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PULMONARY & CRITICAL CARE INSIDER Special Issue 5: 2023 in Review



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Sepsis / Septic shock

- Managing septic shock with a restrictive-fluids approach (preferentially using vasopressors after a single liter crystalloid bolus) led to similar outcomes as the usual practice of administrating large bolus volumes of fluids first. Restrictive-fluids patients did require longer durations of vasopressors. Despite the significant differences in fluids delivered, there was no difference in need for mechanical ventilation between groups. Either approach in severe sepsis with shock seems reasonable. (<u>CLOVERS trial</u>)
- Piperacillin-tazobactam (marketed as Zosyn) did not cause more renal failure than cefepime, but cefepime did result in more delirium and coma than pip-tazo, in a randomized trial of critically ill patients receiving the antipseudomonal antibiotics. (<u>ACORN</u>)
- Corticosteroids (hydrocortisone 200 mg daily for either 4 or 7 days as determined by clinical improvement, followed by tapering for a total of 8 or 14 days) daily reduced mortality from severe community-acquired pneumonia by 50% (6% vs 12%) in the <u>CAPE COD trial</u> in French ICUs. Reasonable to start steroids for CAP patients requiring mechanical ventilation.
- Beta blockers (landiolol) given to patients receiving norepinephrine for septic shock led to worse outcomes; prior trials had suggested beta-blockade might be helpful, by blunting negative effects of vasopressor-induced tachycardia. (<u>STRESS-L</u>)
- <u>Continuous meropenem infusions were not superior to usual dosing in treating</u> <u>critically ill patients with sepsis.</u>
- Inhaled amikacin reduced the incidence of ventilator-associated pneumonia, but whether it improves hard meaningful clinical outcomes including mortality remains unknown. (<u>AMIKINHAL</u>)

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COVID-19

- <u>Convalescent plasma</u>, given early to patients with ARDS due to Covid-19 pneumonia requiring mechanical ventilation 2020-2022, saved lives with a number needed to treat of 10, in <u>Belgian trial</u>.
- Metformin reduced symptoms of long Covid in a <u>derivative study</u> of <u>a large</u> <u>randomized trial</u>. It's the first treatment to appear to do so.
- Vitamin C did not improve outcomes among patients hospitalized with Covid-19 irrespective of severity of illness. (<u>LOVIT-COVID</u> and <u>REMAP-CAP</u>)
- Twice-daily oral zinc reduced mortality, ICU admission rate, and hospital length of stay in patients <u>with Covid-19 in Tunisia in 2022.</u>
- Simvastatin seemed highly likely to have reduced ventilator-days and mortality in critically ill patients with Covid-19 between 2020 and 2022, compared to placebo (<u>REMAP-CAP</u>)
- <u>Paxlovid</u> seems to continue to improve outcomes from Omicron-era Covid-19 in patients at increased risk for progression to severe disease, but not in patients at average risk.
- Inhaled corticosteroids did not improve outcomes from Covid-19 pneumonia in the Omicron era. (<u>ACTIV-6 trial</u>)
- Pulse oximeters are less accurate in darker-skinned patients—often generating falsely high readings—and <u>this led to delays of care in severely ill darker-skinned</u> <u>patients during the Covid-19 pandemic</u>.

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Cardiovascular care & Stroke

- Mechanical thrombectomy was shown to markedly improve functional independence after large ischemic strokes (<u>SELECT2</u>), heralding a new standard of care for the condition.
- For ischemic strokes caused by venus thromboembolism from atrial fibrillation, starting a direct oral anticoagulant early (3-7 days) prevented more subsequent strokes, as compared to waiting longer. (<u>ELAN trial</u>).
- •
- Patients receiving ECMO for cardiogenic shock due to myocardial infarction had no improvement in survival, and more serious complications, compared to patients managed conventionally. (<u>ECLS-SHOCK trial</u>)
- <u>Semaglutide (Wegovy)</u> improved heart failure symptoms along with weight reduction, further raising the sense of optimism for the costly drugs' potential for mitigating the devastating public health consequences of obesity.

Cardiac Arrest

- A <u>Cochrane review</u> did not find a benefit from cooling below 36° after cardiac arrest, but suggested that patients do better if they receive active (i.e., devicebased) cooling to at least 36°.
- After cardiac arrest, a large trial found no benefit to maintaining temperature <37° for 72 hours as compared to 36 hours (after targeting 36° for the first 24 hours), using cooling devices. <u>Read in NEJM</u>.
- <u>Targeted mild hypercapnia</u> did not improve neurologic outcomes in patients resuscitated from out-of-hospital cardiac arrest (OHCA).

