



2025: A Year in Review

Sepsis

Key Article

- Endo A, Yamakawa K, Tagami T, et al. Efficacy of targeting high mean arterial pressure for older patients with septic shock (OPTPRESS): a multicentre, pragmatic, open-label, randomized controlled trial. *Intensive Care Med.* 2025; 51:883-892

Background

- Septic shock is a subset of sepsis with a high mortality rate of approximately 38.5%.
- Optimal target blood pressure, a key factor in circulatory management for septic shock, remains debatable.
- Recent RCTs showed that a MAP of > 65 mm Hg in vasodilatory shock is not always beneficial, however targeting a MAP of 80-85 mm Hg was suggested to benefit septic shock patients with chronic HTN in some studies.

Objective

- To evaluate the effects of a high-target MAP in patients with septic shock aged > 65 years in a population of patients with a high prevalence of chronic HTN.

Methods

- Multicenter, pragmatic, open-label, randomized, controlled trial
- 29 centers in Japan
- Patients - Included
 - 65 years of age or older
 - Septic shock
 - Admitted to an ICU
 - Fluid resuscitation was left to clinician discretion
- Intervention
 - Patients randomized in 1:1 ratio
 - High-Target Group
 - Target 80-85 mm Hg
 - Maintained for 72 hours or until pressors no longer needed
 - Target MAP after 72 hours was at physician discretion
 - BP measured non-invasively in upper arm
 - Concurrent use of vasopressin from an early stage was protocolized to minimize the potential adverse effects of catecholamines
 - If NE > 0.1 mcg/kg/min was needed, vasopressin was initiated
 - If target MAP was not achieved, the treating physician could add another pressor, increase NE, add dobutamine, or hydrocortisone
 - Control Group
 - Target MAP 65-70 mm Hg
- Primary outcome
 - 90-day all-cause mortality

- Secondary outcomes
 - 28-day all-cause mortality
 - Lactate clearance at 24 hours
 - Days free from MV, RRT, and catecholamines at day 28

Results

- Trial stopped early for ineffectiveness and even suggested harm
- A total of 518 patients were included
 - High Target Group: 258 patients
 - Control Group: 260 patients
- Characteristics
 - All patients were Japanese
 - Median age was 78 years
 - Most common source of infection was abdominal (30%), GU (26%), pulmonary (25%)
 - Baseline characteristics were similar between groups
 - Approximately 53% of patients in both groups had chronic HTN
- Primary Outcome – 90-day all-cause mortality
 - High Target Group: 39.3%
 - Control Group: 28.6%
- Secondary Outcomes
 - All lower in the High Target Group
- Safety Outcomes
 - Arrhythmias, VTE, ischemic events, and hemorrhagic events all occurred more frequently in the High Target Group

Limitations Identified by Authors

- Open label, unblinded
- Status of chronic HTN was sometimes incorrect
- No strict titration or tapering protocol for pressors
- Pre-estimated mortality rate used to calculate sample size was higher than observed

Take Home Point

- Among older patients with septic shock in Japan, targeting a MAP of 80-85 mm Hg significantly increased mortality compared with targeting a MAP of 65-70 mm Hg.

Key Article

- *ANDROMEDA-SHOCK-2 Investigators. Personalized hemodynamic resuscitation targeting capillary refill time in early septic shock. JAMA. 2025; 334:1988-1999.*

Background

- Best resuscitation strategy to improve patient-centered outcomes in sepsis remains uncertain.
- Optimal management of fluids and vasopressors is unknown.
- Septic shock resuscitation relies on the assumption that hemodynamic optimization will improve tissue perfusion and revert cell metabolic derangements.
- ANDROMEDA-SHOCK trial used capillary refill time (CRT). A CRT-targeted resuscitation was associated with faster recovery of organ dysfunction, less fluid, and higher likelihood of survival.

Objective

- To assess the efficacy of a personalized hemodynamic resuscitation protocol incorporating sequential multilayered assessments of diverse physiological signals to tailor fluids, vasopressors, and inotropes, targeting CRT normalization.

