Oxygen-Saturation Targets for Critically Ill Adults Receiving Mechanical Ventilation: An embedded cluster-crossover trial

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Disclosures

- **Funding:**

- NHLBI K23HL143053
  Oxygen Saturation Targets during Mechanical Ventilation for Critically Ill Adults
- NIA R21AG063126
  Cognitive Outcomes in the Pragmatic Investigation of Optimal Oxygen Targets

- **Conflicts of Interest:**

  None

Overview

- Background
- Trial Design Considerations
- Methods
- Results
- Discussion

Background

Oxygenation during mechanical ventilation

- >3 million mechanically ventilated ICU patients in US each year
- Universally involves titrating oxygen (FiO_2) to maintain oxygenation
- Oxygenation target that optimizes outcomes has been unknown

Oxygenation target options

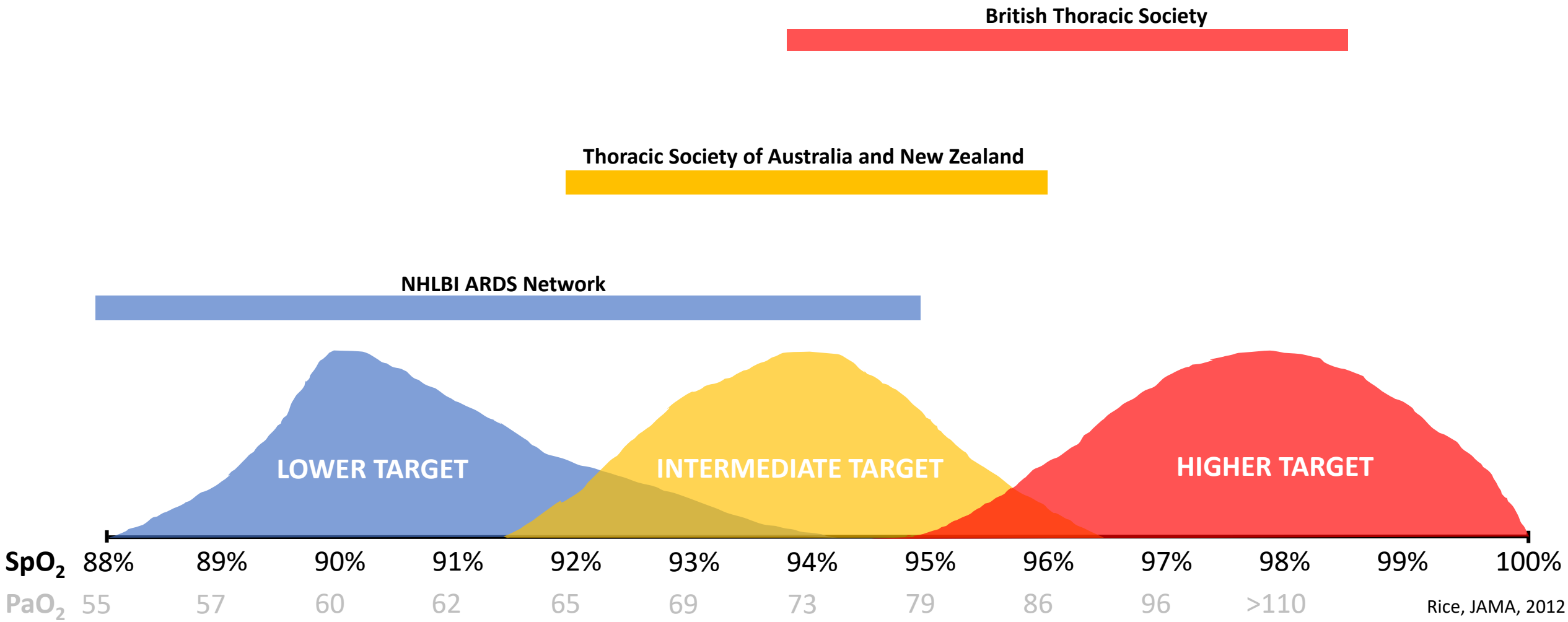
SpO_2	88%	89%	90%	91%	92%	93%	94%	95%	96%	97%	98%	99%	100%
PaO_2	55	57	60	62	65	69	73	79	86	96	>110		

Oxygenation target physiology

	LOWER TARGET	INTERMEDIATE TARGET	HIGHER TARGET
Pro	May avoid excess FiO2, hyperoxemia, hyperoxia	May avoid both hyperoxia and hypoxia (U-shaped curve)	May avoid hypoxia
Con	Hypoxia – impedes ATP production, generates ROI, necrosis & apoptosis	May incur risk of both hyperoxia and hypoxia	Excess FiO_2, - direct lung toxicity Hyperoxemia - vasoconstriction Hyperoxia – ROI, peroxidation, DNA damage

SpO_2	88%	89%	90%	91%	92%	93%	94%	95%	96%	97%	98%	99%	100%
PaO_2	55	57	60	62	65	69	73	79	86	96	>110		

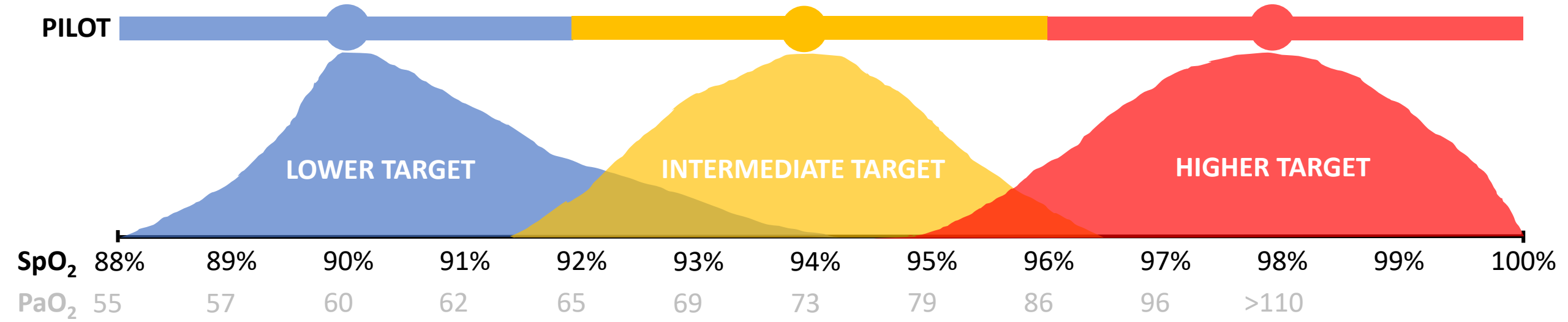
Oxygenation target guidance



Rice, JAMA, 2012
Beasley, Respirology, 2015
O'Driscoll, Thorax, 2017

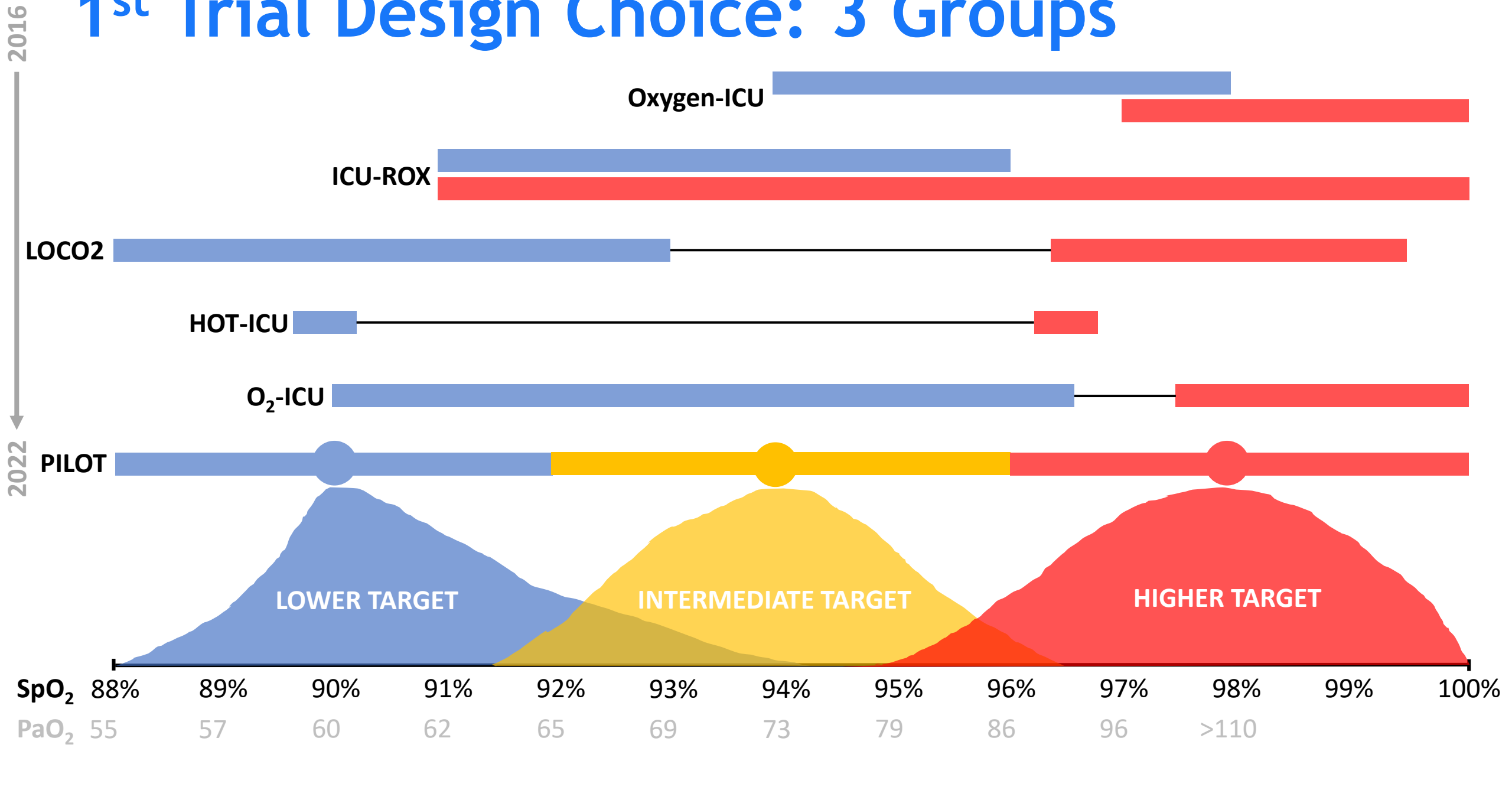
Aim of the PILOT trial

- Determine the effects of lower, intermediate, and higher SpO_2 targets on clinical outcomes for mechanically ventilated critically ill adults.

