The top 100 Critical Care Articles

We believe that inquisitive minds will desire the primary literature from which evidence based practice has been derived. In order to foster education residents must be willing to read, interpret and apply studies to real patients at the bedside. It is also our expectation that you challenge dogma based on your readings, lectures and experiences to help cultivate your own practice habits. This is the only way we can truly assist you in becoming an “evidenced-based” clinician with translational practice habits.

-David & Samir

In a randomized controlled trial of 861 patients with ARDS, mechanical ventilation with a tidal volume of 6 ml/kg and plateau pressure ≤ 30 cmH₂O, in comparison with tidal volume of 12 ml/kg and plateau pressure ≤ 50 cm H₂O, was associated with a 9% absolute mortality decrease (31% vs 40%, P=0.007; NNT=11) and a 2 day increase in ventilator-free days (12±11 vs. 10±11; P=0.007).


In a multicenter, randomized, double-blind trial comparing 0.9% saline or 4% albumin for fluid resuscitation in 6997 critically ill patients in the ICU, there was no difference in mortality (729 v 726, RR 0.99; 95 CI 0.91 to 1.09; P=0.87), new single-organ and multiple-organ failure (P=0.85), mean (SD) numbers of ICU days (6.2±6.2 v 6.5±6.6, P=0.44), hospital days (15.6±9.6 v 15.3±9.6; P=0.30), days of mechanical ventilation (4.3±5.7 v 4.5±6.1; P=0.74), or days of renal-replacement therapy (0.4±2.0 v 0.5±2.3) respectively.


In a randomized controlled trial comparing a red cell transfusion trigger of 7 g/dL versus 10 g/dl in 838 critically ill resuscitated patient, there was no difference in either total 30 day mortality (18.7% vs 23.3%, P=0.11, respectively) or mortality in those with clinically significant cardiac disease (20.5% vs 22.9%; P=0.69). The restrictive transfusion policy was superior for mortality outcome in patients with APACHE II scores of <20 (8.7% vs 16.1%;P=0.03), in patients < 55 years of age (5.7% vs 13.0%; P=0.02), and during hospitalization (22.2% vs 28.1%;P=0.05).

In a blinded randomized controlled trial comparing 6% hydroxyethyl starch 130/0.42 (Voluven) with 0.9% saline for fluid resuscitation in 7000 critically ill patients, this colloid therapy was associated with a 21% increased risk of the requirement for renal replacement therapy (HES RRT requirement 7.0% versus saline 5.8%; relative risk 1.21; 95% CI 1.00 to 1.45; P=0.04 and no mortality benefit (HES mortality 18.0% versus saline mortality 17.0%; relative risk in the HES group, 1.06; 95% CI 0.96 to 1.18; P=0.26). Starch therapy was also associated with increased rates of hepatic failure, rash and pruritus.


In a blinded randomized controlled trial comparing 6% hydroxyethyl starch 130/0.42 (Tetraspan) with Ringers acetate for fluid resuscitation in 804 patients with severe sepsis, at 90 days the use of HES was associated with an 8% absolute increase in mortality (51% v 43%; relative risk: 1.17; 95% CI: 1.01 to 1.36; P=0.03) and a 6% absolute increase in renal replacement therapy (22% v 16%; relative risk: 1.35; 95% CI 1.01 to 1.80; P=0.04).


In a single centre, randomised, controlled trial comparing daily sedation hold with continuous sedation in 128 critically ill mechanically ventilated adults, sedation hold decreased the median durations of mechanical ventilation (4.9 days versus 7.3, p=0.004) and ICU length of stay (6.4 days versus 9.9 days, p = 0.02) as well as the requirement for diagnostic testing for changes in mental status (9% versus 27%, p = 0.02). There were no significant differences in adverse events, including self extubation (intervention group 4% versus control group 7 %, p = 0.88).