Methods

- Investigator initiated, multicenter, randomized clinical trial
- 86 ICUs across 19 countries
- Patients - Included
 - 18 years of age or older
 - Septic shock
 - Suspected or confirmed infection
 - Lactate > 2 mmol/L
 - Requirement of NE to maintain MAP > 65 mm Hg after 1 L of IVFs
 - Could be in the ED, ICU, OR, or ward
- Intervention
 - Patients randomized in a 1:1 ratio
 - CRT-PHR Group
 - Based on 4 pillars
 - CRT normalization
 - Baseline identification of individual hemodynamic patterns of CV dysfunction – hypovolemia, vasoplegia, cardiac dysfunction
 - Pulse pressure
 - DAP
 - Bedside echo
 - Systematic fluid-responsiveness assessment before fluid resuscitation
 - 2 acute (1-hour) hemodynamic tests: a trial of higher MAP target and a trial of fixed low-dose dobutamine
 - Patients in the CRT-PHR group underwent a multilayered personalized resuscitation during a 6-hr period aimed at normalizing CRT
 - Tier 1
 - Evaluation of pulse pressure
 - Those with a pulse pressure < 40 mm Hg had fluid responsiveness assessed.
 - If fluid responsive – got 500 ml of crystalloid and then reassessed. If still fluid responsive – got another 500 ml
 - If pulse pressure > 40 mmHg and a DAP < 50 mm Hg, NE was titrated to reach a DAP of 50 mm Hg or higher
 - If these interventions failed to normalized CRT, moved on to Tier 2
 - Tier 2
 - Basic echo to rule out cardiac dysfunction
 - In patients with L or R ventricular dysfunction, general treatment recommendations were provided and interventions recorded
 - If this failed to normalize CRT, fluid responsiveness was reassessed and further fluid boluses provided
 - If CRT was not normalized, a MAP test was performed only in patients with chronic HTN, by transiently increasing NE to attain a MAP of 80-85 mm Hg for 1 hour. If CRT goal met, then this

- MAP was maintained for 6 hours, otherwise NE decreased to previous dose
 - If CRT failed to normalize, patient moved on to a dobutamine test with a fixed dose for 1 hour.
 - CRT-PHR stages prompted hourly reassessments
 - Usual Care Group
 - Treated according to local protocols and/or guidelines
- Primary outcome
 - Hierarchical composite outcome
 - All-cause mortality within 28-days
 - Duration of vital support (pressors, MV, RRT) truncated at day 28
 - Hospital LOS truncated at day 28
- Secondary outcomes
 - All-cause mortality
 - Vital support free days within 28 days
 - Hospital LOS

Results

- A total of 1,467 patients were included in the final analysis
 - CRT-PHR Group: 720 patients
 - Usual Care Group: 747 patients
- Protocol Interventions
 - 6-hour study period
 - Higher percentage of pts normalized CRT in the CRT-PHR group (86% vs. 62%)
 - 65% achieved in Tier 1 and 35% achieved in Tier 2
 - 36% of patients in the CRT-PHR group had a normal CRT to start and did not receive further intervention
 - Overall...
 - Patients in the CRT-PHR group received less IVFs (by about 250 ml), received more dobutamine, had lower CVPs, and had lower lactate values
 - Protocol deviations occurred in 15%
 - Protocol violations occurred in 6%
- Primary Outcome – utilized a win ratio
 - CRT-PHR Group: 48.9%
 - Usual Care Group: 42.1%
 - Highest win ratio was in vital support; individual wins for death were 19.1% vs. 17.8%, duration of vital support 26.4% vs. 21.1%; hospital LOS 3.4% vs. 3.2%
- Secondary Outcomes
 - No significant difference between 28-day mortality
 - CRT-PHR group had a higher number of mean organ support free days and a faster decrease in SOFA score within 7 days compared with usual care

Limitations Identified by Authors

- Unblinded
- Decisions on RRT, discontinuation of pressors, and extubation were made by the treating team
- Specific measurements, such as CRT, do have interrater variability
- Used PP and DAP thresholds that require prospective clinical validation
- Labor-intensive
- It might be possible that more frequent patient assessments contributed to the observed effect

Take Home Point

- Among patients with early septic shock, a personalized hemodynamic resuscitation targeting CRT was superior to usual care for a composite outcome driven primarily by a shorter duration of organ support.