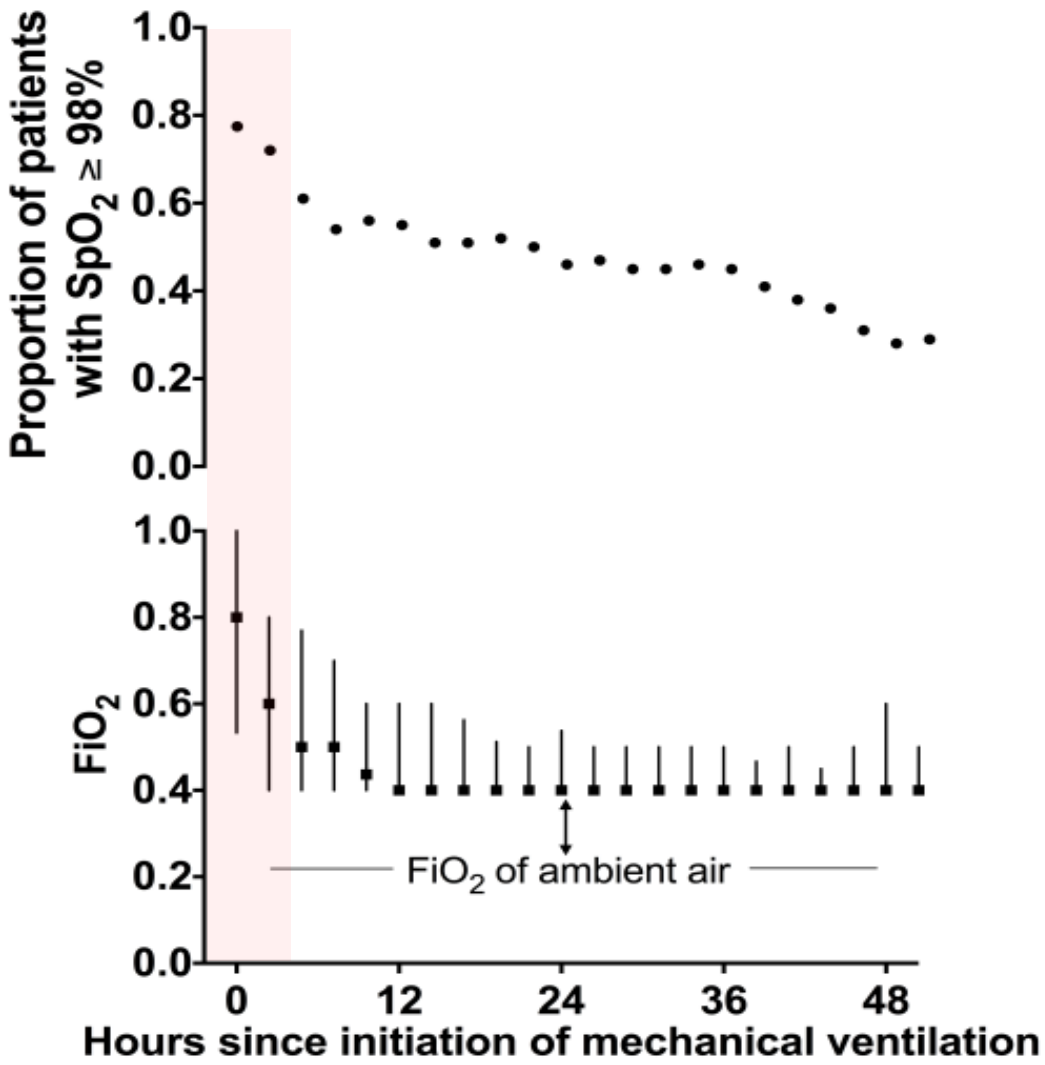


Trial Design Considerations

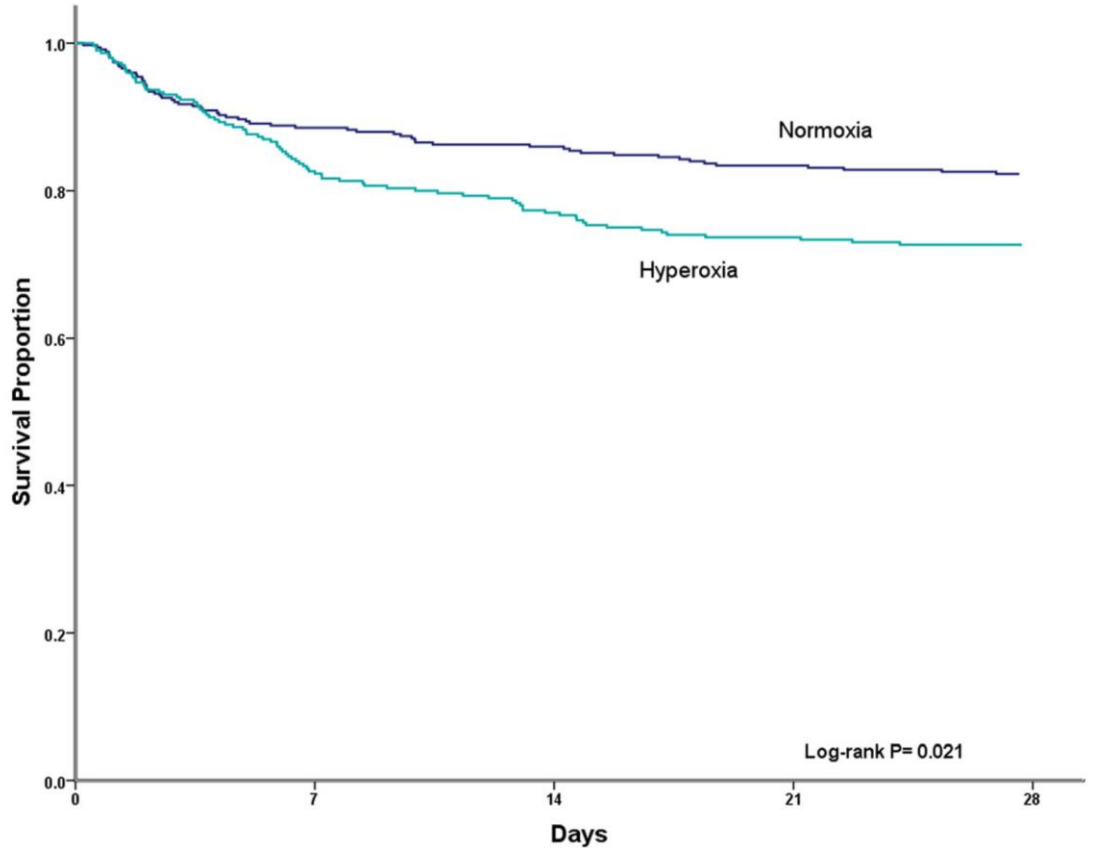
1st Trial Design Choice: 3 Groups



2nd Trial Design Choice: Early Intervention



Emergency department hyperoxia associated with increased mortality in mechanically ventilated patients: a cohort study



3rd Trial Design Choice: Target SpO_2

Big Data for Clinical Trials: Automated Collection of SpO_2 for a Trial of Oxygen Targets during Mechanical Ventilation

	SpO_2 measured	PaO_2 measured
Day 1	Every 1 minute	24% of patients
Day 2	Every 1 minute	13% of patients
Day 3	Every 1 minute	10% of patients
Day 4	Every 1 minute	8% of patients
Day 5	Every 1 minute	6% of patients
Day 6	Every 1 minute	5% of patients
Day 7	Every 1 minute	4% of patients

4^{the} Trial Design Choice: Cluster-Crossover

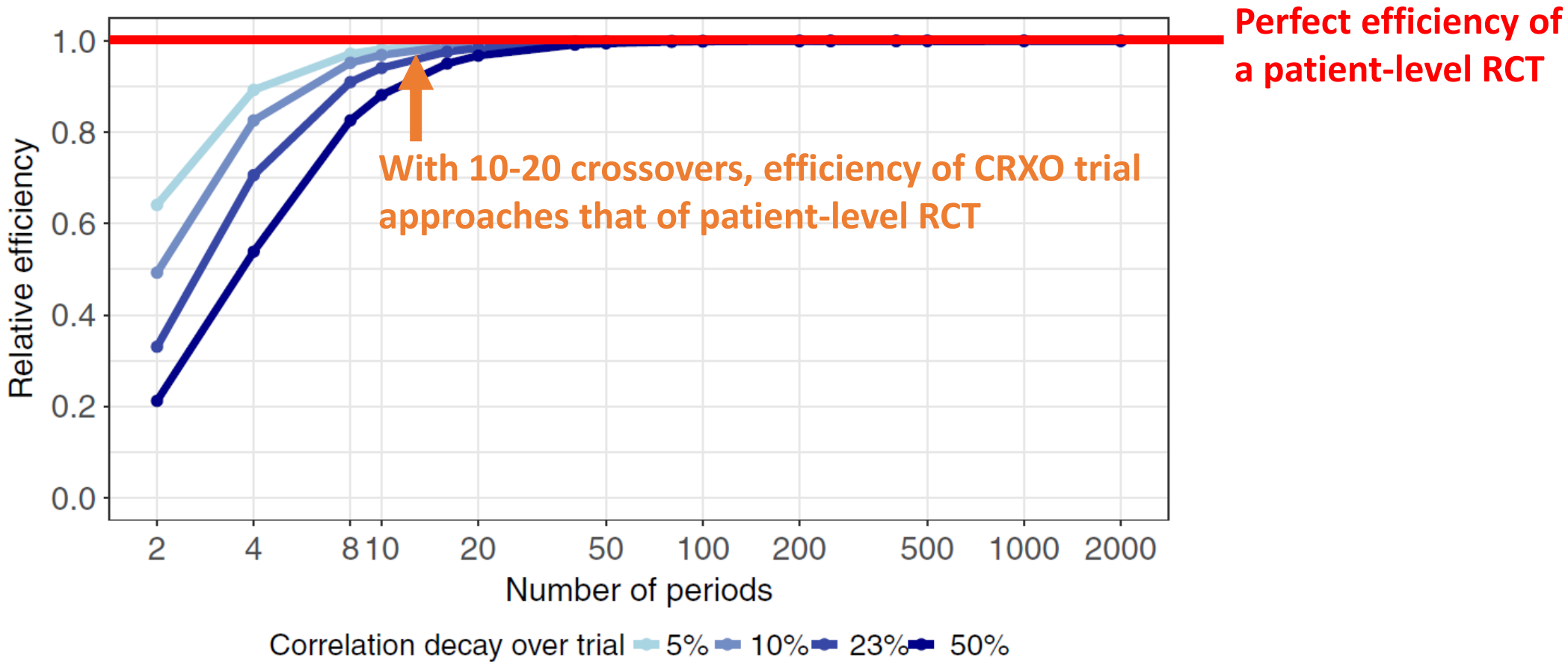
Rationale for cluster-level allocation

- Emulate management in clinical care
  - Titration of FiO_2 for all patients in unit by 2-4 respiratory therapists
  - Management of ventilator via unit-wide protocols (e.g., TV, PEEP, SBT)

- Enrollment immediately at initiation of mechanical ventilation
  - Minimize pre-study exposure to excess FiO2, hyperoxemia, hyperoxia
  - Facilitate on-study separation between groups

Rationale for number of crossovers

How many times should a cluster randomized crossover trial cross over?



