EHR-Embedded Trials (PEET): OCCULT-O2

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PEET Demonstration Project #2 PIs

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Introduction – What Problem Are We Trying to Solve?

Relevance and Background

- **Hidden (occult) hypoxemia (OH)** defined as: Arterial oxygen saturation (SaO2) is lower when the finger probe (SpO2) is higher
- OH is more common at lower SpO2s (90-92%) than higher (96-100%)
- OH is **often unrecognized clinically**
- OH rates are common and may vary by race/ethnicity and exist at **higher rates in patients with darker skin pigmentation**
- Patients with OH can experience a **5-11% higher in-hospital mortality rate** as compared to other ICU patients, suggesting its association with worse outcomes during acute illness

Specific Aims

Aim 1 (Phase 1): To determine the effectiveness of a cluster, stepped-wedge randomized trial to standardize the SpO_2 target range among mechanically ventilated patients in all UCHealth hospital ICUs to shorten ventilator duration and other patient-centered outcomes by mitigating hypoxemia and hyperoxia.

Aim 2 (Phase 2): To evaluate occult hypoxemia (OH) reduction effectiveness of an EPIC-embedded clinical decision support (CDS) tool that recognizes OH in mechanically patients with an ABG in real-time, and then randomly "nudges" the clinical team to augment oxygen delivery to achieve a higher SpO_2 target range.

Overarching Hypothesis

Our **pragmatic trial design hypothesis** was that (1) EPIC embedded interventions can augment clinical workflow to optimize oxygen delivery, and the (2) EPIC/EHR platform can be used measure patient-centered outcomes, without clinical disruption.

Our **research hypothesis** was that two separate intervention(s) to target a higher oxygen saturation target range would reduce occult hypoxemia rates without negatively impacting other outcomes if…

clinical practice demonstrated reasonable adherence to the pre-intervention SpO2 target (88-94%) and intervention SpO2 target (90-96%) and we were able to successfully deliver a timely and instructive CDS tool following real-time and accurate EPIC-based detection of occult hypoxemia (OH).

Methods

Goal: Reduce OH and improve clinical outcomes

- SpO2 range orderset compliance
- SpO2 range adherence
- (1°) Ventilator duration
- (2°) Occult hypoxemia (OH)
  - Clinical ABG
- Post-extubation management