Key Article

- *Kalimouttou A, Kennedy JN, Feng J, et al. Optimal vasopressin initiation in septic shock. The OVISS reinforcement learning study. JAMA. 2025. Published online March 18, 2025.*

Background

- Current international guidelines for the resuscitation of sepsis recommend norepinephrine as the first-line vasopressor agent. Furthermore, they suggest adding vasopressin as a second-line agent when the MAP remains low despite norepinephrine.
- While vasopressin use has increased, there is little literature to guide the optimal timing of its administration.
- Reinforcement learning is a branch of machine learning where a virtual agent learns from trial and error an optimized set of treatment rules to maximize the probability of a good outcome.

Objective

- To derive, validate, and measure the treatment implications of a vasopressin initiation rule optimized to improve both short- and long-term outcomes among critically ill adult patient with septic shock receiving norepinephrine.

Methods

- Derivation and Validation Cohorts
 - Training, testing, and internal validation of the model used data from the UCSF De-Identified Clinical Data Warehouse.
 - External validation of the reinforcement learning model used 3 datasets: MIMIC-IV, eICU-CRD, EHR dataset from UPMC
- Model Training
 - Reinforcement learning model is a specific type of machine learning algorithm where an agent learns how to make decisions by interacting with an environment.
 - Agent aims to maximize rewards over time by choosing actions based on the current state, with the decision-making process guided by likelihood of future outcomes.
 - Investigators defined the action as a binary decision – start vasopressin or do not start vasopressin.
 - The reward was a weighted combination of in-hospital mortality and changes in lactate, MAP, SOFA, and NE dose.
- Primary outcome
 - In-hospital mortality
- Secondary outcomes
 - Use of mechanical ventilation
 - Use of RRT

Results

- A total of 14,453 patients with septic shock were included
 - Derivation cohort: 3,608 patients
 - Validation cohort: 10,845 patients
- Clinician Initiated Vasopressin
 - In the 3 external datasets...
 - Vasopressin initiated in 31% of patients

- Median SOFA score of 9
 - Median of 5 hours after shock
 - NE dose of 0.37 mcg/kg/min
 - Lactate of 3.6
 - In-hospital mortality: 28-43%
- Reinforcement Learning Rule
 - 2,362 patients in whom vasopressin were recommended by the rule and initiated by clinicians
 - 14% had vasopressin initiated in the same hour as the reinforcement rule recommended
 - Compared to clinician-observed action, the reinforcement learning model suggested vasopressin initiation...
 - In more patients
 - Lower median SOFA score (7)
 - Earlier onset after shock (4 hrs)
 - Lower NE dose (0.20 mcg/kg/min)
 - Lower serum lactate (2.5)
 - Results consistent across each of the 3 validation sets
- Primary Outcome
 - The reinforcement learning model outperformed the clinician-observed action.
 - Concordance with the rule in each time block was associated with reduced odds of in-hospital mortality.
- Secondary Outcomes
 - Concordance with the rule was also associated with a reduced odds of requiring RRT at each time point but not with the odds of requiring mechanical ventilation.

Limitations Identified by Authors

- Did not prospectively test the reinforcement learning rule – used existing databases
- May have limited generalizability to patients underrepresented in the derivation data
- Clinician subjectivity cannot be fully captured by the model
- Did not capture infectious source or source control. There likely exist other unmeasured variables.
- The rule recommended the initiation of vasopressin but did not recommend dosing strategy.

Take Home Point

- A reinforcement learning model recommended more frequent and earlier use of vasopressin for adult patients with septic shock receiving norepinephrine.