Methods

PILOT Trial Design

- Pragmatic, unblinded, cluster-randomized, cluster-crossover trial
  - Initiated by the investigators
  - Funded by the NIH/NHLBI
  - Approved by the Institutional Review Board at Vanderbilt University
  - Registered prior to initiation (NCT03537937)
  - Overseen by independent Data and Safety Monitoring Board (DSMB)

- Enrollment (36 months)
  - Began: July 1 2018
  - Paused: April 1 2020 until May 31 2020 due to the COVID-19 pandemic
  - Concluded: August 31 2021

Study Sites and Patients

- Study Sites
  - Emergency department & medical intensive care unit at Vanderbilt

- Patients
  - All adults in medical ICU or in ED with planned medical ICU admission
  - Enrolled at the time of the first receipt of invasive mechanical ventilation
  - Excluded:
    - Age < 18 years
    - Pregnant
    - Prisoner

Randomization and Treatment Allocation

- **Cluster-level allocation:** All patients in the ED & ICU were assigned together to an SpO_2 target
- **Cluster-level crossover:** Every two months, the ED & ICU switched together between SpO_2 targets in a sequence generated by computerized randomization using permuted blocks of 3 to minimize impact of seasonal variation
- **Washout period:** last 7 days of each two-month period

Study Year 1						Study Year 2						Study Year 3					
Jul-Aug	Sep-Oct	Nov-Dec	Jan-Feb	Mar-Apr	May-Jun	Jul-Aug	Sep-Oct	Nov-Dec	Jan-Feb	*Mar & Jun*	Jul-Aug	Sept-Oct	Nov-Dec	Jan-Feb	Mar-Apr	May-Jun	Jul-Aug
2018			2019						2020			2021					
H	I	L	I	L	H	L	I	H	H	I	L	I	H	L	I	H	L

H = Higher; I = Intermediate; L = Lower SpO_2 target group

Informed Consent

1. Patients were enrolled under waiver of informed consent
   - Minimal risk
     - Compared 3 approaches common in clinical care
     - Trial only determined target for patients for whom clinicians were uncertain which target would be best and felt all 3 were reasonable
     - If clinicians felt that the optimal target known for a given patient, that target was used
   - Impracticable to obtain informed consent from every patient in the ED & ICU prior to emergency tracheal intubation & initiation of mechanical ventilation
2. Patients and families were notified of participation with an IRB-approved information sheet
3. Patients or their legally-authorized representatives were approached for informed consent for assessment of long-term outcomes as a part of the independently-funded CO-PILOT study

No research-specific study procedures (e.g., blood draws)

Intervention

- Respiratory therapists titrated FiO2 to achieve SpO2
  - Beginning within 15 minutes of initiation of mechanical ventilation
  - Ending at discontinuation from mechanical ventilation or transfer
  - Except: during transport, procedures, or spontaneous breathing trials

Study Group	SpO_2 target	SpO_2 range	PaO_2 target	PaO_2 range
Lower SpO_2 target	90%	88-92%	60 mm Hg	55-65 mm Hg
Intermediate SpO_2 target	94%	92-96%	70 mm Hg	65-80 mm Hg
Higher SpO_2target	98%	96-100%	110 mm Hg	> 80 mm Hg

Other interventions

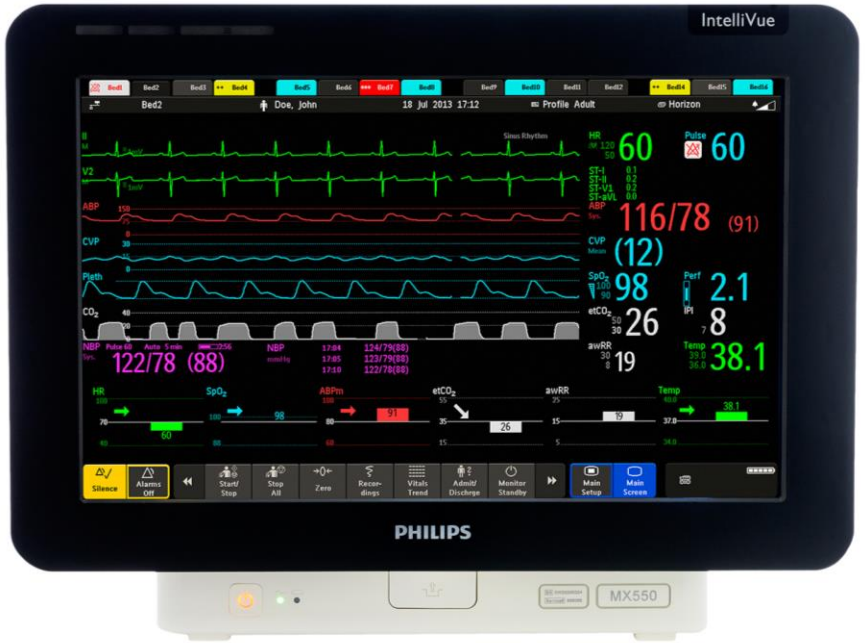
- Modification of the SpO2 target
  - If a clinician, patient, or family member determined that an oxygenation target other than the assigned target would be best for the patient, that target was used (and the reason was recorded)

- Institutional protocols and clinicians determined
  - Tidal volume, PEEP, blood gas measurement
  - Analgesia, sedation
  - Timing of SAT, SBT, and extubation

Data collection

- Study personnel
  - Baseline characteristics, on-study management, in-hospital outcomes

- Automated extraction from bedside monitor
  - SpO_2, FiO_2, ventilator settings <u>every 1 minute</u>



Outcomes

- **Primary Outcome:** Ventilator-free days
  - Days alive and free of mechanical ventilation through study day 28

- **Secondary Outcome:** In-hospital mortality
  - Death from any cause prior to day 28, censored at hospital discharge

- **Exploratory**
  - Clinical: ICU mortality, vasopressor-free days, RRT-free days, ICU-free days
  - Organ Function: Non-respiratory SOFA score, creatinine, lactate, AKI
  - Safety: Arrhythmia, cardiac arrest, pneumothorax, stroke, MI

Sample Size

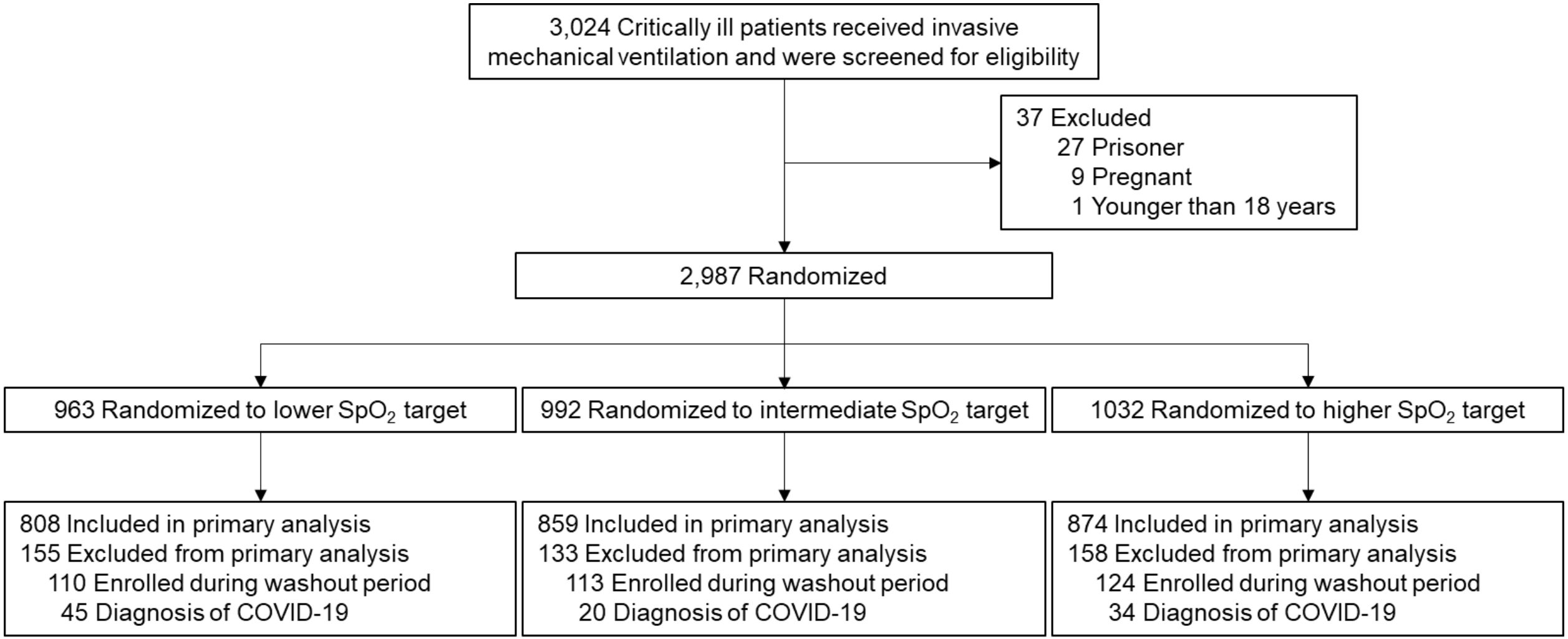
- Assumptions:
  - 2,250 patients over 36 months
  - Median ventilator-free days of 22 [IQR, 0-25]
  - Intra-cluster intra-period correlation of 0.01
  - Alpha of 0.05

- 92% power to detect a difference of 2 ventilator-free days

Statistical Analysis

- Primary Analysis
  - All enrolled patients EXCEPT
    - Admitted during washout period
    - Laboratory-confirmed COVID-19 – majority of trial occurred before pandemic and COVID-19 patients were cared for in a separate COVID ICU not participating in the trial
  - Proportional odds model
    - Dependent variable: ventilator-free days
    - Independent variables: group (lower vs intermediate vs higher) and time