Phase 1 Trial 09/24 – 09/25

Phase 1: Health system, stepped-wedge cluster RCT

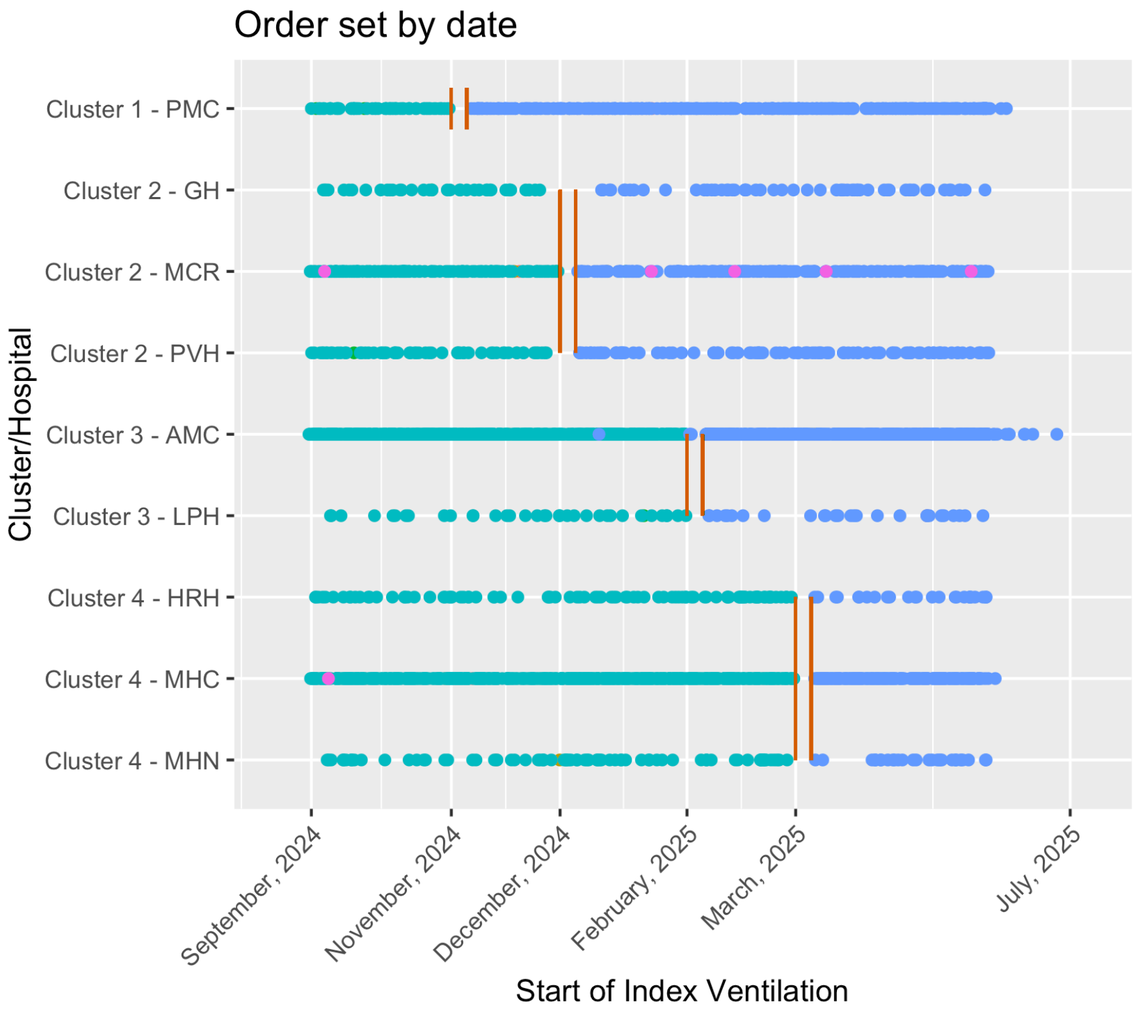
- Hospital clusters = step
- Random, cluster-level SpO2 target change using EHR orderset
- 10-14 day education and run-in period for each step

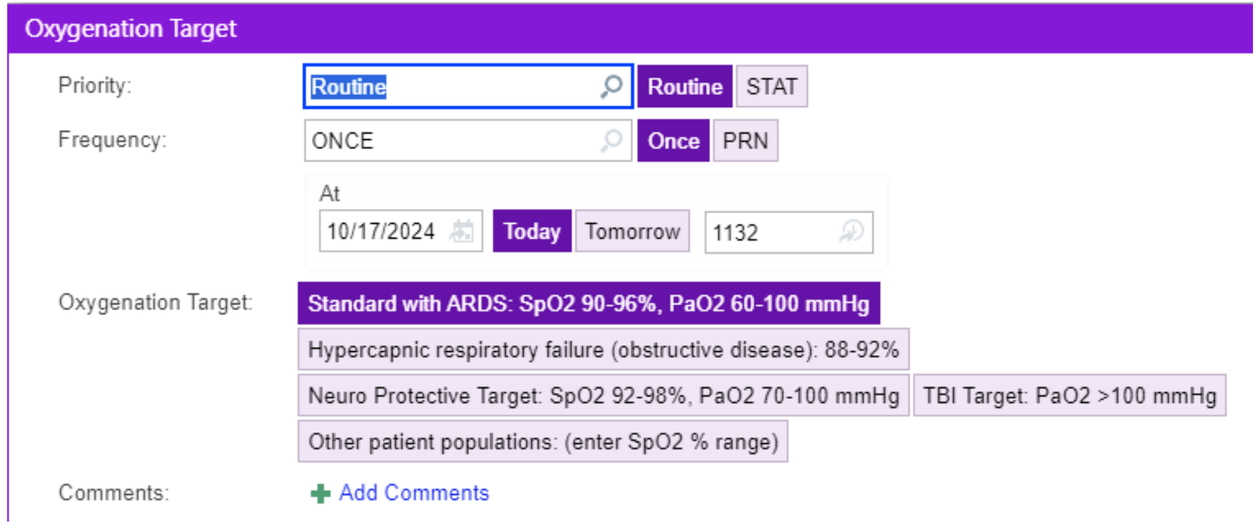
Phase 2 Design & Trial 10/25 – 07/26

Phase 2: EHR-based OH detection & randomized CDS trial

- Real-time, EHR-based OH detection
- Embedded randomization
- Track provider review of CDS tool (OPA)
- Track variation in provider behavior and association with outcomes

