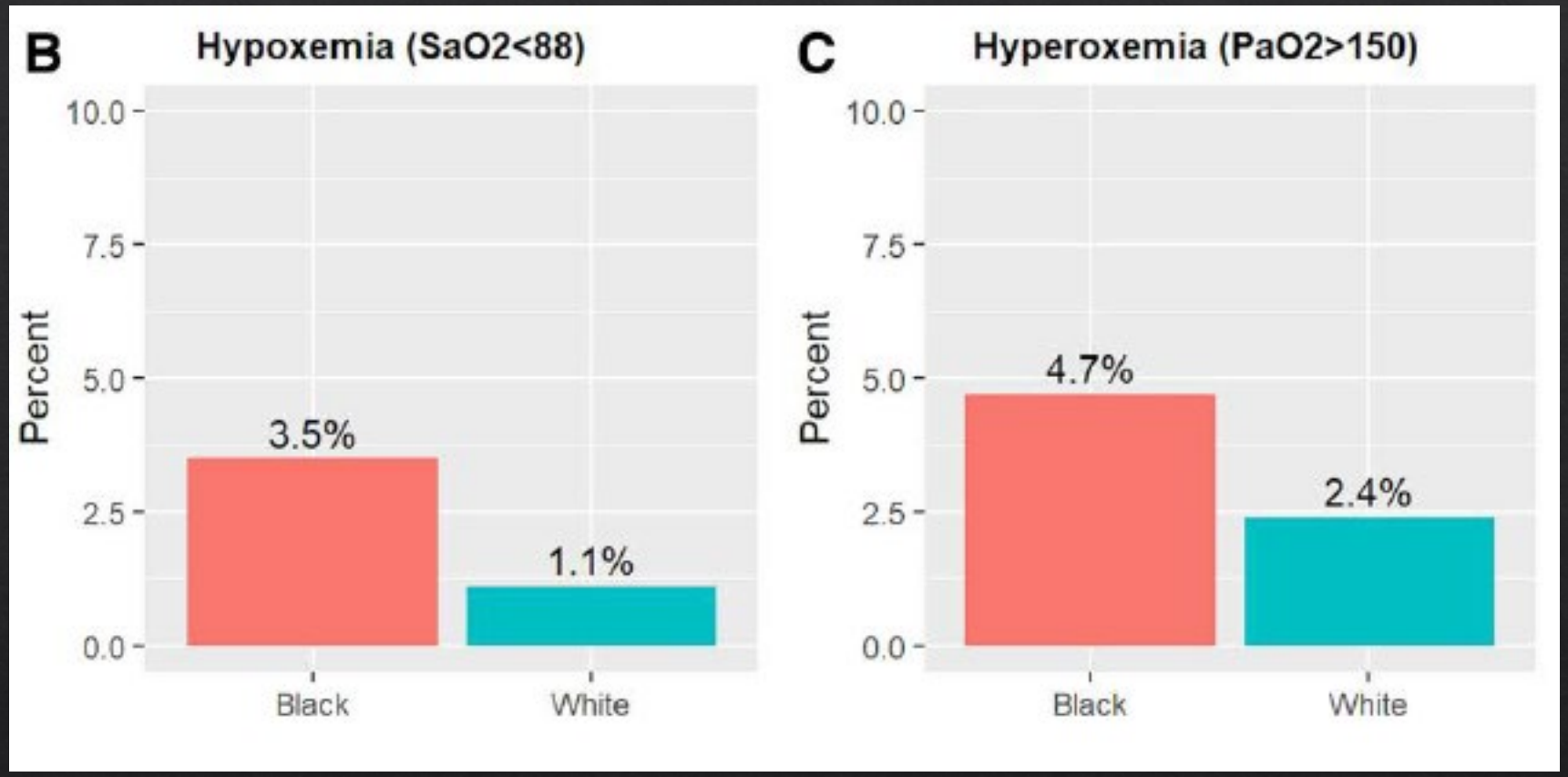
Skin Pigmentation and Unrecognized Hypoxemia



No. of Paired Measurements								
White patients	88	168	219	296	411	530	625	770
Black patients	17	45	59	82	118	124	176	213

Sjoding et al., NEJM, 2020

Skin Pigmentation and Unrecognized Hypoxemia



SaO_2 among 1,024 patients when SpO_2 92-96%

Black patients had a higher incidence of both hypoxemia (3.5% vs 1.1%, p=0.002) and hyperoxemia (4.7% vs 2.4%, p=0.03)