Results

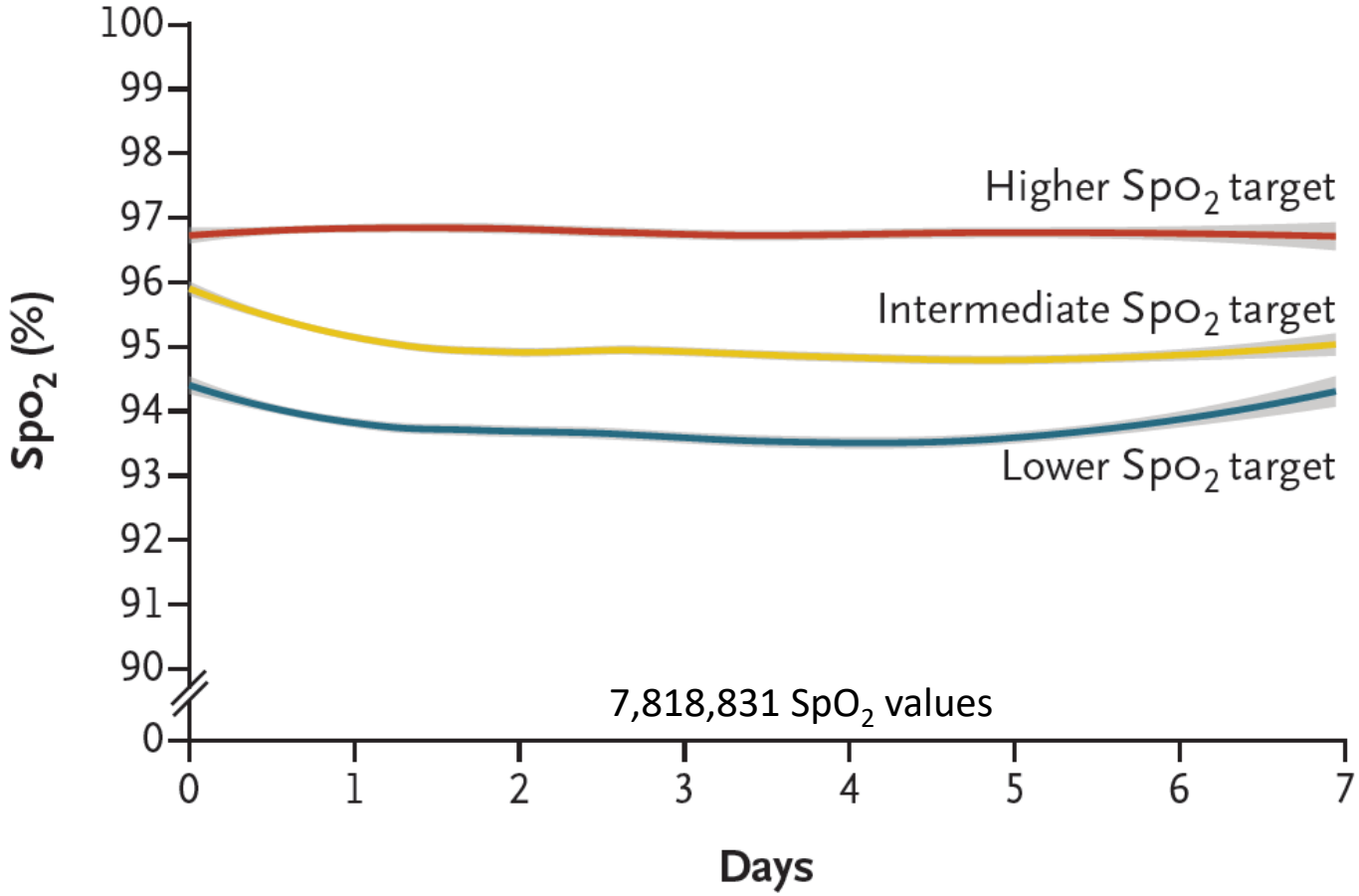


2,541 patients

Table 1. Characteristics of the Patients at Baseline.*

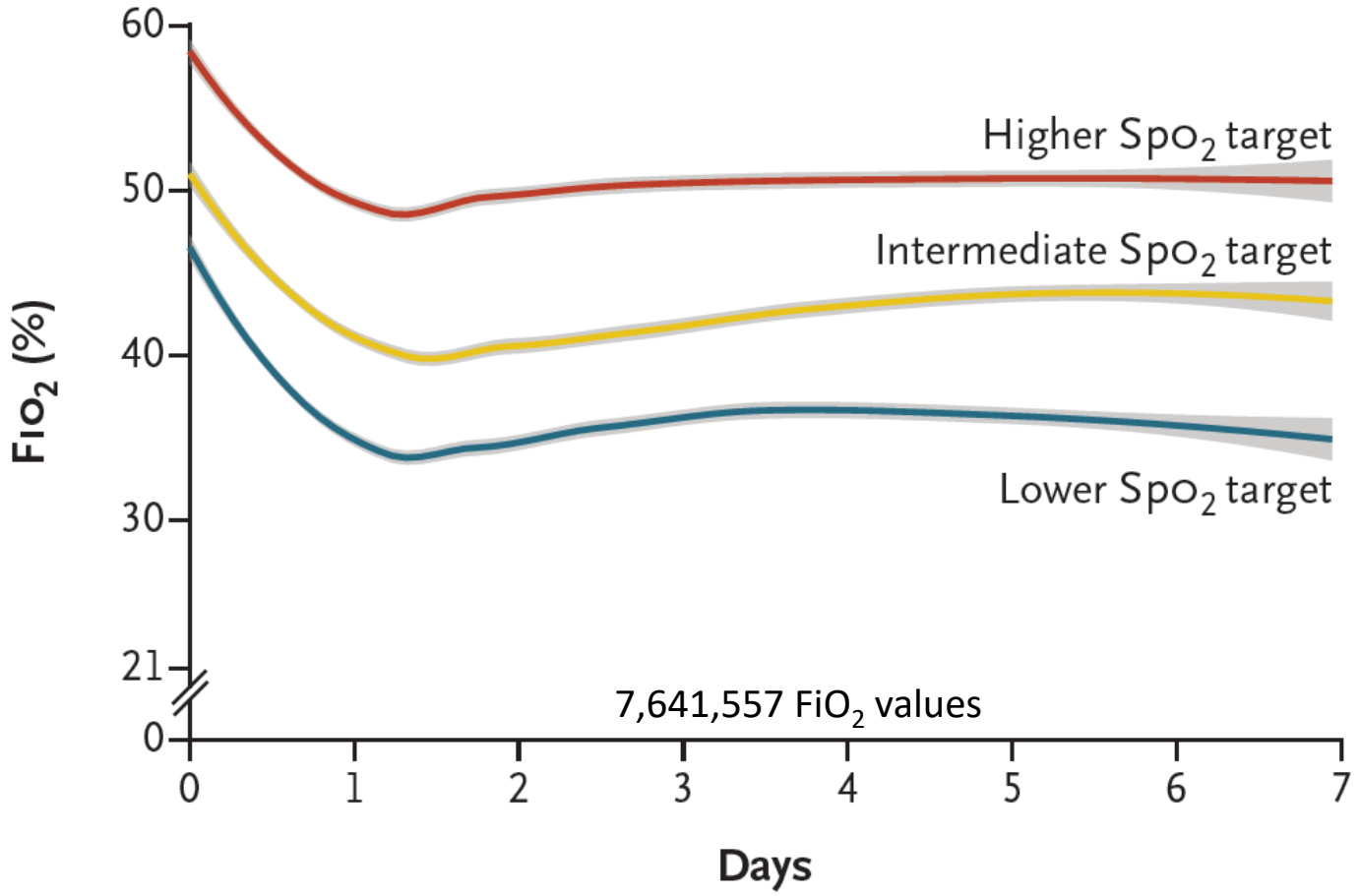
Characteristic	Lower SpO_2 Target (N = 808)	Intermediate SpO_2 Target (N = 859)	Higher SpO_2 Target (N = 874)
Median age (IQR) — yr	57 (44–67)	59 (47–68)	59 (45–68)
Female sex — no. (%)	361 (44.7)	385 (44.8)	409 (46.8)
Race or ethnic group — no. (%)†			
White	649 (80.3)	666 (77.5)	695 (79.5)
Black	121 (15.0)	140 (16.3)	136 (15.6)
Other	38 (4.7)	53 (6.2)	43 (4.9)
Median time from initiation of mechanical ventilation to enrollment (IQR) — hr‡	0.0 (0.0–4.9)	0.0 (0.0–4.5)	0.0 (0.0–5.5)
Location at enrollment — no. (%)			
Emergency department	280 (34.7)	313 (36.4)	282 (32.3)
Intensive care unit	528 (65.3)	546 (63.6)	592 (67.7)
Coexisting conditions — no. (%)			
Chronic obstructive pulmonary disease	148 (18.3)	175 (20.4)	169 (19.3)
Coronary artery disease	145 (17.9)	152 (17.7)	178 (20.4)
End-stage kidney disease, receiving RRT	52 (6.4)	46 (5.4)	39 (4.5)
Acute illnesses§			
Cardiac arrest — no. (%)	125 (15.5)	100 (11.6)	109 (12.5)
Acute myocardial infarction — no. (%)	136 (16.8)	138 (16.1)	145 (16.6)
Sepsis or septic shock — no. (%)	275 (34.0)	247 (28.8)	283 (32.4)
Stage ≥II acute kidney injury — no./total no. (%)	231/756 (30.6)	248/813 (30.5)	243/835 (29.1)
Receipt of vasopressors — no. (%)	160 (19.8)	171 (19.9)	153 (17.5)
Median nonrespiratory SOFA score (IQR)¶	5 (4–8)	5 (4–8)	5 (3–8)

Separation between groups in SpO2



	Lower	Intermediate	Higher
SpO_2 of 99-100% on FiO_2>0.21	6%	8%	33%
SpO_2 < 85%	0.8%	0.6%	0.9%

