UAPM
Journal of Respiratory Diseases
and Allied Sciences

Review Article

Critical Care Medicine: The Journey Back to the Bedside

Jacob George Pulinilkunnathil*

Department of Critical Care, Caritas Hospital and Institute of Health Sciences, Kottayam, Kerala, India

Abstract

Critical care medicine is a relatively new specialty that has been growing over the past seven decades. The specialty has come a long way from the bag-ventilation of polio patients to the modern intensive care units. Over the years, with more understanding of physiology, critical care now means intervening less while monitoring the patient more closely. The article touches upon the evolution of the specialty and the Indian context; and the opportunities artificial intelligence may bring in the coming decades.

Keywords: Critical care, History of medicine, Current updates in intensive care.

Introduction

In 1952, Copenhagen faced the worst poliomyelitis epidemic, and patients were dying of respiratory failure.[1] The most significant change in history stemmed from a change in reasoning that these patients were dying of carbon-dioxide retention and not from metabolic alkalosis.[1] As a result, Bjorn Ibsen proposed a solution of tracheostomy with manual positive-pressure ventilation, resulting in a dramatic drop in mortality. Encouraged by this improvisation, the specialty of intensive care was born in December 1953 in Denmark.[2]

The history of intensive care is probably still older, dating back to the Crimean War when Florence Nightingale arranged her most seriously wounded patients adjacent to the nurses' station, for close monitoring. Later in 1958, Max Harry Weil and Herbert Shubin opened a four-bed "shock ward" at the USC Medical Center, and almost concurrently, Peter Safar established a multidisciplinary ICU in Baltimore.[3] Critical care medicine was thus born out of a crisis, driven by the willingness to support failing organs by whatever available means and to call for teamwork under pressure. Seventy years down the line, the specialty continues to focus on organization of the care built on evidence-based practice.

The Evolution of Organ Support

The history of ventilators began in the nineteenth century with negative-pressure ventilators, including the iron lung and progressed to the positive-pressure ventilation during the polio epidemic.[4] Over years, the understanding of ventilation-induced lung injury also evolved as we learned about barotrauma, volutrauma, atelectrauma, biotrauma, and Ergotrauma[5] (Figure 1). That marked a change in era of ventilation - from targeting normoxia and normocapnia with high tidal volumes, to a more gentle, tolerant approach to hypercapnia and hypoxia. Currently, the spectrum of respiratory support ranges from oxygen to non-invasive ventilation, and high-flow nasal oxygen, the use backed up with evidence, scoring systems and guidelines. A landmark trial in the history of critical care was the publication of the ARMA trial which showed that ventilating injured lungs with tidal volumes of 6 ml/kg of predicted body weight showed a significant mortality benefit vs 12 ml /kg body weight.[6] Later, the PROSEVA trial suggested that prolonged prone positioning in severe ARDS, can result in a relative reduction of mortality by 50%.[7]

Address for correspondence: Jacob George Pulinilkunnathil,
Department of Critical Care, Caritas Hospital and Institute of Health Sciences, Kottayam, Kerala, India
E-mail: hipulian@yahoo.co.in

Access this article online

Quick Response Code

Website: uapmjournal.in

DOI: 10.70192/v3.i2.04

How to cite this article: Pulinilkunnathil JG. Critical Care Medicine: The Journey Back to the Bedside. UAPM J. Respiratory Diseases Allied Sci. 2026;3(2):19-25.
Received: 30-04-2026, **Accepted:** 06-06-2026, **Published:** 15-06-2026