Phase 1: OCCULT O2 Design & Implementation



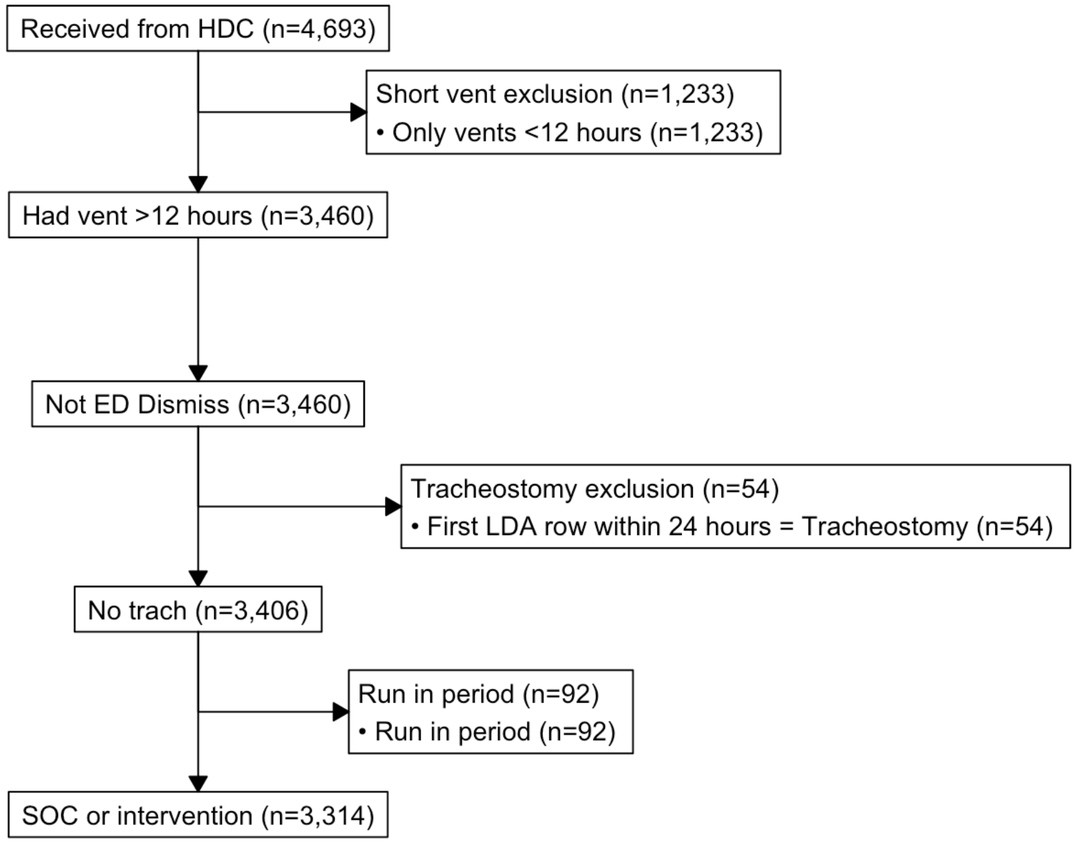


OxygenationTarget

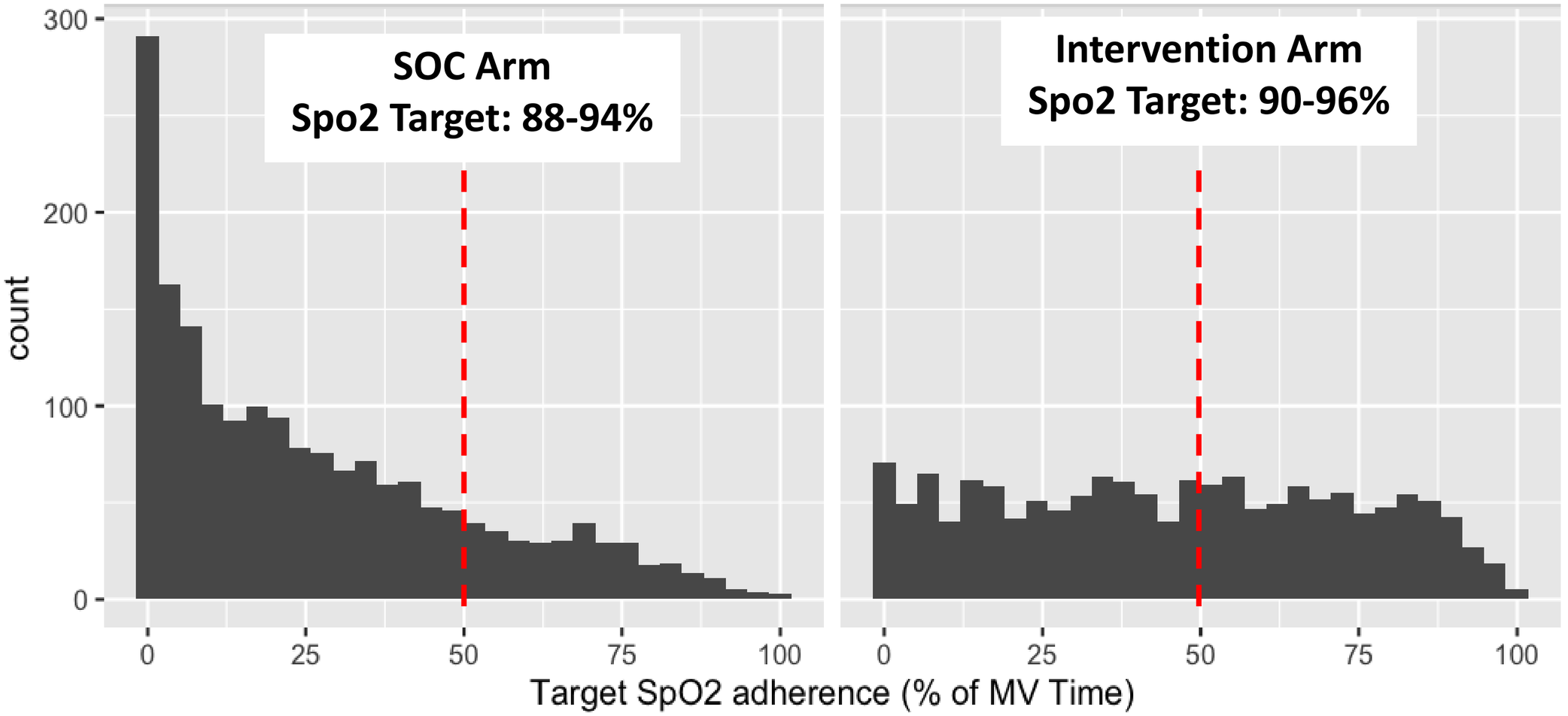
- Standard with ARDS: SpO2 88-94%, PaO2 55-90 mmHg
- Standard with ARDS: SpO2 90-96%, PaO2 60-100 mmHg
- TBI Target: PaO2 >100 mmHg