Metabolic Acidosis

Key Article

- *Jung B, Jabaudon M, De Jong A, et al. Sodium bicarbonate for severe metabolic acidemia and acute kidney injury. JAMA. 2025; 334:2000-2010.*

Background

- Severe acidemia can impair cardiac contractility, produce arrhythmias, induce pulmonary vasoconstriction, induce systemic vasodilation, alter renal blood flow, induce cerebral edema, and cause diaphragmatic dysfunction.
- BICARICU-1 was a randomized controlled trial in which unselected critically ill patients with severe metabolic acidemia received an infusion of 4.2% sodium bicarbonate.

- The primary outcome of BICARICU-1 of 28-day mortality or organ failure at day 7 did not differ between those who received bicarbonate and those who did not.
- However, a preplanned analysis of patients with moderate to severe AKI did show an improvement in mortality.
- Subsequent observational trials also suggested benefit of sodium bicarbonate for patients with severe acidemia and severe AKI.

Objective

- To assess whether sodium bicarbonate infusion improved 90-day all-cause mortality for critically ill patients with both severe metabolic acidosis and moderate to severe AKI.

Methods

- Randomized, open-label, parallel-group, clinical trial
- 43 ICUs in France
- Patients - Included
 - 18 years of age or older
 - SOFA score > 4 or lactate > 2 mmol/L within 48 hrs of ICU admission
 - Within 6 hours before enrollment
 - pH 7.20 or less
 - Sodium bicarbonate level of 20 mEq/L or less
 - PaCO₂ of 45 mm Hg or less
 - Moderate to severe AKI defined as Stage 2 or 3 KDIGO classification
- Patients – Excluded
 - Respiratory acidosis (PaCO₂ > 45 mm Hg)
 - Proven bicarbonate wasting via the GI or urinary tract
 - GFR of 10 ml/min or less
 - Exogenous acid poisoning
- Intervention
 - Patients randomized in a 1:1 ratio
 - Bicarbonate Group
 - IV infusion of 4.2% sodium bicarbonate
 - Targeting an arterial pH of 7.30 or higher
 - Each infusion was 125 to 250 ml within 30 minutes
 - Maximum amount of bicarbonate was 1 L
 - ABG 1 to 4 hours after each infusion
 - No Bicarbonate Group
 - No bicarbonate infusion
 - Indications for RRT were standardized in both groups
- Primary outcome
 - 90-day all-cause mortality
- Secondary outcomes
 - 28-day and 180-day all-cause mortality
 - Use of RRT
 - Use of vasopressors
 - Need for MV
 - ICU and hospital LOS
 - Fluid balance

Results

- A total of 640 patients underwent randomization
 - Bicarbonate Group: 314 in the primary analysis
 - No Bicarbonate Group: 313 in the primary analysis
- Characteristics
 - Groups well balanced
 - Median pH at enrollment was 7.15
 - Patients in the bicarbonate group received a median of 750 ml of 4.2% bicarbonate within the first 48 hours
- Primary Outcome
 - Bicarbonate Group: 62.1%
 - No Bicarbonate Group: 61.7%
- Secondary Outcomes
 - Initiation of RRT
 - Bicarbonate Group: 31 hours
 - No Bicarbonate Group: 16 hours
 - No change in ICU or hospital LOS, vasopressor use, or need for MV

Limitations Identified by Authors

- Open-label design
- Sodium bicarbonate dose was not computed according to lab testing or weight, rather individualized to target a pH of 7.30 or higher.
- 47 of patients in the No Bicarbonate Group received bicarbonate

Take Home Points

- Sodium bicarbonate therapy did not reduce 90-day all-cause mortality in critically ill patients with severe metabolic acidemia and moderate to severe AKI.
- Patients in the bicarbonate group received RRT less often.