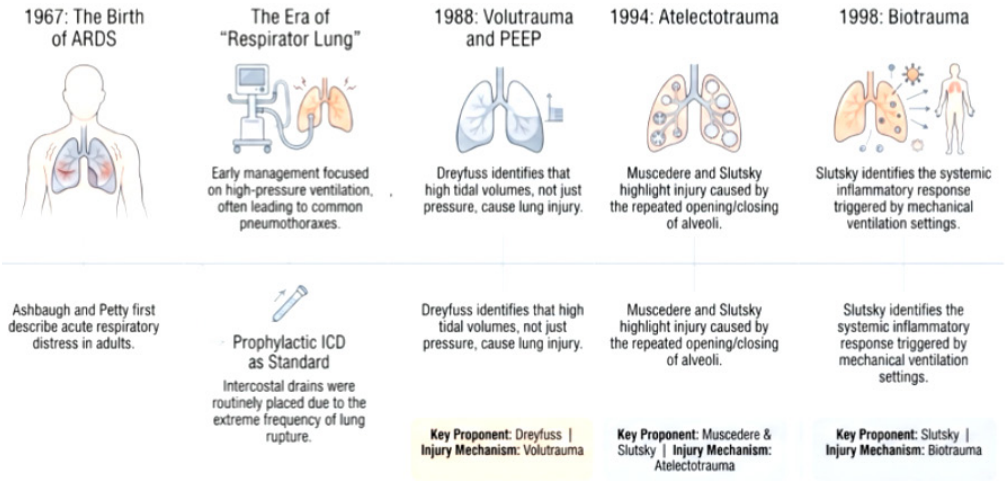

Figure 1: The evolution of respiratory support in the ICU. The trajectory from aggressive strategies to the gentle patient friendly strategies.

Extracorporeal Life Support (ECMO)

The concept of ECMO to tide over failure of heart or lungs evolved from the heart–lung machine, in 1953.[8] However, the first survivor on ECMO was reported only in 1972, and later, a child in 1975.[8] In 1979, the first randomized trial on ECMO in adults was published which turned out to be negative.[9] The resurgence of ECMO was later observed during the 2009 influenza pandemic, with the CESAR trial (2009) showing a benefit from referring ARDS patients to a center capable for performing ECMO[10] and later by the EOLIA in 2018 which further defined the role of ECMO in severe ARDS.[11]

Circulatory Support

The pulmonary artery catheter (PA catheter) developed and introduced in 1970[12] helped clinicians to reliably understand the pressures inside the heart and decide on therapeutics including fluids or modification of vasopressors. The PA catheter remained the gold standard of hemodynamic monitoring for over 20 – 25 years till adverse effects like arrhythmias, infection, and pulmonary artery rupture and a failure to improve clinical outcomes resulted in its downfall. Esophageal Doppler to measure blood flow in the aorta, Pulse Contour Analysis to estimate cardiac output from arterial waveforms, Impedance Cardiography, and later bedside point of care ultrasound and echocardiography brought the objectivity in day-to-day hemodynamic assessment. The use of mixed venous oxygen saturation, central venous oxygen saturation, lactate, and the arterio -venous CO2 gap (A-VCO2 gap) also improved the way we perform hemodynamic resuscitation.

Renal Support

The principle of dialysis was first described in 1854, and the first successful dialysis was performed in 1945.[13] In 1946 the first documented clinical peritoneal dialysis (PD) on a patient suffering from acute renal failure was reported and PD remained a widely accepted treatment for renal failure inside critical care settings till the early 1980s.[14] In 1977 Peter Kramer performed the first continuous arteriovenous hemofiltration and allowed more precision in fluid removal and solute clearance.[15] Owing to the high costs and non-availability of CRRT machines, sustained low-efficiency dialysis was introduced in late 90s.[16] These modalities of renal support have been repeatedly and rigorously tested trial after trial regarding the timing, mode of renal support, dose of renal replacement therapy, type of filters, etc. Similar to ECMO, acute peritoneal dialysis saw a revival during the COVID pandemic, with good outcomes and lower costs. The renewed interest in peritoneal dialysis for critically ill patients with acute kidney injury reiterates that in dire situations, proper application of physiology in appropriate patient groups with coordinated teamwork can help simple solutions transform outcomes.[17]