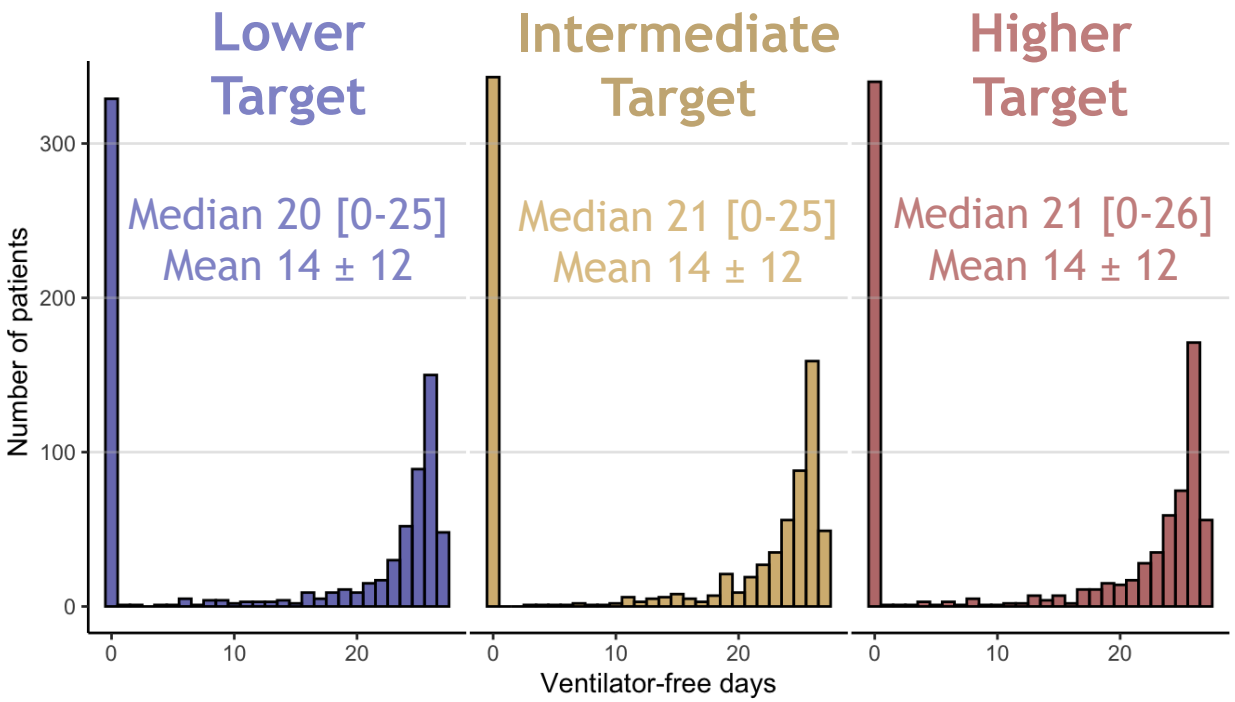
Separation between groups in FiO2



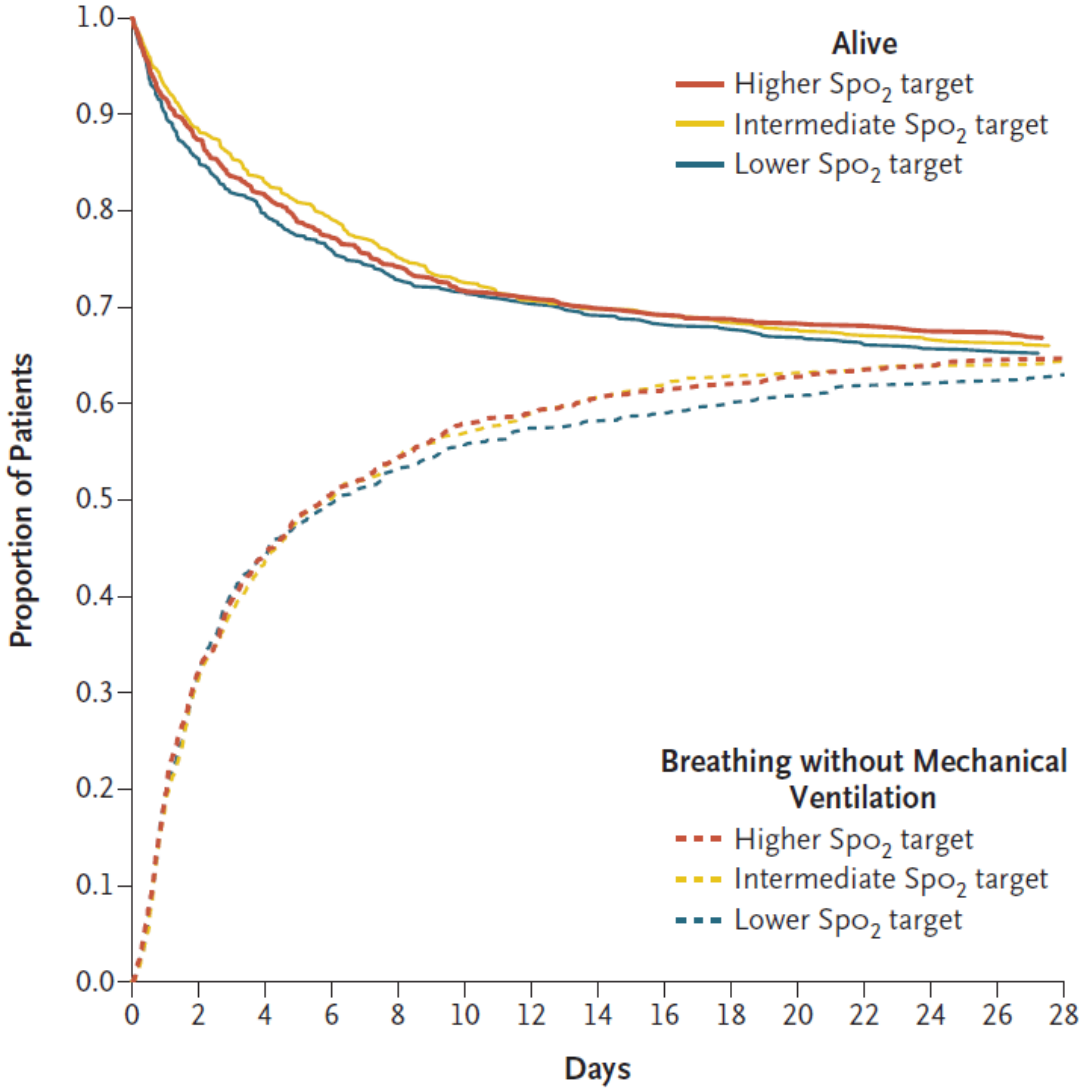
	Lower	Intermediate	Higher
FiO2 ≥ 0.40	33%	45%	69%
FiO2 of 0.21	34%	22%	4%

Primary Outcome

Primary Outcome

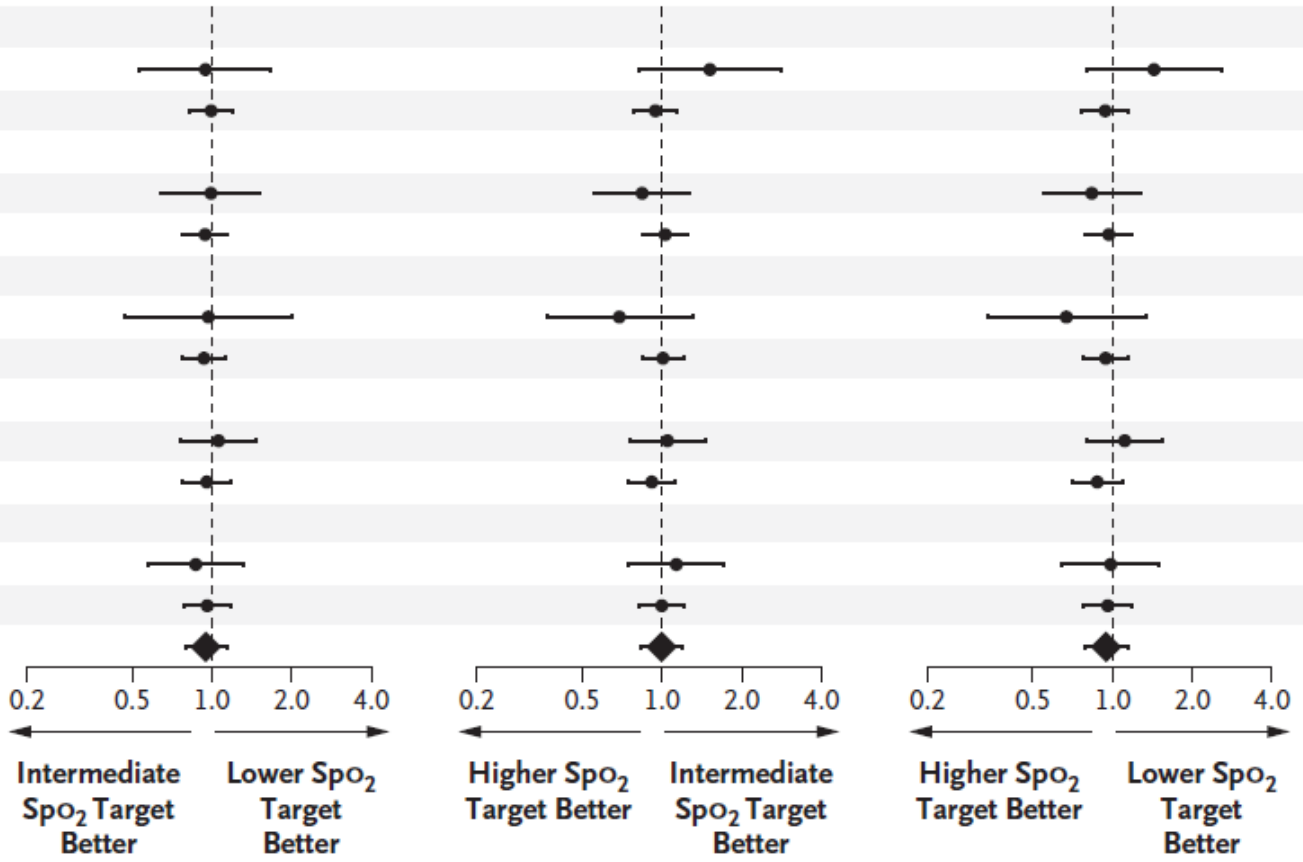


P value for a difference between 3 groups = 0.81



No differences in any subgroup

Subgroup	No. of Patients	Lower SpO_2 Target	Intermediate SpO_2 Target	Higher SpO_2 Target
		median ventilator-free days (IQR)		
Cardiac arrest				
Yes	334	0 (0–16)	0 (0–20.5)	0 (0–0)
No	2207	23 (0–26)	22 (0–26)	22 (0–26)
Acute myocardial infarction				
Yes	419	13 (0–25)	15 (0–24)	21 (0–25)
No	2122	21 (0–26)	21 (0–26)	21 (0–26)
Acute respiratory distress syndrome				
Yes	190	0 (0–16)	0 (0–19)	0 (0–22.75)
No	2351	21 (0–26)	22 (0–26)	22 (0–26)
Sepsis or septic shock				
Yes	805	0 (0–24)	0 (0–22)	0 (0–23)
No	1736	23 (0–26)	23 (0–26)	24 (0–26)
Receipt of vasopressor				
Yes	484	0 (0–22)	0 (0–23)	0 (0–22)
No	2057	23 (0–26)	22 (0–26)	22 (0–26)
Overall	2541	20 (0–25)	21 (0–25)	21 (0–26)