Baseline Characteristics

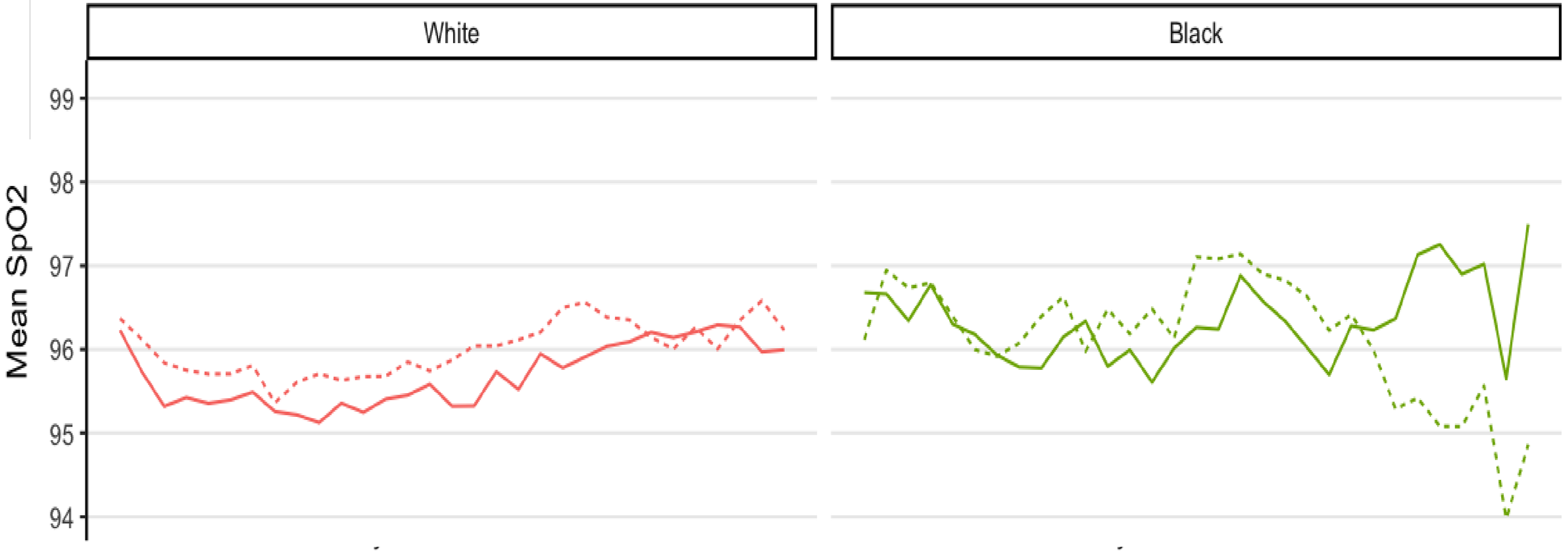
Characteristic	SOC N = 1,823[1]	Intervention N = 1,491[1]	Total N = 3314[1]
Age at admission	63 (47, 73)	63 (49, 73)	63 (48, 73)
Race			
Black	157 (8.6%)	110 (7.4%)	267 (8.1%)
Other	322 (18%)	291 (20%)	613 (18%)
Unknown	66 (3.6%)	54 (3.6%)	120 (3.6%)
White	1,278 (70%)	1,036 (69%)	2,314 (70%)
Ethnicity			
Hispanic	320 (18%)	290 (19%)	610 (18%)
Sex			
Female	760 (42%)	588 (39%)	1,348 (41%)
Insurance type			
Medicaid	400 (22%)	319 (21%)	719 (22%)
Medicare/Private	1,238 (68%)	1,052 (71%)	2,290 (69%)
Other	185 (10%)	120 (8.0%)	305 (9.2%)
ABG count	4 (2, 10)	5 (2, 11)	5 (2, 11)
Highest initial SOFA score	8 (6, 11)	8 (6, 11)	8 (6, 11)
Weighted comorbidity	26 (15, 39)	27 (15, 40)	26 (15, 40)
Index SpO2/FiO2	167 (100, 240)	167 (100, 240)	167 (100, 240)
Index PaO2/FiO2	172 (111, 255)	177 (112, 260)	174 (111, 258)
[1]Median (Q1, Q3); n (%)			



Intervention Adherence



SpO2 Mean Values During Intervention Phase



Phase 1: OCCULT O2 Outcomes

Characteristic	SOC N = 1,823[1]	Intervention N = 1,491[1]	Total N = 3314[1]
Ventilator free days to 30	**24 (-1, 29)**	**24 (-1, 29)**	**24 (-1, 29)**
Occult Hypoxemia (OH)*	**177 (9.7%)**	**150 (10%)**	**327 (9.9%)**
Hospital free days to 30	10 (-1, 22)	11 (-1, 23)	10 (-1, 22)
ICU free days to 30	21 (-1, 27)	22 (-1, 27)	22 (-1, 27)
Mortality to day 90	663 (36%)	540 (36%)	1,203 (36%)
New tracheostomy	175 (9.6%)	135 (9.1%)	310 (9.4%)
HHFNC within 24 hours	256 (14%)	195 (13%)	451 (14%)
NIV within 24 hours	167 (9.2%)	128 (8.6%)	295 (8.9%)
New home oxygen order	221 (12%)	171 (11%)	392 (12%)
Discharge disposition			
Home	769 (42%)	631 (42%)	1,400 (42%)
Acute care	111 (6.1%)	113 (7.6%)	224 (6.8%)
Intermediate care	363 (20%)	285 (19%)	648 (20%)

[1]Median (Q1, Q3); n (%); *Encounter level; HHFNC = heated high flow nasal cannula; NIV = non-invasive ventilation