Procedures

Key Article

- *Muller G, Contou D, Ehrmann S, et al. Deferring arterial catheterization in critically ill patients with shock. N Engl J Med. 2025; 393:1875-88. (EVERDAC Trial)*

Background

- An arterial catheter is often recommended for the treatment of patients with shock, although evidence from randomized trials is lacking.
- Continuous, real-time, accurate blood pressure measurements obtained by means of an a-line are presumed to enable earlier detection of hypotensive episodes, prompt initiation of volume expansion, and timely vasopressor dose adjustment, thereby minimizing the duration of undertreatment or overtreatment and potentially influencing the course of organ failure and ultimately survival.
- These assumptions are based on expert opinion and not bested in RCTs.
- Arterial catheterization carries its own risks, including ischemia, hematoma, pseudoaneurysm, and bloodstream infections
- Non-invasive cuff measurements are commonly used, even in patients with unstable conditions
- However, non-invasive cuff monitoring can yield inaccurate blood pressure readings that may lead to temporarily inappropriate therapeutic actions.
- Non-invasive cuff measurements may also be associated with pain or discomfort.

Objective

- To evaluate whether management of shock without early arterial catheterization is noninferior to the practice of early catheter insertion with regard to 28-day all-cause mortality.

Methods

- Open-label, investigator-initiated, pragmatic, multicenter, parallel-group, noninferiority, randomized, controlled trial
- 9 ICUs in France (6 university hospitals and 3 general hospitals)
- Patients - Included
 - 18 years of age or older
 - Had acute circulatory failure
 - Persistent hypotension (SBP < 90 mm Hg or MAP < 65 mm Hg for more than 15 minutes or initiation of vasopressor therapy)
 - At least 1 sign of hypoperfusion
- Intervention
 - Patients randomized in a 1:1 ratio
 - Noninvasive strategy group
 - Insertion of an a-line was not permitted until the 28th day after randomization unless one of predefined criteria was present
 - Inability of bedside monitor to display a value for SpO₂ or noninvasive BP
 - Absolute need for ABG measurement after 5 consecutive failed attempts
 - Need for ECMO
 - Vasopressor dose > 2.5 mcg/kg/min of NE
 - If a-line in place prior to randomization it had to be removed within 1 hr
 - Frequency of BP measurements left to treating clinician
 - Invasive strategy group
 - A-line inserted within 4 hours after randomization
 - Use of noninvasive BP monitoring was not allowed except during insertion or replacement of the catheter
 - All aspects of the patient's care unrelated to management of the catheter were left to treating clinical teams
- Primary outcome
 - 28-day all-cause mortality
- Secondary outcomes
 - SOFA score over first 7 days
 - Number of days free from ventilator support
 - Number of days free from RRT
 - Number of days free from vasopressor therapy
 - Number of infections related to the arterial catheter
- Adverse events
 - Pain and discomfort

Results

- A total 1,010 underwent randomization
 - Noninvasive strategy group: 506
 - Invasive strategy group: 504
- Characteristics

- Mean age 66 years
- Predominantly male
- 94% medical admission vs surgical
- Source – 25-30% from the ED; 25% direct from ambulance; 28% from the floor; 19% from another hospital
- Causes – sepsis in more than 50%; cardiogenic in 11%; post-arrest shock 8-10%; obstructive 1%
- 86% receiving pressors on admission to the ICU
- ITT population – 1,006 patients
 - Noninvasive strategy group: 504
 - Invasive strategy group: 502
 - 74 patients (14.7%) in the noninvasive strategy group underwent a-line placement at a median time of 22 hours after randomization. 68 of these met a prespecified criteria
- Primary Outcome
 - Noninvasive strategy group: 34.3%
 - Invasive strategy group: 36.9%
 - Noninferiority met
- Secondary Outcomes
 - No change in median SOFA scores over first 7 days
 - 90-day mortality was no different
 - 28-day median number of days free from MV, RRT, and vasopressors was similar
 - Hematoma/hemorrhage at arterial catheter insertion site
 - Noninvasive strategy group: 1.0%
 - Invasive strategy group: 8.2%
 - Incidence of arterial puncture attempts for blood sampling
 - Noninvasive strategy group: 742
 - Invasive strategy group: 269
- Adverse events
 - Serious pain or discomfort
 - Noninvasive strategy group: 13.1%
 - Invasive strategy group: 9%