Seitz et al., Crit Care Explorations, 2022

Skin Pigmentation and Unrecognized Hypoxemia

Ultimate solution is likely an improved pulse-oximeter (Co-Oximetry) – at least 5-10 years away

However, race/ethnicity is a poor surrogate for skin pigmentation

FDA Executive Summary

Prepared for the
February 2, 2024, meeting of the
Anesthesiology and Respiratory Therapy Devices Panel of the
Medical Devices Advisory Committee
Center for Devices and Radiological Health (CDRH)
United States Food and Drug Administration

Performance Evaluation of Pulse Oximeters Taking into Consideration Skin Pigmentation, Race and Ethnicity

GUIDANCE DOCUMENT

Pulse Oximeters for Medical Purposes – Non-Clinical and Clinical Performance Testing, Labeling, and Premarket Submission Recommendations

Draft Guidance for Industry and Food and Drug Administration Staff

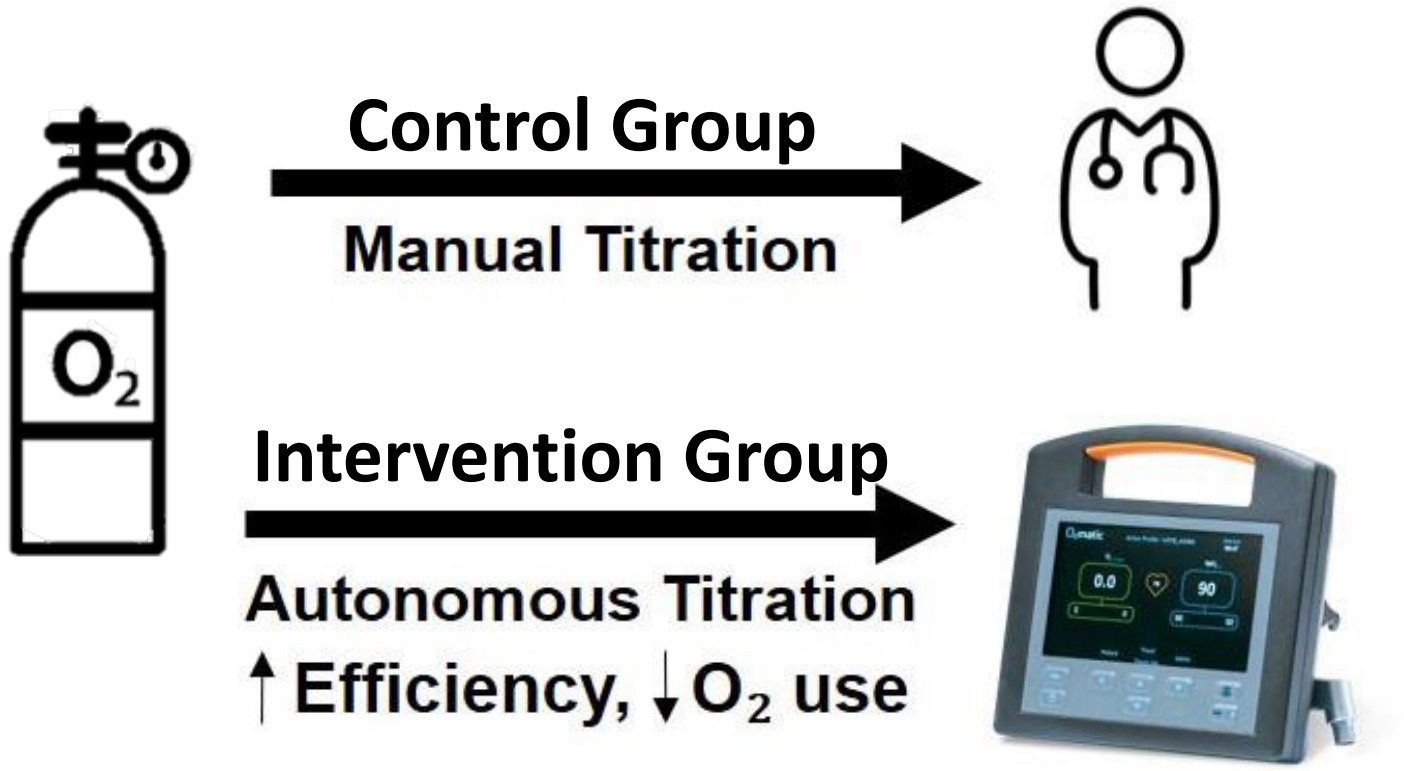
JANUARY 2025

SAVE-O_2

STRATEGY TO AVOID EXCESSIVE OXYGEN

USING AUTONOMOUS OXYGEN TITRATION INTERVENTION (AI)