Sepsis Management

Sepsis is one area where critical care has focused, resulting in important changes in management and outcome. The early goal-directed therapy (EGDT) trial by Rivers et al. that demonstrated a significant mortality benefit by a protocolized early recognition and management of sepsis.[18] The routine use of central venous pressure and mixed venous oxygen saturation (SvO_2) was later refuted by subsequent trials.[19] But EGDT had already transformed sepsis care by reinforcing the early identification, timely intervention, and structured resuscitation. Kumar et al. showed that every hour of delay in the administration of appropriate antibiotics was associated with a significant increase in mortality.[20] Understanding the pharmacodynamics and pharmacokinetics (PK- PD) principles of antibiotics, and their application in practice based on the trials like DALI – ICU, BLING series, BLISS, and MERCY, along with rapid molecular diagnostics has also contributed to a paradigm change in sepsis management.[21]

These trial results have significantly changed the practice, and the mortality of sepsis and septic shock has reduced over years.

Gastrointestinal support and nutrition

Over the years, nutritional support has also evolved in critical care. Initially, most critically ill patients were kept fasting during the acute phase, and nutrition never received the same priority as the other forms of organ support. In the late 1960s, total parenteral nutrition was introduced by Dr. Stanley Dudrick, which revolutionised the field.[22] The understanding of the role of GI tract and its integrity to maintain immune function, later shifted the practice again towards enteral feeding. Trials such as EDEN, PermiT, EPaNIC, TARGET, NUTRIREA-2 and NUTRIREA-3 demonstrated that aggressive early calorie delivery, particularly during shock, does not improve outcomes while permissive hypocaloric feeding during the acute phase is safe. NUTRIREA-3 trial also suggests that temporary restriction of both calories and protein during the early phase of shock may reduce gastrointestinal complications and facilitate recovery[23] (Table 1).

Oncology critical care

Historically, patients with malignancy were not considered for ICU admission, owing to a prevailing therapeutic nihilism about their outcomes. Advancements in critical care – in technology and in the refinement of practice – along with advances in oncology such as better chemotherapy, targeted therapies, immunotherapy, and haematopoietic stem cell transplantation, have changed this significantly. Dedicated onco-critical care units demonstrated that acute organ failure in cancer patients can be reversed, with good patient outcomes. Time-limited trials of ICU admission further helped decision-making in patients with uncertain prognosis. Newer agents such as CAR-T cell therapy and immune checkpoint inhibitors are promising but rely heavily on critical care to recognize and manage their treatment-related toxicities.[24]

The Evidence Era: Trials That Changed Practice

If the early decades gave critical care some ideas and rationale, the 1990s and 2000s gave it evidence. The randomized controlled trials were applied at the bedside, and critical care matured from the application of plausible physiology into application of tested outcomes. Some trials established a beneficial practice (Table 2) while other trials demonstrated that some widely used interventions were either useless or harmful. (Table 3).

Is Less More? Monitoring Closely, Intervening Less

With increasing experience in critical care, we have significantly moved from a goal of attaining normal physiological parameters to a tolerant limit of normal. Multiple high-quality trials have shown that tolerating mild degree of physiological abnormality can be lifesaving than aggressive intervention. As good critical care physicians, we now realize that every intervention, drug, and device carries a risk that must be justified by a genuine expected benefit. Less is more is now a dictum in Critical care, which now supports lower tidal volumes, restrictive transfusion thresholds, lighter sedation with daily awakening, conservative fluid strategies once shock has resolved, moderate oxygen targets, shorter antibiotic courses.[33] Doing "less" safely demands more aggressive, continuous, attentive monitoring of the disease trajectory (Table 4).