Limitations Identified by Authors

- Unblinded
- Evaluation of pain and discomfort may not be complete – only a limited number of patients were awake and capable of self-assessment
- Did not record the satisfaction and workload of healthcare workers
- Did not include many trauma or post-surgical patients and no patient with a BMI of 40 or higher

Take Home Point

- A strategy of delaying arterial catheterization in favor of noninvasive BP monitoring was noninferior to early invasive BP monitoring in patients with shock

Post-Intubation Sedation

Key Article

- *Walsh TS, Parker MSc, Aitken LM, et al. Dexmedetomidine- or clonidine-based sedation compared with propofol in critically ill patients. The A2B randomized clinical trial. JAMA. 2025; Published online May 19, 2025.*

Background

- Critically ill patients receiving mechanical ventilation require sedation.
- At present, propofol is the most widely used sedative medication for ventilated patients.
- Recent trials have suggested that dexmedetomidine (alpha-2-adrenergic receptor agonist) may reduce delirium and duration of MV.
- To date, there is no high-quality research that has evaluated dexmedetomidine or clonidine-based sedation to propofol in critically ill ventilated patients.

Objective

- To compare the effectiveness and safety of dexmedetomidine- and clonidine-based sedation vs. propofol-based sedation as the primary sedation for mechanically ventilated critically ill patients.

Methods

- Pragmatic, multicenter, open-label, randomized trial
- 41 ICUs in the UK
- Patients - Included
 - 18 years of age or older
 - Receiving mechanical ventilation in the ICU
 - Were sedated with propofol after intubation
 - Were within 48 hours of initiation of MV
 - Were expected to require a further 24 hrs or more of MV
- Intervention
 - Patients randomized in a 1:1:1 ratio
 - Dexmedetomidine
 - Initial dose 0.7 mcg/kg/hr
 - Max dose 1.4 mcg/kg/hr
 - Clonidine
 - Initial dose 1.0 mcg/kg/hr
 - Max dose 2.0 mcg/kg/hr
 - Propofol (Usual Care)
 - No specific dose guidance given
 - Medical staff determined whether deep sedation (RASS -4 or -5) was indicated. If deep sedation was not indicated or requested, a RASS of -2 to 1 was targeted.
 - RASS measured every 4 hours, CAM-ICU measured every 12 hrs
 - Choice of an opioid for analgesia was determined by the clinical team.
 - Other sedatives (benzos) were discouraged.
 - ****Propofol was permitted if the max dose of either dexmedetomidine or clonidine was reached or because of dose-limiting side effects.**
 - MV weaning, sedation discontinuation, and assessing readiness for extubation guidance was provided but not protocolized.
- Primary outcome
 - Time from randomization to successful extubation
- Secondary outcomes
 - 180-day all-cause mortality
 - ICU LOS
 - Time to first RASS of -2 or greater
 - Time to first day without agitation, deep sedation, or pain behavior

- Rates of delirium or coma
- Safety outcomes
 - Severe bradycardia
 - Cardiac arrhythmia
 - Cardiac arrest

Results

- A total 1404 patients were included in the analysis
 - Dexmedetomidine: 457 patients
 - Clonidine: 476 patients
 - Propofol: 471 patients
 - Baseline characteristics well balanced
- Primary Outcome
 - Dexmedetomidine vs. propofol: HR 1.09 (not statistically significant)
 - Clonidine vs. propofol: HR 1.05 (not statistically significant)
 - No significant difference in the number of patients receiving MV 7 days after randomization
- Secondary Outcomes
 - 180-day all-cause mortality
 - Dexmedetomidine vs. propofol: HR 0,98 (not statistically significant)
 - Clonidine vs. propofol: HR 1.04 (not statistically significant)
 - ICU LOS
 - No difference in time to ICU discharge among survivors
 - Time to first RASS -2 or greater
 - Median number of 12-hr nursing shifts to first achieve a RASS of -2 was 2 across all 3 groups
 - Time to first day without agitation, deep sedation, or pain behavior
 - Median of 3 days across all 3 groups
 - *Rates of agitation were higher over 7 days after randomization with both dexmedetomidine and clonidine
 - Rates of delirium or coma
 - No difference between the groups
- Safety Outcomes
 - Prevalence of bradycardia
 - Dexmedetomidine group: 33%
 - Clonidine group: 33%
 - Propofol group: 20%
 - Cardiac arrhythmia
 - Higher rates reported with dexmedetomidine vs. propofol (RR 1.27)