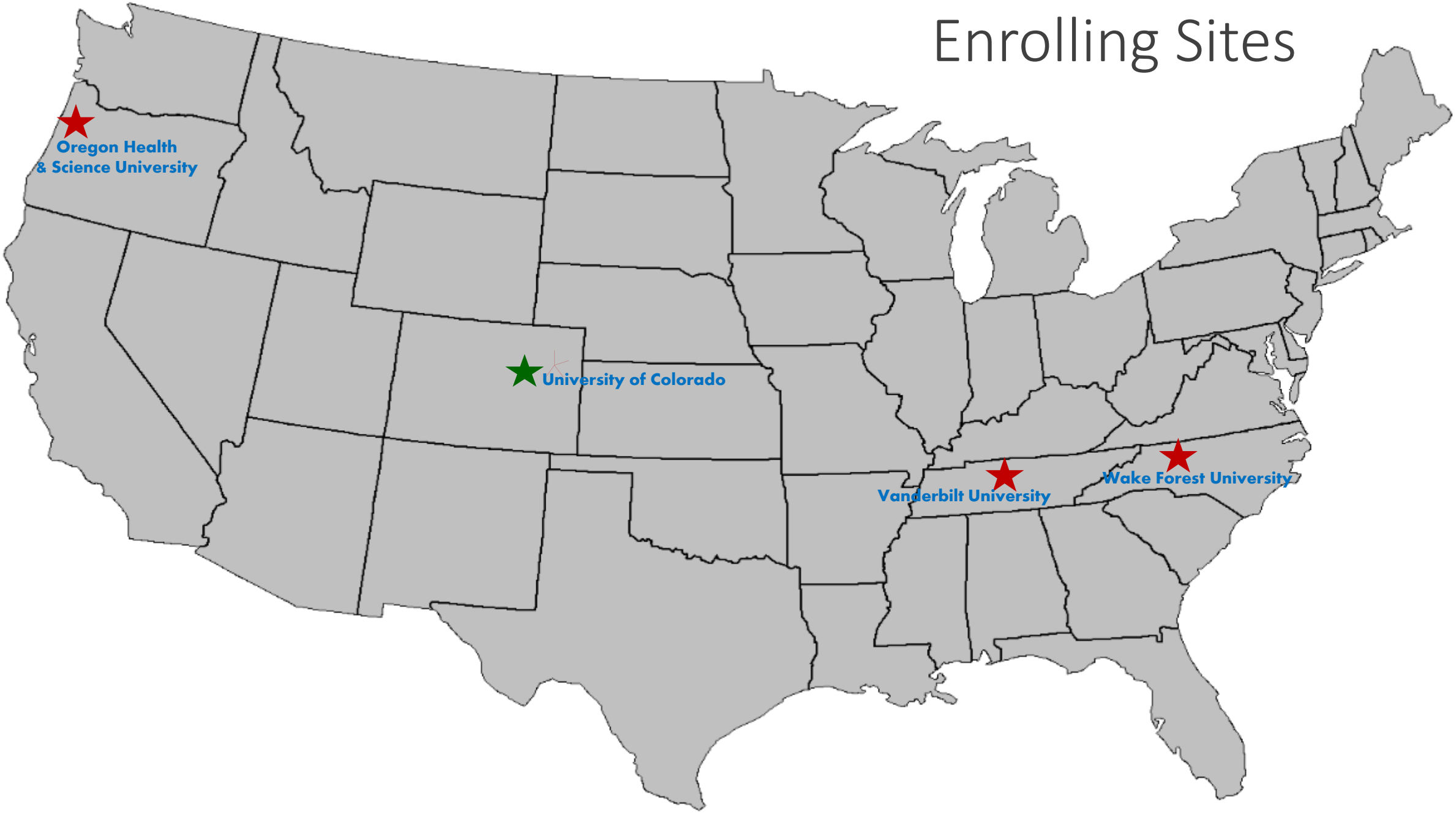
NCT06374225



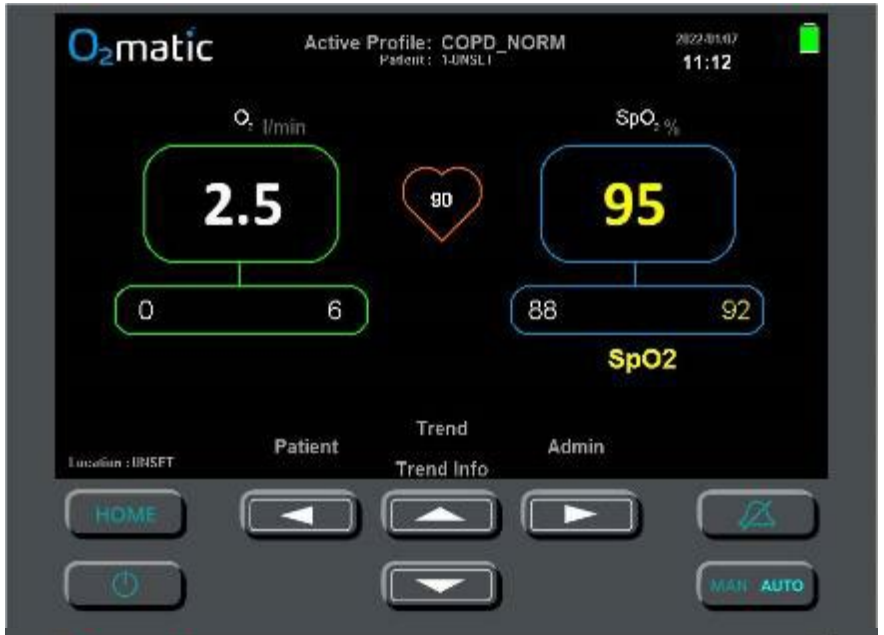
Study Design

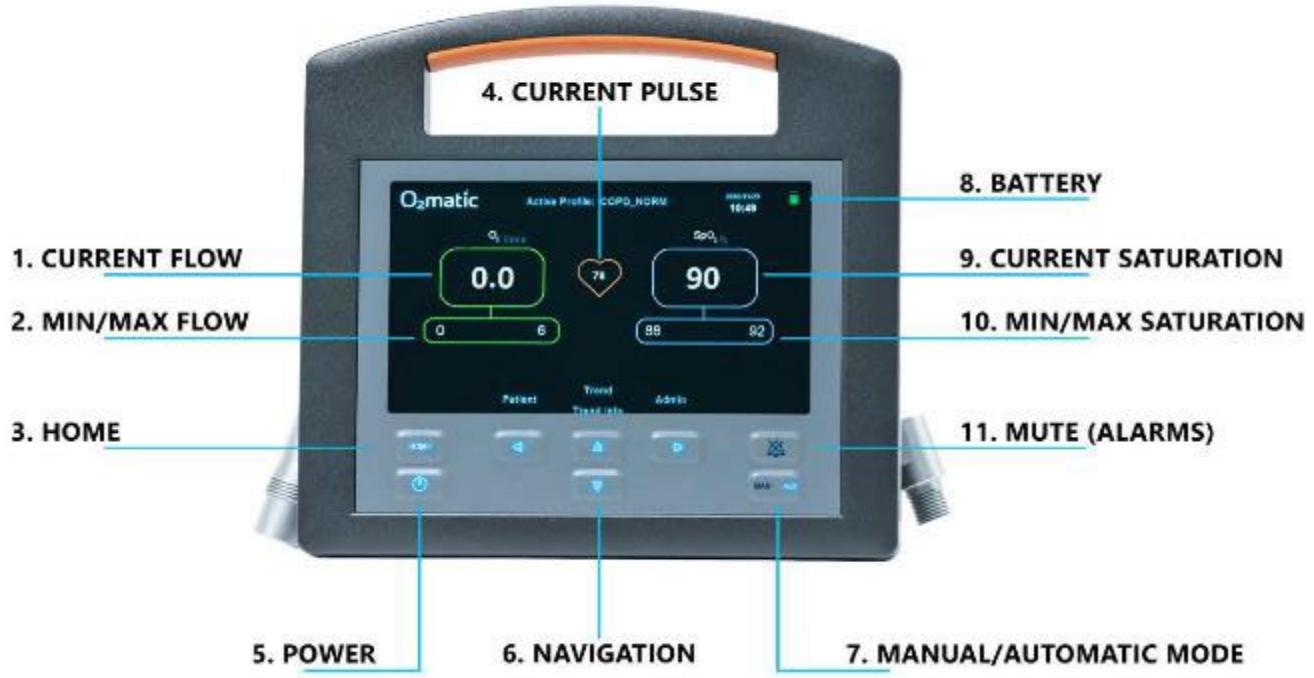
- Multicenter randomized controlled trial
  - Oversight by FDA, IRB, DSMB
  - 300 patients at four level 1 trauma centers in the U.S.
- Manual titration (control) versus automated titration with PRO100 (intervention)
  - Goal SpO2 range 90-96%, target 93% for all patients
  - Enroll within 36 hours of hospital arrival