In a multicentre, randomized controlled trial comparing intensive glucose control (81-108 mg/dL / 4.5-6.0 mmol/L) with conventional glucose control
(≤180 mg/dL / ≤ 10.0 mmol/L) in 6,104 adult medical and surgical patients, intensive glucose control increased mortality (27.5% vs 24.9%; odds ratio 1.14; 95% CI 1.02 to 1.28; P=0.02). There was no significant difference between medical and surgical patients (odds ratio 1.31 and 1.07 respectively; P=0.10). Severe hypoglycaemic episodes (blood glucose level ≤40mg/dL / 2.2 mmol/L) were more common in the intensive glucose control group (6.8% vs 0.5%; P<0.001). There were no significant differences in the median number of days of mechanical ventilation (P=0.56) or renal-replacement therapy (P=0.39), or days in ICU (P=0.84) or hospital (P=0.86).


In a multicentre, randomised, controlled, double-blind study comparing low-dose dopamine (2μg/kg/min) infusion with placebo in 328 patients with at least two SIRS criteria and early renal dysfunction, there were no differences in peak serum creatinine concentration (dopamine 245 vs placebo 249 μmol/L; p=0.93), increase in serum creatinine from baseline to highest value (62 vs 66 μmol/L; p=0.82), patients whose serum creatinine concentration exceeded 300 μmol/L (56 vs 56; p=0.92), requirement for renal replacement therapy (35 vs 40; p=0.55), duration of ICU stay (13 vs 14 days; p=0.67), duration of hospital stay (29 vs 33 days; p=0.29), or mortality (69 deaths versus 66 deaths).


In a multicenter, randomized, control trial, comparing temperature management at 33°C with 36°C in 939 comatose patients after out-of-hospital cardiac arrest of presumed cardiac cause, there was no difference in mortality at the end of the trial (33°C group 50% vs 36°C group 48%; hazard ratio with 33°C, 1.06; 95% CI 0.89 to 1.28; P = 0.51), 180-day composite of mortality and poor neurological function (54% vs. 52%, respectively; RR 1.02; 95% CI 0.88 to 1.16; P = 0.78), or serious adverse events (93% vs. 90%, respectively; RR 1.03; 95% CI 1.00 to 1.08; P = 0.09).

Prasad et al reviewed 2,044 original articles published from 2001 to 2010 in the New England Journal of Medicine, and found of 1,344 articles which investigated a medical practice, 73.0% examined a new medical practice, and 27.0% tested an established practice; while 70.5% had positive findings, and 29.5% had negative findings. Of the 1,344 articles addressing a medical practice, 56% demonstrated a new practice surpassed a standard of care, 12% demonstrated a new practice was no better than current practice, 11% showed an existing practice was no better than a lesser therapy, 10% showed an existing practice was better than a lesser standard, while 10% were inconclusive. Of the 363 articles testing standard of care, 146 (40.2%) reversed that practice, whereas 138 (38.0%) reaffirmed it.


In a multicentre, double-blind, randomized placebo-controlled trial comparing hydrocortisone (50mg IV 6 hourly, then tapered) with placebo in 499 patients with septic shock, there was no significant difference in 28-day mortality (hydrocortisone group 34.3% vs placebo group 31.5%; P=0.51). Subgroup analyses of 28-day mortality based on response to corticotropin also showed no difference between study groups. Hydrocortisone hastened reversal of shock compared to placebo, however, with more episodes of superinfection, including new sepsis and septic shock.


In a multicentre, randomised control trial, comparing prolonged periods of prone position ventilation with ongoing supine position ventilation, in 466 patients with moderate-to-severe ARDS, prone positioning was associated with reduced 28 day mortality (16% versus 32.8%, hazard ratio 0.39, 95% CI 0.25 to 0.63, P<0.001), reduced 90 day mortality (23.6% versus 41%, HR 0.44, 95% CI 0.29 to 0.67, P<0.001), and less cardiac arrests (31 patients versus 16 patients, P=0.02), with no difference in other complications.