Phase 1: OCCULT O2 Outcomes

	Adjusted Model			Sensitivity Analysis: SpO2 Adherence (>50%)		
Characteristic	**Estimate**	**95% CI**	**p-value**	**Estimate**	**95% CI**	**p-value**
Ventilator Free Days (d30)*	**1.08**	**0.86, 1.35**	**0.5**	**1.00**	**0.66, 1.52**	**>0.9**
Hospital Free Days (d30)*	0.95	0.74, 1.20	0.6	0.82	0.55, 1.22	0.3
ICU Free Days (d30)*	0.99	0.79, 1.23	0.9	0.91	0.61, 1.36	0.6
Death within 90 Days*	1.09	0.83, 1.42	0.5	1.12	0.70, 1.78	0.6
Discharge Disposition*	1.13	0.85, 1.50	0.4	0.76	0.46, 1.24	0.3
New Home O2 Order*	1.12	0.73, 1.72	0.6	0.74	0.35, 1.54	0.4
Occult Hypoxemia^	**1.15**	**0.80, 1.67**	**0.5**	**1.36**	**0.75, 2.46**	**0.3**
30-day In-Hospital Mortality^	1.09	0.89, 1.34	0.4	1.09	0.77, 1.52	0.7
90-day Mortality^	1.04	0.84, 1.29	0.7	1.13	0.78, 1.63	0.5

Phase 1: OCCULT O2 Outcomes

Encounters that experienced occult hypoxemia				
Race	**Total Encounters**	**Overall**	**SOC**	**Intervention**
White	2,314	222 (9.6%)	118 (9.2%)	104 (10%)
Black	267	26 (9.7%)	13 (8.3%)	13 (11.8%)
Other	613	63 (10.3%)	37 (11.5%)	26 (8.9%)
Unknown	120	16 (13.3%)	9 (13.6%)	7 (13%)
Ethnicity				
Non-Hispanic	2,595	247 (9.5%)	134 (9.3%)	113 (9.8%)
Hispanic	610	65 (10.7%)	36 (11.2%)	29 (10%)
Unknown	109	15 (13.8%)	7 (12.1%)	8 (15.7%)

Interim Assessment:
Raising SpO2 target did not negatively impact outcomes, but also did not improve adherence, nor sufficiently lower OH rates

Phase 2: EHR Real-Time OH Detection

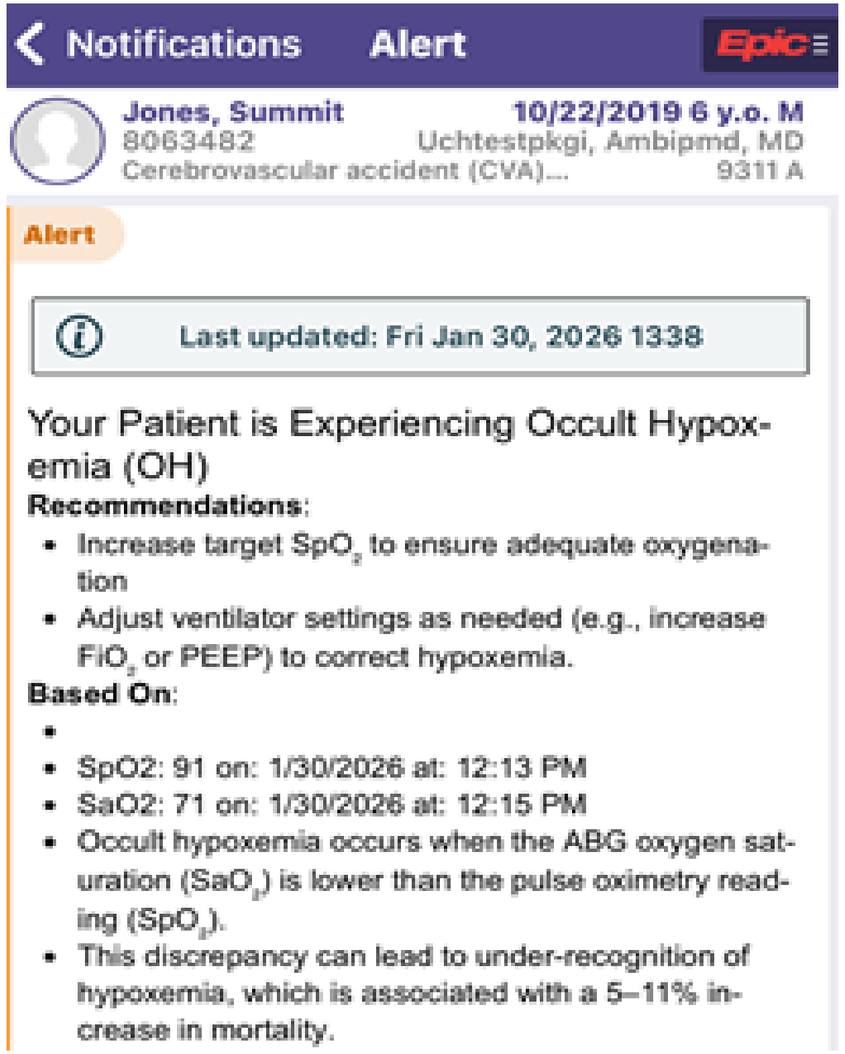
- Given unchanged ***residual*** OH rates after the EHR (EPIC) MV orderset SpO2 change (90-96%), we developed an embedded, second intervention specifically targeting OH
- Use EPIC to identify real-time (OH) among mechanically ventilated ICU patients and provide a clinician decision support tool
- Systematically track related behavioral responses and clinical outcomes using EPIC study record