Table 1: summary of nutrition trials in critical care

Trial (Year)	Study population	Nutrition strategy tested	Major findings
EDEN (2012)	Mechanically ventilated patients with acute lung injury/ARDS	Trophic enteral feeding versus full enteral feeding during the first 6 days	No difference in mortality, ventilator-free days, or infections.
EPaNIC (2011)	Critically ill adults with insufficient enteral intake	Early supplemental parenteral nutrition (within 48 hours) versus delayed parenteral nutrition (after day 7)	Delayed parenteral nutrition resulted in fewer infections, shorter ICU stay, and faster recovery
PermiT (2015)	Critically ill adults requiring nutritional support	Permissive underfeeding (40–60% of calculated calorie target) versus standard feeding (70–100% target) with similar protein intake	No difference in 90-day mortality or major clinical outcomes
TARGET (2018)	Mechanically ventilated ICU patients	enteral nutrition targeting full calories versus enteral nutrition with lower calorie delivery	Increased calorie delivery did not improve survival or functional outcomes
NUTRIREA-2 (2018)	Mechanically ventilated ICU patients with shock receiving vasopressors	Early full-dose enteral nutrition versus early parenteral nutrition	Similar mortality; enteral nutrition group had increased complications
NUTRIREA-3 (2023)	Mechanically ventilated ICU patients with shock	Early low-calorie and low-protein feeding versus standard calorie and protein targets during the first week	No significant mortality reduction

Table 2: Selected landmark trials that established a beneficial practice

Trial (year)	*Question*	*Practice-changing result*
TRICC, 1999[25]	Restrictive vs liberal red-cell transfusion	Transfusion at a hemoglobin threshold of 7 g/dl was as safe or safer in critically ill patients
ARDS Network (ARMA), 2000[6]	Low vs traditional tidal volume in ARDS	~9% absolute mortality reduction with 6 ml/kg; lung-protective ventilation vs 12 ml/kg
Rivers (EGDT), 2001[18]	Early protocolized resuscitation in sepsis	Stressed early recognition and timely resuscitation of sepsis worldwide.
PROSEVA, 2013[7]	Prolonged prone positioning in severe ARDS	28-day mortality 16% vs 33% with prone positioning in severe ARDS.
EOLIA 2018[11]	Whether early veno-venous ECMO improved survival compared to conventional mechanical ventilation in patients with severe ARDS	Secondary analyses suggested benefit in selected severe ARDS patients.
DEXA ARDS 2020[26]	Dexamethasone for treatment of ARDS	Early administration of dexamethasone reduces mortality in moderate-to-severe ARDS

Table 3: Influential "negative" trials that changed practice

Trial (year)	*Intervention tested*	*Result & consequence*
PAC-Man, 2005[27]	Pulmonary artery catheter	No benefit from routine use; invasive catheter use was largely abandoned.
CORTICUS, 2008[28]	Corticosteroids in septic shock	No overall mortality benefit; steroids reserved for refractory shock.
VISEP 2008; NICE-SUGAR 2009[29,30]	Tight glycemic control	No benefit, more hypoglycemia and excess mortality; tight control was abandoned.
OSCAR OSCILLATE (2013)[31,32]	High frequency oscillatory ventilation vs mechanical ventilation in ARDS	High mortality in HFOV group – abandonment of HFOV
PROCESS / ARISE / PROMISE(2014–15)[19]	Protocolized early goal-directed therapy in sepsis	No benefit over good usual care; rigid sepsis protocols were relaxed, though early recognition endured.

Still a Doctor: The Art of Critical Care

It is tempting to imagine the intensivist as superhuman who reads fancy machines and is skilled at lines and tubes. The reverse is true. A good intensivist is one who realizes that behind every trace on the monitor is a patient with a history, and if the physician doesn't ask where the story began, he is likely to be like Don Quixote fighting windmills of numbers and alarms while missing the real enemy.

In critical care, every source of information is eagerly sought into – the history from a reliable relative, the previous medical record, the unmentioned travel history or silent pet at home. Along with the eliciting of a good history, a focused objective clinical examination continues to remain the foundation of critical care. Point-of-care ultrasound, procedural skills in airway management, and vascular access, although considered sine qua non for critical care, have never replaced the physician's understanding of the disease pathophysiology. Knowing when not to order the test, not to start the drug, not to escalate, is among the most refined skills in the unit. Critical illness has thus probably raised the stakes of the art of clinical medicine.