No differences in any subgroup

Subgroup*	n	Lower (n=808)	Intermediate (n=859)	Higher (n=874)	Lower vs Intermediate OR (95% CI)	Intermediate vs Higher OR (95% CI)	Lower vs Higher OR (95% CI)
Race							
Hispanic	45	22 [0-26]	23 [0-25]	23 [3-26]	1.11 (0.27-4.62)	0.70 (0.15-3.32)	0.77 (0.22-2.66)
Non-Hispanic Black	392	18 [0-25]	22 [0-26]	21 [0-25]	0.71 (0.46-1.10)	1.13 (0.74-1.71)	0.80 (0.51-1.24)
Non-Hispanic White	1940	21 [0-26]	21 [0-25]	21 [0-26]	0.97 (0.79-1.19)	1.03 (0.84-1.26)	1.00 (0.81-1.23)
Other	164	12 [0-25]	6 [0-25]	22 [0-26]	1.22 (0.59-2.49)	0.59 (0.30-1.14)	0.71 (0.33-1.52)
Source of admission to the ICU							
Emergency department	1194	23 [0-26]	23 [0-26]	24 [0-26]	0.95 (0.74-1.22)	0.82 [0.64-1.06]	0.78 [0.6-1.02]
Transfer from another hospital	651	19 [0-25]	19 [0-25]	17 [0-24]	0.98 (0.68-1.39)	1.33 (0.95-1.87)	1.30 (0.92-1.83)
Hospital ward	338	0 [0-22]	0 [0-23]	0 [0-23]	0.71 (0.42-1.21)	1.12 (0.68-1.86)	0.80 (0.47-1.35)
Another ICU within the hospital	205	14 [0-25]	14 [0-24]	18 [0-24]	1.09 (0.59-2.03)	0.96 (0.55-1.69)	1.05 (0.56-1.96)
Operating room	153	25 [0-26]	24 [0-26]	25 [4-26]	1.07 (0.53-2.17)	0.63 (0.31-1.30)	0.68 (0.33-1.37)
Home supplemental oxygen							
Yes	362	13 [0-25]	7 [0-25]	15 [0-25]	1.08 (0.68-1.74)	0.84 (0.53-1.33)	0.91 (0.56-1.47)
No	2172	21 [0-25]	21 [0-26]	21 [0-26]	0.92 (0.76-1.11)	1.02 (0.85-1.24)	0.94 (0.77-1.15)
Coronary disease or heart failure							
Yes	524	18 [0-25]	17 [0-25]	19 [0-25]	1.04 (0.70-1.54)	1.01 (0.70-1.48)	1.05 (0.72-1.55)
No	2017	21 [0-26]	21 [0-25]	21 [0-26]	0.93 (0.76-1.13)	0.98 (0.81-1.20)	0.91 (0.74-1.13)

Secondary, Exploratory, Safety Outcomes

	Lower	Intermediate	Higher	Lower vs Higher OR (95% CI)
In-hospital mortality	**34.8%**	**34.0%**	**33.2%**	**1.16 (0.93-1.45)**
Stage II-III AKI	30.4%	30.8%	30.0%	0.99 (0.78-1.25)
Receipt of RRT	14.8%	14.5%	11.6%	1.28 (0.93-1.77)
RRT-free days	28 [0-28]	28 [0-28]	28 [0-28]	0.88 (0.71-1.08)
Vasopressor-free days	25 [0-28]	25 [0-28]	25 [0-28]	0.87 (0.72-1.05)
ICU-free days	20 [0-24]	19 [0-24]	20 [0-24]	0.94 (0.78-1.14)
Hospital-free days	10 [0-20]	11 [0-21]	10 [0-20]	0.98 (0.81-1.19)

No differences in cardiac arrest, arrhythmia, MI, stroke, or pneumothorax

Discussion

Comparison to prior trials

Trial characteristic	PILOT	HOT-ICU	ICU-ROX	Oxygen-ICU	O_2-ICU	LOCO-2
Patients ventilated at enrollment	2,541	1,704	965	291	295	201
Time-to-enrollment	At initiation of ventilation in ED or ICU	Median of 4 hours after ICU admission	After ICU admission, median 3 hours after ventilation	At ICU admission	Median of 4 hours after ICU admission	After ICU admission, exact interval not reported
Target	SpO_2	PaO_2	SpO_2	PaO_2	PaO_2	PaO_2
SpO_2 target in lower group	90%	About 90%	91-96%	94-98%	About 90-97%	88-92%
SpO_2 target in higher group	98%	About 97%	91-100%	97-100%	About 98-100%	96-100%
Oxygenation achieved						
Median SpO_2 in lower group	94%	93%	Not reported	Not reported	96%	About 93%
Median SpO_2 in higher group	97%	96%	Not reported	Not reported	97%	About 97%
Difference between groups	-3%	-3%	Not reported	Not reported	-1%	-3.8%
Median FiO_2 in lower group	0.31	0.43	About 0.30	0.36	0.40	About 0.40
Median FiO_2 in higher group	0.45	0.56	About 0.35	0.39	0.51	About 0.50
Difference between groups	-0.15	-0.13	About -0.05	-0.03	-0.09	-0.15
Mortality	In-hospital (28d)	90 days	90 days	In-hospital	In-hospital	28 days
In lower target group	34.8%	42.9%	34.7%	24.2%	32.2%	34.3%
In higher target group	33.2%	42.4%	32.5%	33.9%	31.3%	26.5%
Difference between groups	1.6%	0.5%	2.2%	-9.7%	0.9%	7.8%

Trial characteristic	PILOT	HOT-ICU	ICU-ROX	Oxygen-ICU	O_2-ICU	LOCO-2
Patients ventilated at enrollment	2,541	1,704	965	291	295	201
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Target	SpO_2	PaO_2	SpO_2	PaO_2	PaO_2	PaO_2
SpO_2 target in lower group	90%	About 90%	91-96%	94-98%	About 90-97%	88-92%
SpO_2 target in higher group	98%	About 97%	91-100%	97-100%	About 98-100%	96-100%
Oxygenation achieved						
Median SpO_2 in lower group	94%	93%	Not reported	Not reported	96%	About 93%
Median SpO_2 in higher group	97%	96%	Not reported	Not reported	97%	About 97%
Difference between groups	-3%	-3%	Not reported	Not reported	-1%	-3.8%
Median FiO_2 in lower group	0.31	0.43	About 0.30	0.36	0.40	About 0.40
Median FiO_2 in higher group	0.45	0.56	About 0.35	0.39	0.51	About 0.50
Difference between groups	-0.15	-0.13	About -0.05	-0.03	-0.09	-0.15
Mortality	In-hospital (28d)	90 days	90 days	In-hospital	In-hospital	28 days
In lower target group	34.8%	42.9%	34.7%	24.2%	32.2%	34.3%
In higher target group	33.2%	42.4%	32.5%	33.9%	31.3%	26.5%
Difference between groups	1.6%	0.5%	2.2%	-9.7%	0.9%	7.8%

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Target	SpO_2	PaO_2	SpO_2	PaO_2	PaO_2	PaO_2
SpO_2 target in lower group	90%	About 90%	91-96%	94-98%	About 90-97%	88-92%
SpO_2 target in higher group	98%	About 97%	91-100%	97-100%	About 98-100%	96-100%
Oxygenation achieved						
Median SpO_2 in lower group	94%	93%	Not reported	Not reported	96%	About 93%
Median SpO_2 in higher group	97%	96%	Not reported	Not reported	97%	About 97%
Difference between groups	-3%	-3%	Not reported	Not reported	-1%	-3.8%
Median FiO_2 in lower group	0.31	0.43	About 0.30	0.36	0.40	About 0.40
Median FiO_2 in higher group	0.45	0.56	About 0.35	0.39	0.51	About 0.50
Difference between groups	-0.15	-0.13	About -0.05	-0.03	-0.09	-0.15
Mortality	In-hospital (28d)	90 days	90 days	In-hospital	In-hospital	28 days
In lower target group	34.8%	42.9%	34.7%	24.2%	32.2%	34.3%
In higher target group	33.2%	42.4%	32.5%	33.9%	31.3%	26.5%
Difference between groups	1.6%	0.5%	2.2%	-9.7%	0.9%	7.8%

Trial characteristic	PILOT	HOT-ICU	ICU-ROX	Oxygen-ICU	O_2-ICU	LOCO-2
Patients ventilated at enrollment	2,541	1,704	965	291	295	201
Time-to-enrollment	At initiation of ventilation in ED or ICU	Median of 4 hours after ICU admission	After ICU admission, median 3 hours after ventilation	At ICU admission	Median of 4 hours after ICU admission	After ICU admission, exact interval not reported
Target	SpO_2	PaO_2	SpO_2	PaO_2	PaO_2	PaO_2
SpO_2 target in lower group	90%	About 90%	91-96%	94-98%	About 90-97%	88-92%
SpO_2 target in higher group	98%	About 97%	91-100%	97-100%	About 98-100%	96-100%
Oxygenation achieved						
Median SpO_2 in lower group	94%	93%	Not reported	Not reported	96%	About 93%
Median SpO_2 in higher group	97%	96%	Not reported	Not reported	97%	About 97%
Difference between groups	-3%	-3%	Not reported	Not reported	-1%	-3.8%
Median FiO_2 in lower group	0.31	0.43	About 0.30	0.36	0.40	About 0.40
Median FiO_2 in higher group	0.45	0.56	About 0.35	0.39	0.51	About 0.50
Difference between groups	-0.15	-0.13	About -0.05	-0.03	-0.09	-0.15
Mortality	In-hospital (28d)	90 days	90 days	In-hospital	In-hospital	28 days
In lower target group	34.8%	42.9%	34.7%	24.2%	32.2%	34.3%
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Strengths and Weaknesses