Limitations Identified by Authors

- Unblinded clinical trial; primary outcome measured by unblinded researchers
- Most patients in the dexmedetomidine and clonidine groups received propofol (approximately 77% of days), though at a lower dose than those in the propofol only group.
- Best practices for weaning, use of analgesia, and sedation targets were not protocolized.
- Findings cannot be extrapolated to patients with acute brain injury

Take Home Point

- A dexmedetomidine-based or clonidine-based sedation did not reduce the time to successful extubation in critically ill patients receiving mechanical ventilation when compared to propofol.

- Higher rates of agitation and severe bradycardia in both the dexmedetomidine and clonidine groups

Mechanical Ventilation

Key Article

- *Martin DS, et al. Conservative oxygen therapy in mechanically ventilated critically ill adult patients. The UK-ROX Randomized Clinical Trial. JAMA. 2025. Published online June 12, 2025.*

Background

- Oxygen is one of the most commonly delivered therapies to ICU patients.
- We know that hypoxemia is bad for critically ill patients. As such, a liberal approach to the administration of supplemental oxygen is common.
- However, we also have evidence to suggest that too much oxygen may also be harmful to critically ill patients.
- Achieving a balance between too little and too much oxygen is critical to ensure optimal outcomes for critically ill patients.
- To date, clinical trials have not been able to conclusively determine whether a conservative or liberal approach to oxygen delivery is beneficial for ICU patients.

Objective

- To assess whether a conservative oxygen therapy strategy by targeting an SpO2 88%-92% reduced 90-day mortality compared to usual oxygen therapy in adult ICU patients receiving mechanical ventilation.

Methods

- Multicenter, pragmatic, registry-embedded, randomized trial
- 97 adult ICUs in England, Wales, and Northern Ireland
- Patients - Included
 - 18 years of age or older
 - Receiving invasive mechanical ventilation following an unplanned ICU admission OR
 - Where invasive mechanical ventilation was started in the ICU
 - Were able to be enrolled within 12 hours of initiation of ventilation
- Intervention
 - Patients randomized in a 1:1 ratio
 - Conservative oxygen therapy
 - Received the lowest FiO2 possible to maintain an SpO2 at 90%
 - Sites instructed to set alarms if the SpO2 fell below 88% or exceeded 92% once the patient was within range
 - Usual oxygen therapy
 - Patients received supplemental oxygen at the discretion of the treating clinician.
 - No minimal FiO2 was mandated and no upper limit SpO2 alarm was set.
- Primary outcome
 - All-cause mortality at 90 days
- Secondary outcomes
 - ICU LOS
 - Hospital LOS
 - Days alive and free of organ support at 30 days
 - ICU and hospital mortality at hospital DC
 - 60-day and 1-year mortality

Results

- A total of 16,434 patients were included in the primary analysis
 - Conservative oxygen therapy: 8,230 patients
 - Usual oxygen therapy: 8,204 patients
 - Groups were similar at baseline
- Oxygen Exposure
 - Median FiO₂
 - Conservative oxygen therapy: 0.31
 - Usual oxygen therapy: 0.35
 - Total exposure was 29% lower in the conservative oxygen therapy group
 - Median SpO₂
 - Conservative oxygen therapy: 93%
 - Usual oxygen therapy: 95%
 - Time spent within an SpO₂ range of 88%-92%
 - Conservative oxygen therapy: 63 hours
 - Usual oxygen therapy: 27 hours
- Primary Outcome – All-cause 90-day mortality
 - Conservative oxygen therapy: 35.4%
 - Usual oxygen therapy: 34.9%
- Secondary Outcomes
 - No differences
- Serious Adverse Events
 - Conservative oxygen therapy: 0.7%
 - Usual oxygen therapy: 0.4%

Limitations Identified by Authors

- Unblinded clinical trial
- Large number of patients excluded due to the intervention either being indicated or contraindicated
- Large % of nonadherence to conservative oxygen therapy protocol
- Usual care comparator? Was there enough separation between the groups?