A Day at the Bedside

My day begins in my bed, scrolling through overnight events posted in the WhatsApp groups. This gives me a head's-up, but I don't compromise on a bedside-focused handover. The multidisciplinary rounds are deliberately brief. The nurse, the respiratory therapist, the dietitian, the trainees and the relevant consultants voice their opinion at the bed. I often act as the buffer. A sick patient often carries four consultants with four plans; and as an intensivist, I must hold the whole picture, reconcile the contradictions, and keep the patient from being pulled in four directions. I tend to focus a lot on clinical microbiology, appropriate antibiotics and try to draw a line between colonization and true infection. Every day, at the bed side the charts are revisited, reading the trends, so that we are always in anticipation of tomorrow's trajectory.

Clinical examination includes a deliberate examination under the blanket to expose the limbs so that mottling, a cold periphery, pedal edema, or an early cellulitis are picked up. In patients with shock, the touch on extremities and the capillary refill aid a focused ultrasound of the heart, lungs, and kidneys. Again, I run through the blinking monitors,

Table 4: Current evidence of "Less is more in critical care."

Area / Intervention (Less is More)	*Major Trial(s)*	*Evidence*
Avoid supranormal oxygen delivery goals[34]	Gattinoni SVO2 trial	Targeting supranormal cardiac index/DO_2 did not improve outcomes; excessive fluids/inotropes may cause harm
Restrictive transfusion strategy[25]	TRICC Trial (1999)	Hb trigger 7 g/dL was at least as safe as liberal transfusion (10 g/dL); reduced unnecessary blood exposure
Less synthetic starch in resuscitation[35]	VISEP, 6S, CHEST Trials	Hydroxyethyl starch increased risk of renal injury/RRT without survival benefit
Lower tidal volume ventilation in ARDS[6]	ARMA Trial (ARDSNet, 2000)	6 mL/kg predicted body weight reduced mortality compared with traditional high tidal volumes
Conservative fluid strategy in ARDS[36]	FACTT Trial (2006)	Conservative fluid management improved ventilator-free days without increasing shock or renal failure
Less sedation[37]	Daily interruption trial (Kress)	Daily awakening and spontaneous breathing trials reduced ventilation duration and ICU stay
Lower oxygen targets / avoid hyperoxia[38]	Oxygen-ICU	Conservative O_2 reduced mortality
Avoid intensive glucose normalization[30]	NICE-SUGAR Trial (2009)	Tight glucose control increased mortality and hypoglycemia; moderate targets preferred
Shorter antibiotic duration[39]	Balance trial	Short-course antibiotics often equivalent and reduce resistance/adverse effects

infusion pumps, charts, labs, and case files, so that nothing is skipped. Drug interactions, drug deescalations, dose modifications, and drug reconciling happens at this point. Then the second part begins – discussion with the relatives, truthfully, clearly, in their own language, with respect. In our context, communication is an art, and we need to address concerns from the decision-maker, the confused relatives, and maybe an unknown person over the phone. As intensivists we must express the possible complications, yet infuse them with confidence, avoid conflicts, and still help to take the decisions that remain tangled culturally and legally, such as palliative care and, at times, futility without being paternalistic.

This daily routine is not sustainable on willpower alone, and it comes with a cost – burnout — the triad of emotional exhaustion, depersonalization, and a diminished sense of accomplishment.[40] It is universal but more common in high-intensity areas like ICUs, due to an occupational response to the work, repeated exposure to death, moral distress, and interpersonal conflict. If not cared for, its consequences can negatively affect the workforce turnover and even patient safety.[41] As a leader of the team, I need to constantly look into the daily structure of the duty pattern, nature of the duty and provide genuine, healthy, and collaborative team environments, with ready access to support.