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Intubation and mechanical ventilation

- Video laryngoscopy was superior to direct laryngoscopy in first-pass success among ED residents and CCM fellows intubating critically ill patients (<u>DEVICE</u> <u>trial</u>). Besides confirming video laryngoscopy's shorter learning curve, this result may also in part represent the decay in direct laryngoscopy skills in the post-video era.
- **Does oxygen target matter?** In a large, complicated pragmatic cluster-crossover study at a single academic center, there was no difference in any meaningful outcome (death, ventilator-free days, or severe complications) between patients randomized to an oxygen saturation target of 90%, 94%, or 98%. (PILOT trial)
- In the ICONIC trial, <u>targeting paO2 55-80 mm Hg (low oxygenation) or 110-150 mm Hg (high oxygenation) in mechanically ventilated patients did not affect mortality</u>, although the trial was cut short and possibly underpowered.
- Is etomidate harmful? A meta-analysis of 11 randomized trials suggested etomidate increased the risk of death, with a number need to harm of 31. Adrenal suppression is the putative mechanism. Meta-analyses are prone to falsely amplifying small (or absent) effects, by compounding publication bias.
- During spontaneous breathing trials, there was no apparent advantage to using more-cumbersome T-pieces over the usual practice of pressure support ventilation in achieving successful ventilator liberation. (<u>TIP-EX trial</u>)
- Patients planned for extubation who were receiving tube feedings had equivalent rates of reintubation/extubation failure whether or not their tube feedings were stopped 6 hours prior, or continued through extubation. (<u>REVA network</u>)
- <u>An expert panel broadened the definition</u> of acute respiratory distress syndrome (ARDS), to include patients on high-flow oxygen, and made other small tweaks.

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Hematology and hemorrhages

- Tranexamic acid's short-term survival benefits in traumatic hemorrhage were confirmed, with most of the benefit still persisting after six months. (<u>PATCH trial</u>)
- Direct oral anticoagulants (DOACs) were found to be appropriate alternatives to injected enoxaparin for secondary prevention of venous thromboembolism in patients with invasive solid cancers or blood cancers. (<u>CANVAS trial</u>)
- Giving extra cryoprecipitate to trauma patients undergoing massive transfusion did not help. (<u>CRYOSTAT-2</u>)
- Patients with severe thrombocytopenia who need central lines had a 5% rate of major bleeding if not transfused platelets (vs. 2% severe bleeding in those who were transfused), but most of that risk accrued to patients with blood cancers.

Neurology and neurosurgery

- For subdural hematoma requiring surgical evacuation, either craniotomy (replacing the bone flap immediately) or decompressive craniectomy (leaving the flap off temporarily) led to similar outcomes. (<u>RESCUE-ASDH</u>)
- <u>Haldol was found to be safe</u> and appropriate to use for selected patients with hyperactive delirium in the ICU, in the AID-ICU trial.

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Nutrition in Critical Illness, Intensive Insulin Therapy

- Intensive insulin therapy was convincingly shown to be unhelpful at improving any meaningful outcome in critically ill patients, in a massive trial in Belgium. Rather, the study suggested an even more permissive approach to hyperglycemia (glucose of 215 mg/dL rather than the common target of 180 mg/dL) might be reasonable. (<u>TGC-FAST</u>)
- Another large trial showed no benefit of a high dose protein nutrition strategy in critically ill patients; there was possible harm among those with acute kidney injury who received high dose protein. (<u>EFFORT Protein</u>)
- And another trial suggested there may be no benefit to the high-caloric targets advised in critical care guidelines. Patients on mechanical ventilation and highdose vasopressors restricted to ~420 kcal/day for the first 7 days did as well as those provided ~1750 kcal/day. (<u>NUTRIREA-3</u>)

Post-ICU Disability

- Functional outcomes after critical illness, especially ARDS with mechanical ventilation, are much worse than most physicians recognize. (<u>Review</u>)
- Intensive early mobilization did not lead to improved functional outcomes after critical illness, although the control group received much more physical therapy than is typical in U.S. ICUs, in the multicenter <u>TEAM study</u> by ANZICS.
- Patients receiving intensive early mobilization had better cognitive outcomes, but no greater rates of functional independence, <u>in a single center study at University</u> <u>of Chicago</u>.





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