Phase 2 Design

- **Cohort:** Mechanically ventilated ICU patients
- **Trigger:** EPIC to identify patients experiencing OH by:
  - Clinical ABG resulted in EPIC triggers evaluation of the **SaO2 <88%,**
  - Look back for all SpO2 values within 30 min of the time ABG drawn
  - If all recorded **SpO2s ≥90%, labeled as OH**
- When EPIC identifies OH, **randomize 1:1 to an active vs. silent OPA**
- Patients with silent or active OPA will be tracked in **EPIC study record**

EPIC Push Notification Language & Recipient(s)

- For patients with OH who were randomized to “active”, an EPIC push notification will **immediately notify providers**
- Goal to communicate within the existing framework of Uchealth hospital/region
- Track notification viewing (and by whom)
- Parallel notification on story board will provide an “acknowledge” radio button to remove and lockout the notification



Post-Alert Monitoring & Evaluation Of Success

- Following the randomized EPIC notification, will track:
  A. Seen +/- acknowledged/dismissed
  B. Behavioral action decision (within 4 hours):
     Management
     a. Mechanical ventilation orderset change and vent parameters
     b. Medication changes that can impact oxygenation
     Procedures
     a. ABG, CXR, A-line (safety parameter)
  C. **Endpoints (clinical outcomes as in Phase 1)**
- Use **EPIC study record** with timed OH detection & randomized notification
- Existing data analyst support through PEET core team and project team

EHR Integration Features

PEET PROJECT	OCCULT O2	
Embedded Feature	Phase 1	Phase 2
Cohort Identification	✓	✓
Portal-based Recruitment		✓
E-consent		
Randomization		✓
Intervention Delivery	✓	✓
Real-time Accrual Monitoring		
Real Time Dashboards		
Outcomes Evaluation	✓	✓
Patient Reported Outcomes		

CTS Roadblocks Addressed

- Using automated EHR cohort detection and randomization, along with waiver of IC, we minimized participant and provider burden
- High efficiency, low-cost of trial enrollment with more than 3000 participants enrolled in less than one year
- Leveraged UCHealth system on the same instance of EPIC, allowing for RCT participation across all UCHealth hospitals with local project champions
- Participation of “North” and “South” regions of UCHealth has increased the proportion of rural patients

Future Plans

- **Manuscripts:**

  (1) Protocol paper, phase 1 trial design – *revision submitted*

  (2) Primary outcomes paper for phase 1 stepped wedge RCT – *near-final draft*

  (3) OH-focused outcome paper to understand risk factors for OH and outcomes associated with OH – *outline form, preliminary data review*

  (4) Pilot trial phase 2 behavioral & clinical outcomes – *trial ongoing*

  (5) Heterogeneity of treatment effect (HTE) in phase 1 cohort – *collaboration, early stages*

- **Grants:**

  (1) R01 focused on causal inference models related to OH – *June or October 2026*

  (2) R61/R33 trial to evaluate EHR-based strategies to mitigate OH and related clinical endpoints, adopting from PEET-funded pilot, phase 2 trial) – *Winter 2026 / Spring 2027*