In an unblinded, single center, randomized control trial comparing selective digestive tract decontamination (oral and enteral polymyxin E, tobramycin, and amphotericin B combined with an initial 4-day course of intravenous cefotaxime) with standard treatment in 934 critically ill patients, SDD was associated with reductions in ICU mortality (15% versus 23%, \( P=0.002 \)), hospital mortality (24% versus 31%, \( P=0.02 \)) and colonization with resistant gram-negative bacteria (16% versus 26%, \( P=0.001 \)), with equal colonization of vancomycin resistant enterococcus (1% versus 1% \( p=1.0 \)) and absence of methicillin resistant staphylococcus aureus colonization.


In an ICU population in which the mortality rate associated with standard care was 27.5% at day 28, the rate was reduced by an estimated 3.5 percentage points with selective digestive tract decontamination and by 2.9 percentage points with selective oropharyngeal decontamination.


In a multicenter trial conducted in the tertiary care setting, protocol-based resuscitation of patients in whom septic shock was diagnosed in the emergency department did not improve outcomes.


In a multicenter, randomized control trial comparing critical care management with a pulmonary artery catheter to management without a pulmonary artery catheter in 1,014 general ICU patients, there was no difference in hospital mortality (68% versus 66%, hazard ratio 1.09, 95% CI 0.94 to 1.27, \( P=0.39 \)) or complications, with the incidence of non-fatal complications secondary to pulmonary artery catheterization being 9.5%.

Maitland et al performed a stratified (severe hypotension or not), multicenter, randomized control trial, in a resource-limited setting in sub-Saharan Africa, comparing a fluid bolus (20 to 40 ml of 5% albumin or 0.9% saline) with no fluid bolus at admission to hospital in 3,141 children with febrile illness and impaired perfusion, and found fluid bolus therapy was associated with a higher mortality at 48 hours (albumin 10.6%, saline 10.5%, no bolus 7.3%; relative risk bolus therapy versus no bolus 1.45, 95% CI 1.13 to 1.86, P=0.003), and 28 days (12.2%, 12.0% & 8.7%, respectively; RR bolus therapy versus no bolus p=0.004), with similar incidences of pulmonary oedema, increased intracranial pressure (2.6%, 2.2% versus 1.7% P=0.17), and neurological sequela in the three groups (P=0.92).


In a blinded, multicenter, randomized control trial, comparing noradrenaline plus dobutamine with adrenaline in 330 patients with septic shock, aiming to maintain mean arterial pressure at 70 mmHg, there were no significant differences in 28 day mortality (34% vs. 40%, relative risk 0.86, 95% CI 0.65 to 1.14, P=0.31), ICU mortality (47%vs 75, p=0.69), hospital mortality (52% vs 49%, p=0.51), 90 day mortality (52% vs 50%, p=0.73), time to haemodynamic success (p=0.67), time to vasopressor withdrawal (p=0.09), or rates of serious adverse events.


In a multicenter, randomized control trial, comparing ongoing conventional mechanical ventilation in a non-ECMO centre with transfer to an ECMO centre for respiratory support with either conventional mechanical ventilation or ECMO in 180 patients with severe hypoxic respiratory failure, ECMO centre management, where only 75% of the transferred patients actually received ECMO, was associated with increased 6-month survival (63% vs. 47%, relative risk 0.69, 95% CI 0.05 to 0.97, P=0.03) and a gain of 0·03 quality-adjusted life-years at 6-months, with a lifetime model predicting the cost per QALY of ECMO to be £19 252 (95% CI 7622—59 200) at a discount rate of 3·5%.

In a blinded, multicenter, randomized, control trial, comparing activated protein C (24 µg/kg/hr for 96 hours) with a placebo, in 1,697 adults with septic shock, there were no significant differences in mortality at 28 (26.4% vs. 24.2%, relative risk with APC 1.09, 95% CI 0.92 to 1.28 P=0.31) or 90 days (34.1% versus 32.7%, relative risk with APC 1.04, 95% CI 0.90 to 1.19, P=0.56), including those with initially low levels of APC (28 day mortality 28.7% vs. 30.8%, RR 0.93, 95% CI 0.74 to 1.17; p=0.54), or difference in serious bleeding (APC 10 patients versus placebo 8 patients, P=0.81).