Beyond Survival: ICU Liberation and Post-Intensive Care Syndrome

Over the years, the goal of critical care has changed from survival to the quality of survival. It is now clear that surviving the ICU and recovering from it are not the same. Factors such as deep sedation and prolonged immobility in the ICU result in weakness, delirium, and lasting harm. A substantial proportion of survivors suffer from post-intensive care syndrome (PICS), affecting physical, cognitive, and mental-health domains (Table 5). The ABCDEF bundle, appropriate pain control, minimizing sedation, pharmacological and non-pharmacological methods to manage delirium, mobilizing patients early, and engaging the family early during the disease course all help in improving the quality of ICU survival. The syndrome does not stop at the patient: family members may develop their own anxiety, depression, and grief — termed PICS-F which also requires a targeted management.[42,43]

Becoming a Critical Care Physician

The entry of a trainee into critical care can be from internal medicine, anesthesia, pulmonary medicine, and emergency medicine, each carrying forward the instincts of its parent specialty. In India, a formal super-specialty degree is offered via a three-year DM in Critical Care Medicine, or its National

Table 5: The domains of post-intensive care syndrome (PICS and PICS-F). Critical illness is a family event; its effects persist for months to years after discharge in a large proportion of survivors.

Physical impairment	*Cognitive impairment*	*Mental health impairment*	*PICS-F (Family impact)*
ICU-acquired weakness	Memory impairment	Anxiety	Caregiver anxiety
Fatigue and deconditioning	Poor concentration	Depression	Depression
Reduced mobility	Slowed information processing	Post-traumatic stress symptoms	Complicated grief
Breathlessness	Executive dysfunction	Sleep disturbance	Financial strain

Board equivalent, the DrNB, or through the fellowship pathway of the Indian Society of Critical Care Medicine, the IDCCM diploma, and IFCCM fellowship.

The Indian Context: Capacity and Disparity

The intensive care in India remains scarce and an unevenly distributed resource. Surveys estimate roughly 2.3 ICU beds per 100,000 population — one among the lowest figures in Asia and a small fraction of the capacity in high-income countries.[44] Critical-care capacity remains concentrated in private hospitals and large cities, with rural populations comparatively underserved — a disparity displayed during the COVID-19 pandemic's second wave. The response has pointed towards an urgent unmet need of scalable, lower cost "small ICU" models for smaller towns, and tele-ICU networks that extend expertise to the remote units.

Lessons from a Pandemic

If the polio epidemic gave birth to the specialty of intensive care, the COVID-19 pandemic revealed its importance to the world. Words such as ventilator, ARDS, proning, ECMO, saturation monitoring entered daily conversation of common man and among national policy makers. The pandemic exposed the existing lacunae in availability of trained personnel, infrastructure including reliable oxygen supply, ICU beds, ventilators, and PPE availability which saw measures for urgent redressal. It also reaffirmed that the best care was delivered through teamwork, and not paternalism.

The Future

The future is probably on predictive analytics and artificial intelligence that assist critical care physicians through early warning systems, pattern recognition, aiding early decision support, and optimization of therapies. Developments such as closed-loop ventilation and infusion systems, continuous and wearable monitoring, are also evolving which will result in personalized approach to critical illness. However, challenges will also arise, the most important being to avoid automation bias, preserve clinical reasoning, and ensure that technology does not replace human judgement. Along with an astute physician, I foresee Artificial intelligence providing an incremental, system-level gains with optimal timing, earlier diagnosis, better organization, and the disciplined withdrawal of therapy that does not help.

Conclusion

Critical care medicine began with fatigued clinicians at the bedside during a pandemic, squeezing a bag to keep a life going. Seven decades later, its essence remains unchanged: continuous monitoring, deep physiological understanding, teamwork, and compassion for the sickest patients. Although technology has grown exponentially, the discipline remains rooted in clinical medicine, calm, yet confident. The aim continues to be that to monitor patients closely, intervene only when it truly helps, and never forget that there are patients, relatives, and teammates in the ICU who need understanding, confidence, and support.