Strengths

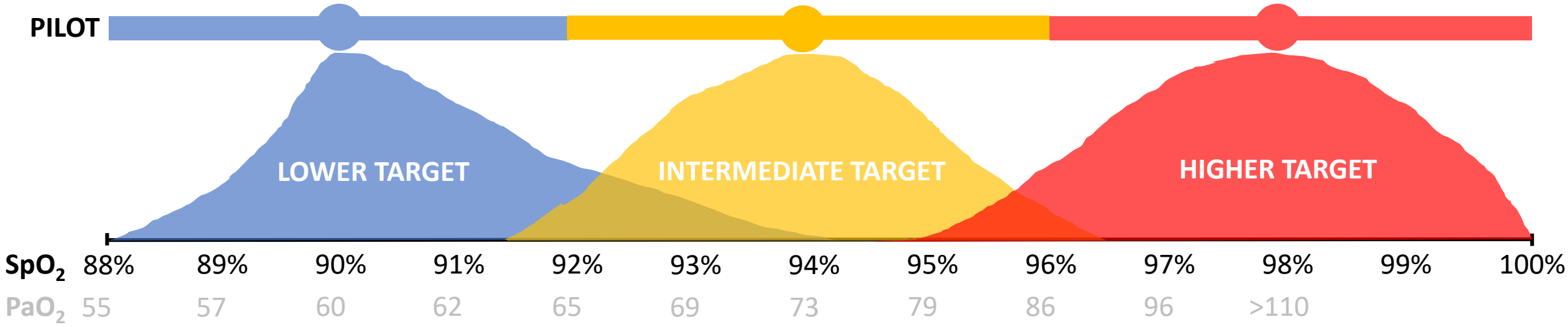
- Moderately large sample size
- Key subgroups represented
- Few exclusion criteria
- Within clinical care
- Early enrollment

Weaknesses

- Single center
- Early enrollment precluded some baseline assessments
- Non-blinded
- SpO2 vs PaO2
- Collection of long-term outcomes is ongoing

Conclusion

- For mechanically ventilated critically ill adults, clinical outcomes do not differ between lower, intermediate, and higher SpO_2 targets.



Future Research (Methods)

- Cluster-crossover design & delivery of intervention by clinicians
  - Early intervention (at time of intubation in ED)
  - Separation between groups (despite 3 trial groups)

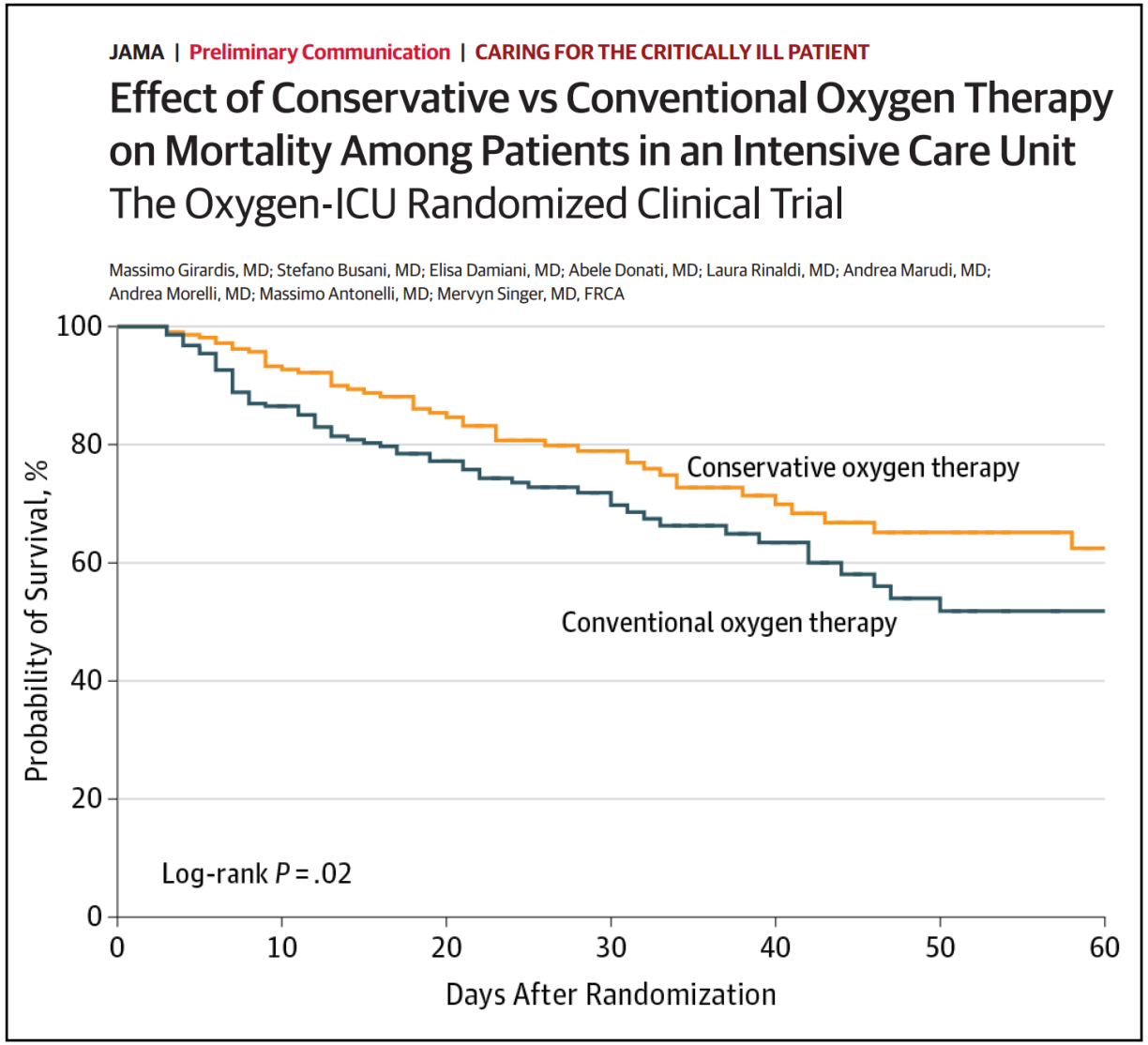
- Multiple crossovers
  - Understanding the trade off in statistical efficiency vs practicality

- Automated data collection from EHR every 1 minute:
  - Granular data on separation between groups, hypoxemia, hyperoxemia


Thank you.
@PCCRG

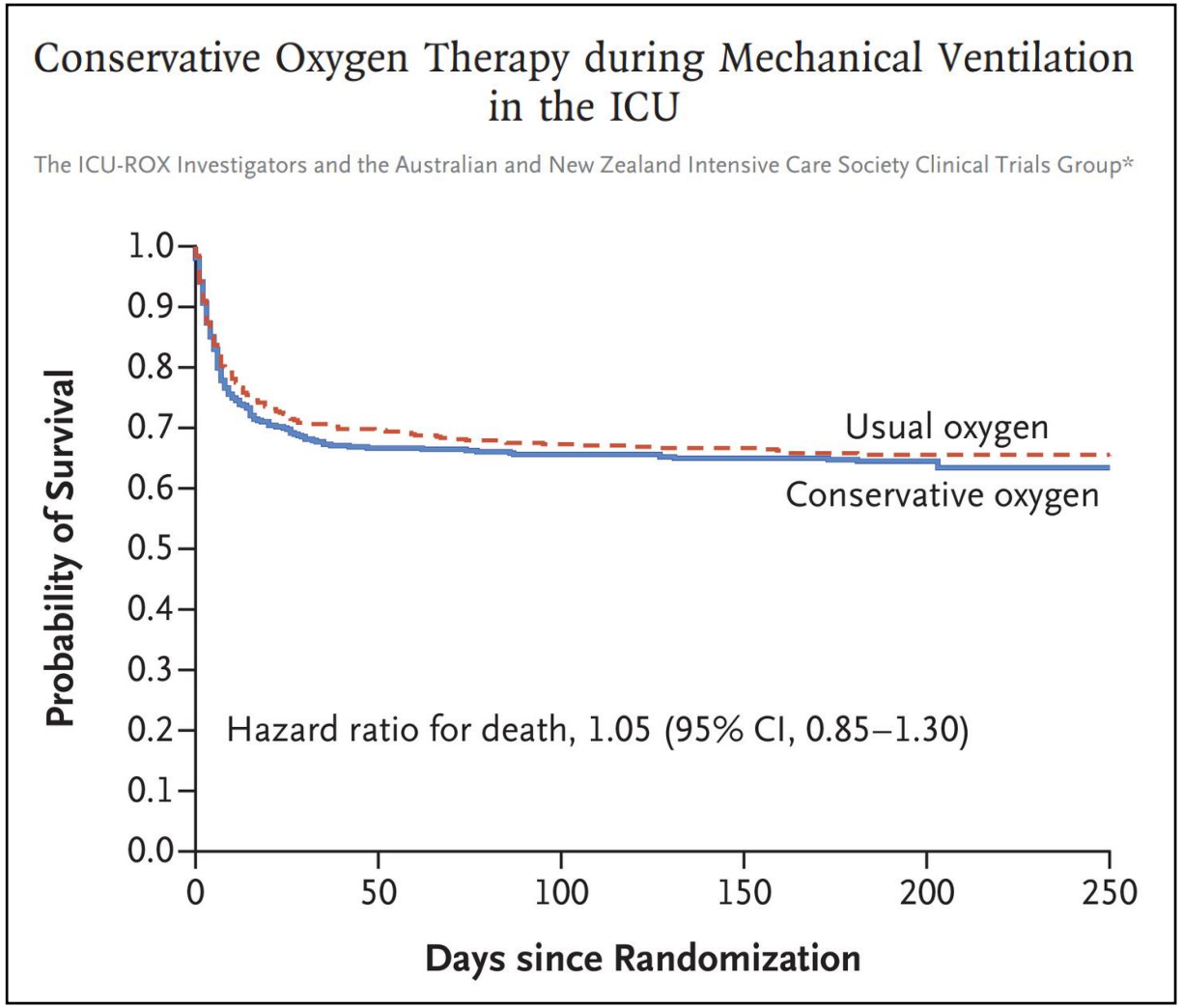
Oxygen-ICU

- Population
  - 434 patients in single ICU w/ expected LOS>72h
  - 60% surgical
  - 55% respiratory failure
  - 66% mechanical ventilation
- Intervention
  - PaO_2 70-100; SpO_2 94-98%
- Control
  - PaO_2 up to 150; SpO_2 97-100%
  - $FiO_2 \geq 0.4$
- Outcomes
  - ICU mortality: 12% vs 20% (RR 0.57, 95%CI 0.37-0.90)
  - Less bacteremia, liver failure, shock
- Notes
  - Single center
  - Stopped early at unplanned interim