Take Home Points

- A conservative oxygen therapy approach that targeted an SpO₂ of 90% did not reduce 90-day all-cause mortality in adult ICU patients receiving mechanical ventilation when compared to usual oxygen therapy.

Palliative Care in the ED

Key Article

- Grudzen CR, Siman N, Cuthel AM, et al. Palliative Care Initiated in the Emergency Department. *JAMA*. 2025; 333:599-608.

Background

- Among pts 65 years and older, approximately 75% visited an ED within 6 months of their death.
- Palliative care teams are now present in approximately two-thirds of hospitals in the US.
- Unfortunately, these teams are often not available 24/7.
- There is an opportunity for emergency care to improve our ability to meet the needs and goals of older adults with serious illness who prefer to have care delivered at home.
- Specialty palliative care is provided by a specialty-trained or board-certified palliative care health worker. Benefits of specialty palliative care include greater quality of life, improvement

in symptom burden and satisfaction with care, and an increased chance of patients dying in their preferred location. Palliative care can also reduce unnecessary hospitalizations, diagnostic and treatment interventions, and avoid subsequent ED visits or ICU admissions.

- Specialty palliative care is often not available in many locations due to workforce shortages.
- Primary palliative care skills are basic skills and competencies that can be taught and delivered to emergency care workers across a diverse group of EDs and settings.

Objective

- To assess the effectiveness of a multicomponent primary palliative care intervention in the ED.

Methods

- Pragmatic, cluster, randomized, stepped-wedge design
- 29 EDs across the US
- Emergency physicians, physician assistants, nurse practitioners, and nurses
- Patients - Included
 - Aged 66 years or older
 - Visit to 1 of the 29 EDs between May 2018 and December 2022
 - Had 12 months of prior Medicare enrollment with inpatient and outpatient claims and a Gagne comorbidity score > 6 (represented a short-term mortality > 30%)
- Intervention
 - Intervention
 - Evidence-based multidisciplinary primary palliative care education (MDs/PAs/NPs and RNs had different education modules)
 - Simulation-based workshops on serious illness communication
 - Clinical decision support
 - Audit and feedback
 - Randomization
 - Sequence of intervention start dates determined by randomly assigning unique start times to each ED site
- Primary outcome
 - Hospital admission
- Secondary outcomes
 - 6-month health care use (ICU admission, additional ED visits, hospice use, home health visits, or hospital readmission)
 - 6-month survival

Results

- A total 98,922 ED visits were included in the analysis
 - Preintervention period: 51%
 - Postintervention period: 49%
 - Median age: 77 years
 - Median Gagne comorbidity score: 8
 - < 25% visits during the preintervention period occurred during COVID-19, whereas 90% of postintervention visits occurred during the pandemic.
- Primary Outcome – Hospital admission
 - Preintervention period: 64.4%
 - Postintervention period: 61.3%
 - Not significant
- Secondary Outcomes
 - No significant differences

Limitations Identified by Authors

- Stepped-wedge trial design – vulnerable to external factors that influence the primary outcome
- Use of an alternative study design not possible due to the human resources needed to deliver the small group, simulation-based training.
- Global pandemic altered the landscape of ED care during this trial – likely affected illness severity of patients, likelihood of hospital admission, availability of home health and hospice services, etc.

Take Home Point

- A multicomponent primary palliative care intervention did not reduce hospital admissions, subsequent health care use, or short-term mortality for older ED patients with life-limiting illness.