Enrolling Sites



O2matic PRO100 Device

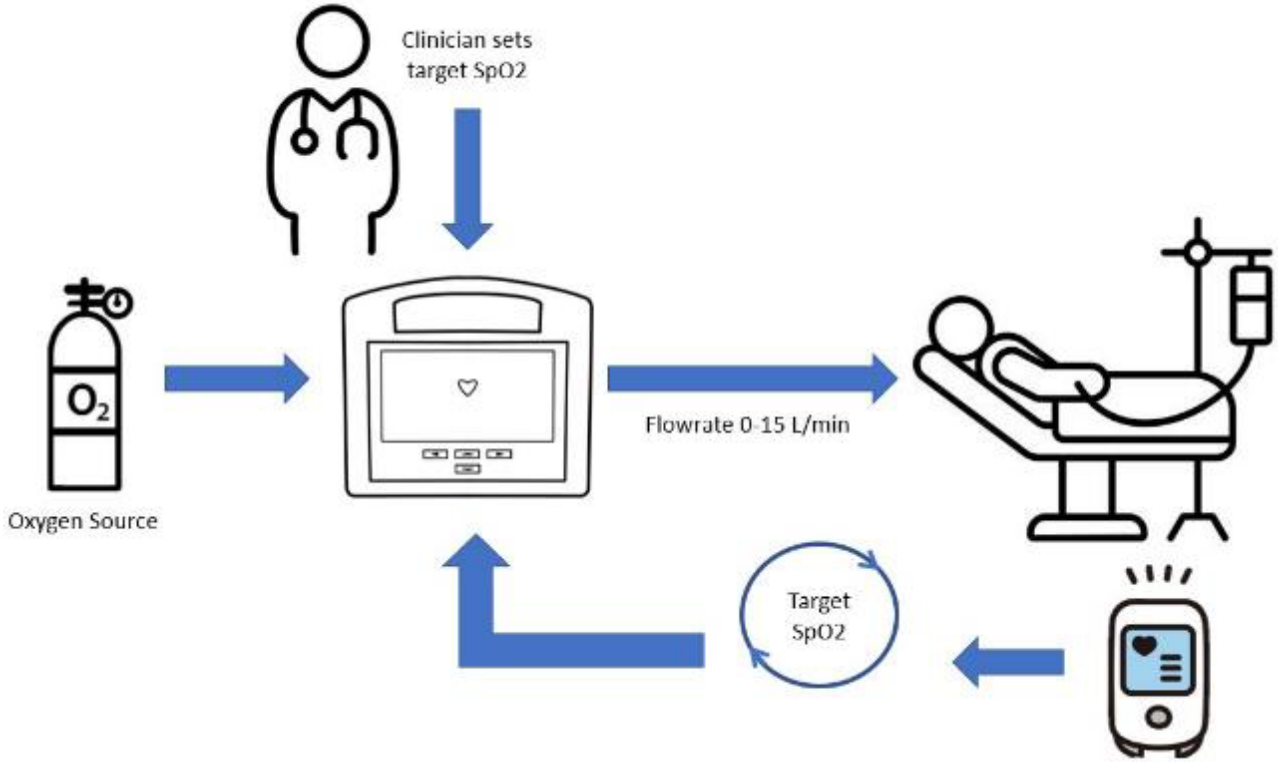




Implementation

- Usual Care

- Automated Titration

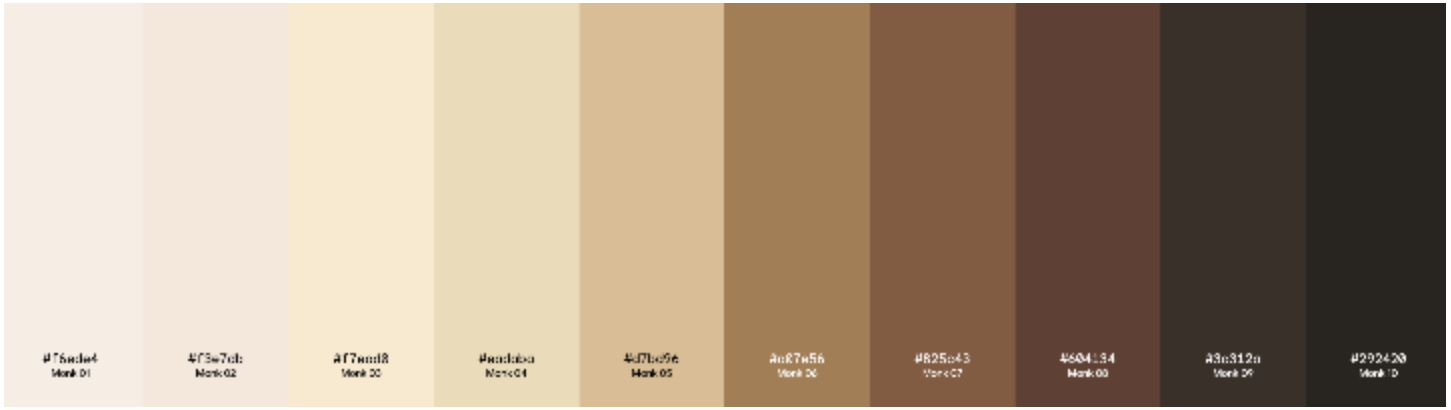


Skin Pigmentation

Fitzpatrick Skin Type Scale

Type I	Type II	Type III	Type IV	Type V	Type VI
Light, pale white	White, fair	Medium, white to olive	Olive, moderate brown	Brown, dark brown	Black, very dark brown to black
Always burns, never tans	Usually burns, tans with difficulty	Sometimes mild burn, gradually tans to olive	Rarely burns, tans with ease to a moderate brown	Very rarely burns, tans very easily	Never burns, tans very easily, deeply pigmented

Monk Skin Tone Scale



Nix Spectro 2 (5 mm)

Outcomes

1. **Primary Outcome:** Proportion of time spent within targeted normoxemia range (SpO_2 90-96%, target 93%)

2. **Secondary Outcomes**
   - **Amount of supplemental oxygen administered**, in first 72 hrs
   - **Proportion of time spent in hypoxemia** (SpO_2 <88%) in first 72hrs
   - **Proportion of time spent in hyperoxemia** (SpO_2 >96%) in first 72hrs
   - **Time to Room Air**, time from hospital presentation to first episode of no supplemental oxygen (room air)

USING AUTONOMOUS OXYGEN TITRATION INTERVENTION (AI)

NCT06374225

Estimated to complete enrollment of 300 patients in <u>early 2026</u>

Conclusions

- SpO_2 90-98% is appropriate for most critically ill adults
- Targeting normoxemia (SpO_2 90-96%) is safe and maintains/improves outcomes for critically ill trauma patients
  - Likely improves outcomes for non-MV patients
- Unrecognized hypoxemia ($SaO_2 < 88\%$ when $SpO_2 \geq 92\%$) is more common among darker skin patients
  - But, race/ethnicity is a poor surrogate for skin pigmentation
- Autonomous oxygen titration solutions may be coming
  - already available in Europe/Australia/NZ

SAVE-O2
STRATEGY TO AVOID EXCESSIVE OXYGEN

Team and Collaborators

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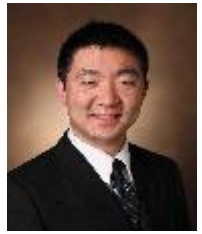
John Rice, PhD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ATLAS
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Thank you!

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SAVE-O_2
STRATEGY TO AVOID EXCESSIVE OXYGEN
USING AUTONOMOUS OXYGEN TITRATION INTERVENTION (AI)