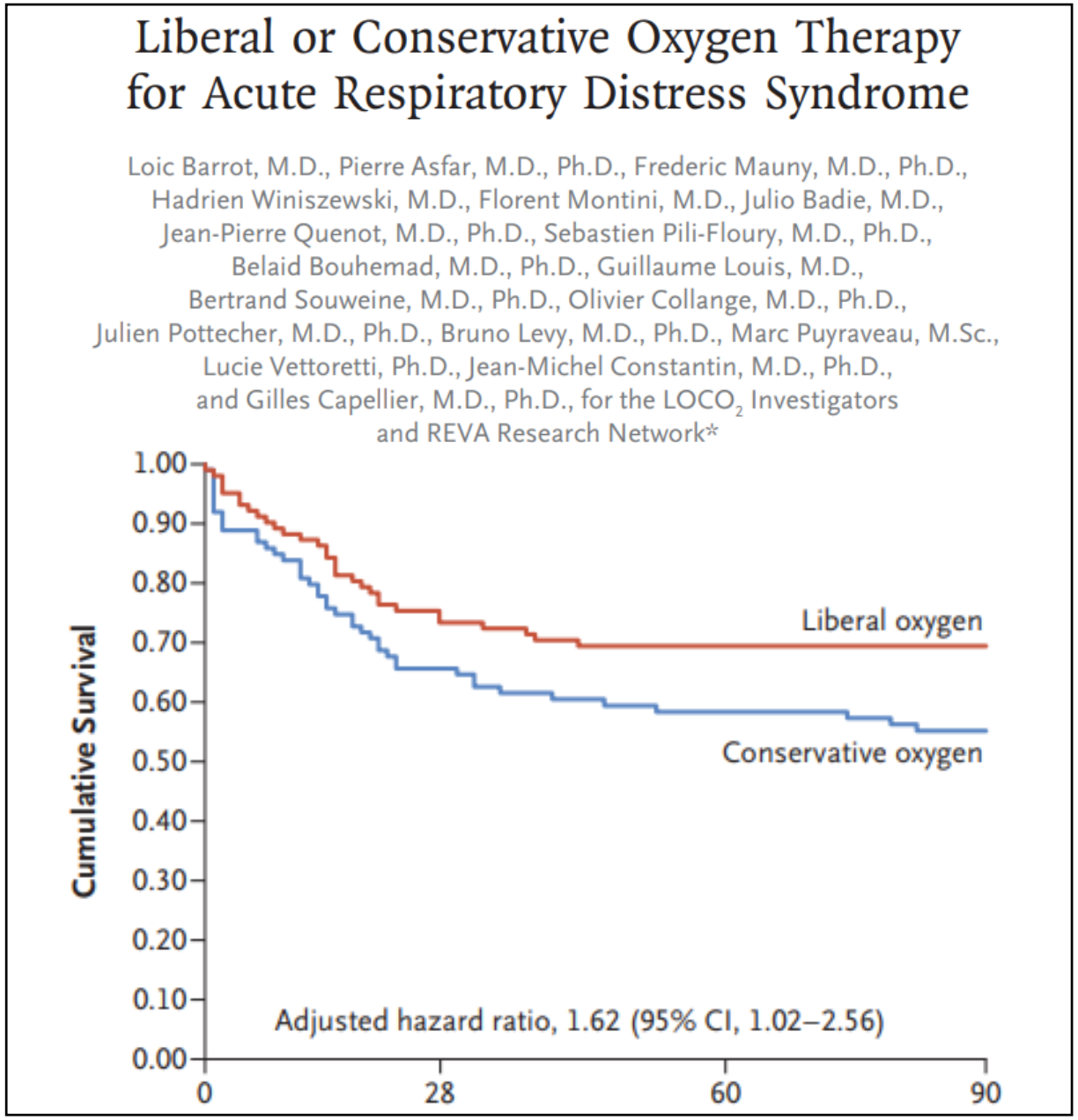
ICU-ROX

- Population
  - 1,000 mechanically ventilated ICU pateints
  - 30% surgical; 17% hypoxic ischemic encephalopathy
  - 66% P/F<300
- Intervention
  - SpO2 target: 91-96%
    - FiO2 decreased to 0.21 if SpO2 >91%
    - Alarm for SpO2 values >96%
- Control
  - SpO2 target: 91-100%
    - FiO2 < 0.3 discouraged
- Outcomes
  - VFDs: 21 [0-26] vs 22 [0-26] (P=0.80)
  - No difference in mortality or LTO
- Notes
  - Lower SpO2 target potentially better in hypoxic ischemic encephalopathy



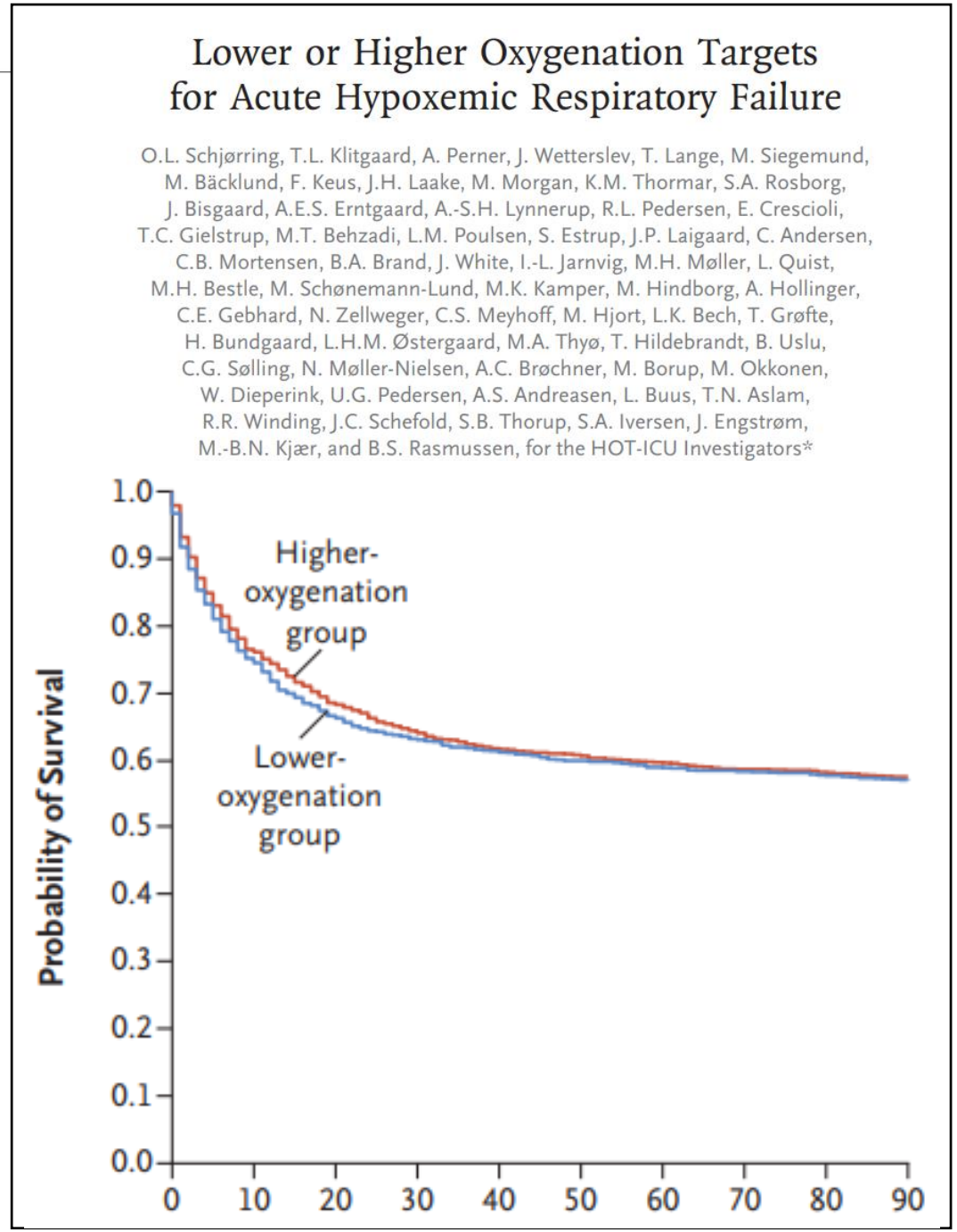
LOCO-2

- Population
  - 201 mechanically ventilated ARDS patients
  - Median P/F 120
  - 70% on vasopressors
- Interventions
  - Higher PaO_2 target: 90-105 (SpO_2 96-100%)
  - Lower PaO_2 target: 55-70 (SpO_2 88-92%)
- Outcomes
  - 28-day mortality: 34% vs 27%
  - 90-day mortality: 44% vs 30%
  - Mesenteric ischemia: 5 vs 0 events
- Notes
  - Trial stopped prematurely at interim



HOT-ICU

- Population
  - 2,928 ICU patients w/ AHRF on >10LPM O2 or >0.5 FiO2
    - 14% surgical
    - 60% mechanical ventilation
    - Median P/F ratio 117
- Interventions
  - Higher PaO_2 target: 90 (range 82.5-97.5)
  - Lower PaO_2 target: 60 (range 52.5-57.5)
- Outcomes
  - 90-day mortality: 43% vs 42% (RR 1.02, 95%CI 0.94-1.11)
  - No difference in subgroups or secondary outcomes
- Notes
  - No difference in intestinal ischemia



O2-ICU

- Population
  - 400 ICU patients with SIRS
  - 25% surgical
  - 75% invasive or non-invasive mechanical ventilation
- Intervention
  - Higher PaO_2 target: 105-135 (with max FiO2 0.6)
  - Lower PaO_2 target: 60-90
- Outcomes
  - SOFArank: -35 (-63 to 0) vs -40 (-76 to -5) (median difference 10 [0 to 21]; P=0.06)
  - 90-day mortality: 35% vs 34% (P=0.91)
- Notes
  - Single center
  - Stopped early at unplanned interim

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Low-Normal vs High-Normal Oxygenation Targets on Organ Dysfunction in Critically Ill Patients
A Randomized Clinical Trial

Harry Gelissen, MD, MBA; Harm-Jan de Grooth, MD, PhD; Yvo Smulders, MD, PhD; Evert-Jan Wils, MD, PhD; Wouter de Ruijter, MD, PhD; Roel Vink, MD, PhD; Bob Smit, PhD; Jantine Röttgering, MD; Leila Atmowihardjo, MD; Armand Girbes, MD, PhD; Paul Elbers, MD, PhD; Pieter-Roel Tuinman, MD, PhD; Heleen Oudemans-van Straaten, MD, PhD; Angelique de Man, MD, PhD