References

1. West JB. The physiological challenges of the 1952 Copenhagen poliomyelitis epidemic and a renaissance in clinical respiratory physiology. J Appl Physiol Bethesda Md 1985. 2005 Aug;99(2):424–32.
2. Reisner-Sénélar L. The birth of intensive care medicine: Björn Ibsen's records. Intensive Care Med. 2011 Jul 1;37(7):1084–6.
3. Tang W, Sun S. Resuscitation great. Max Harry (Hal) Weil - a leader, mentor, friend, and wonderful colleague. Resuscitation. 2011;82(12):1481–2.
4. Slutsky AS. History of Mechanical Ventilation. From Vesalius to Ventilator-induced Lung Injury. Am J Respir Crit Care Med. 2015;191(10):1106–15.
5. Marini JJ, Jaber S. Dynamic predictors of VILI risk: beyond the driving pressure. Intensive Care Med. 2016;42(10):1597–600.
6. Acute Respiratory Distress Syndrome Network, Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000;342(18):1301–8.
7. Guérin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med. 2013;368(23):2159–68.
8. Kanchi M, Bangal K, PVS P, Patangi SO. Extracorporeal Membrane Oxygenation (ECMO) for Pulmonary and/or Cardiopulmonary Support—a Brief Review and Our Experience. Indian J Surg. 2022;1–10.
9. Zapol WM, Snider MT, Hill JD, Fallat RJ, Bartlett RH, Edmunds LH, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure. A randomized prospective study. JAMA. 1979;242(20):2193–6.
10. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. The Lancet. 2009;374(9698):1351–63.
11. Combes A, Hajage D, Capellier G, Demoule A, Lavoué S, Guervilly C, et al. Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome. N Engl J Med. 2018;378(21):1965–75.
12. Swan HJ, Ganz W, Forrester J, Marcus H, Diamond G, Chonette D. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med. 1970;283(9):447–51.
13. Sharma N, Khav E, Elahmadi A, Ong J, Parag S. Dr. Willem Kolff: The Father of the Artificial Kidney. Cureus. 16(9):e69098.
14. Frank HA, Seligman AM, Fine J. Treatment of uremia after acute renal failure by peritoneal irrigation. J Am Med Assoc. 1946;130:703–5.
15. Kramer P, Wigger W, Rieger J, Matthaei D, Scheler F. [Arteriovenous haemofiltration: a new and simple method for treatment of over-hydrated patients resistant to diuretics]. Klin Wochenschr. 1977;55(22):1121–2.
16. Marshall MR, Golper TA, Shaver MJ, Alam MG, Chatoth DK. Sustained low-efficiency dialysis for critically ill

patients requiring renal replacement therapy. Kidney Int. 2001;60(2):777–85.
17. Cullis B. Peritoneal dialysis for acute kidney injury: back on the front-line. Clin Kidney J. 2023;16(2):210–7.
18. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early Goal-Directed Therapy in the Treatment of Severe Sepsis and Septic Shock. N Engl J Med. 2001;345(19):1368–77.
19. Rowan KM, Bailey M, Barnato AE, Bellomo R, Canter RR, Coats TJ, et al. Early, Goal-Directed Therapy for Septic Shock - A Patient-Level Meta-Analysis. N Engl J Med. 2017;376(23):2223–34.
20. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006;34(6):1589–96.
21. Abdul-Aziz MH, Hammond NE, Brett SJ, Cotta MO, De Waele JJ, Devaux A, et al. Prolonged vs Intermittent Infusions of β-Lactam Antibiotics in Adults With Sepsis or Septic Shock: A Systematic Review and Meta-Analysis. JAMA. 2024;332(8):638–48.
22. Dudrick SJ. History of Parenteral Nutrition. J Am Coll Nutr. 2009;28(3):243–51.
23. Gunst J, Casaer MP, Preiser JC, Reignier J, Van den Berghe G. Toward nutrition improving outcome of critically ill patients: How to interpret recent feeding RCTs? Crit Care. 2023;27:43.
24. Divatia JV, Pulinilkunnathil JG. Onco-Critical Care. In: Garg R, Bhatnagar S, editors. Textbook of Onco-Anesthesiology [Internet]. Singapore: Springer; 2021 [cited 2026 Jun 4]. p. 439–57.
25. Hébert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med. 1999;340(6):409–17.
26. Villar J, Ferrando C, Martínez D, Ambrós A, Muñoz T, Soler JA, et al. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. Lancet Respir Med. 2020;8(3):267–76.
27. Harvey S, Harrison DA, Singer M, Ashcroft J, Jones CM, Elbourne D, et al. Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomised controlled trial. Lancet. 2005;366(9484):472–7.
28. Sprung CL, Annane D, Keh D, Moreno R, Singer M, Freivogel K, et al. Hydrocortisone Therapy for Patients with Septic Shock. N Engl J Med. 2008;358(2):111–24.
29. Brunkhorst FM, Engel C, Bloos F, Meier-Hellmann A, Ragaller M, Weiler N, et al. Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis. N Engl J Med. 2008;358(2):125–39.
30. NICE-SUGAR Study Investigators, Finfer S, Chittock DR, Su SYS, Blair D, Foster D, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009;360(13):1283–97.
31. Ferguson ND, Cook DJ, Guyatt GH, Mehta S, Hand L, Austin P, et al. High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome. N Engl J Med. 2013;368(9):795–805.
32. Sklar MC, Fan E, Goligher EC. High-Frequency Oscillatory Ventilation in Adults With ARDS: Past, Present, and Future. Chest. 2017;152(6):1306–17.
33. Auriemma CL, Van den Berghe G, Halpern SD. Less is more in critical care is supported by evidence-based medicine. Intensive Care Med. 2019;45(12):1806–9.
34. Gattinoni L, Brazzi L, Pelosi P, Latini R, Tognoni G, Pesenti A, et al. A Trial of Goal-Oriented Hemodynamic Therapy in Critically Ill Patients. N Engl J Med. 1995;333(16):1025–32.
35. Zarychanski R, Abou-Setta AM, Turgeon AF, Houston BL, McIntyre L, Marshall JC, et al. Association of Hydroxyethyl Starch Administration With Mortality and Acute Kidney Injury in Critically Ill Patients Requiring Volume Resuscitation: A Systematic Review and Meta-analysis. JAMA. 2013;309(7):678–88.
36. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, Hayden D, et al. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med. 2006;354(24):2564–75.
37. Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily Interruption of Sedative Infusions in Critically Ill Patients Undergoing Mechanical Ventilation. N Engl J Med. 2000;342(20):1471–7.
38. Girardis M, Busani S, Damiani E, Donati A, Rinaldi L, Marudi A, et al. Effect of Conservative vs Conventional Oxygen Therapy on Mortality Among Patients in an Intensive Care Unit: The Oxygen-ICU Randomized Clinical Trial. JAMA. 2016;316(15):1583–9.
39. BALANCE Investigators, for the Canadian Critical Care Trials Group, the Association of Medical Microbiology and Infectious Disease Canada Clinical Research Network, the Australian and New Zealand Intensive Care Society Clinical Trials Group, and the Australasian Society for Infectious Diseases Clinical Research Network, Daneman N, Rishu A, Pinto R, Rogers BA, Shehabi Y, et al. Antibiotic Treatment for 7 versus 14 Days in Patients with Bloodstream Infections. N Engl J Med. 2025;392(11):1065–78.
40. Maslach C, Jackson SE. The measurement of experienced burnout. J Organ Behav. 1981;2(2):99–113.
41. Moss M, Good VS, Gozal D, Kleinpell R, Sessler CN. An Official Critical Care Societies Collaborative Statement-Burnout Syndrome in Critical Care Health-care Professionals: A Call for Action. Chest. 2016;150(1):17–26.
42. Needham DM, Davidson J, Cohen H, Hopkins RO, Weinert C, Wunsch H, et al. Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. Crit Care Med. 2012;40(2):502–9.
43. Davidson JE, Jones C, Bienvenu OJ. Family response to critical illness: postintensive care syndrome-family. Crit Care Med. 2012;40(2):618–24.
44. Phua J, Faruq MO, Kulkarni AP, Redjeki IS, Detleuxay K, Mendsaikhan N, et al. Critical Care Bed Capacity in Asian Countries and Regions. Crit Care Med. 2020;48(5):654–62.