In a blinded, international, multicenter, randomized control trial, largely in resource limited healthcare systems, comparing administration of tranexamic acid (TXA) within 8 hours of traumatic injury (1g over 10 min, then infusion of 1g over 8 hours) with placebo in 20,211 adult patients, with or at risk of significant haemorrhage (SBP <90 mmHg or HR >110 bpm, or both), TXA was associated with reduced mortality (14.5% versus 16.0%; relative risk 0.91, 95% CI 0.85 to 0.97; p=0.0035), including reduced bleeding-related mortality (4.9% versus 5.7%; RR 0.85, 95% CI 0.76 to 0.96; p=0.0077), despite no difference in requirement for blood transfusions (50.4% vs. 51.3%) or vascular-occlusive events. In a subsequent post hoc analysis, the bleeding-related mortality reduction with TXA was time dependent, and actually reversed with late administration after 3 hours of injury (TXA 4.4% vs. placebo 3.1%, p=0.004).


Targeting a mean arterial pressure of 80 to 85 mm Hg, as compared with 65 to 70 mm Hg, in patients with septic shock undergoing resuscitation did not result in significant differences in mortality at either 28 or 90 days. In a prespecified subgroup analysis of patients with chronic hypertension there was an association with reduced need for renal replacement therapy in the higher target group.
23. Casaer. Early versus Late Parenteral Nutrition in Critically Ill Adults. NEJM 2011;365:506-517

In a multicenter, randomized trial comparing early parenteral nutrition (within 48 hours of ICU admission) with late parenteral nutrition (within day 8 of ICU admission) to supplement inadequate enteral nutrition, in 4,640 critically ill patients, late parenteral nutrition was associated with multiple improvements, including shorter durations of ICU (3 days vs. 4 days; p=0.02) and hospital (14 vs. 16 days, p=0.004) stay, fewer ICU infections (22.8% vs. 26.2%, P=0.008), lower incidence of cholestasis (P<0.001), reduced requirement for ventilation for > 2 days (36.3% vs. 40.2%, P=0.006), less duration of renal-replacement therapy (7 vs. 10 days, P=0.008) and mean reduction in health care costs of £910 (P=0.04).


Doig et al performed a multicenter, randomized trial comparing standard care with early parenteral nutrition in 1,372 critically ill patients with relative contraindications to enteral nutrition remaining in ICU for > 2 days, and found no difference in 60 day mortality (standard care 22.8% vs. early PN 21.5%; risk difference −1.26%; 95% CI −6.6 to 4.1; P = 0.60). Early parenteral nutrition patients required fewer days of mechanical ventilation (7.73 versus 7.26, risk difference −0.47; 95% CI −0.82 to −0.11; P = 0.01), less muscle wasting based on subjective global assessment (0.43 versus 0.27; mean difference −0.16; 95% CI −0.28 to −0.038; P = 0.01) and less fat loss (0.44 versus 0.31; mean difference −0.13; 95% CI −0.25 to −0.01; P = 0.04). Day-60 quality of life (RAND-36 General Health Status) was statistically higher in the early PN group, which was not clinically meaningful. (45.5 versus 49.8; mean difference 4.3; 95% CI 0.95 to 7.58; P = 0.01).


Mechanical ventilation with conventional tidal volumes is associated with sustained cytokine production, as measured in plasma. Our data suggest that mechanical ventilation with conventional tidal volumes contributes to the development of lung injury in patients without ALI at the onset of mechanical ventilation.

In a multicentre, randomised controlled trial comparing paired daily sedation hold plus daily spontaneous breathing trial (intervention) versus uninterrupted sedation plus a daily spontaneous breathing trial (control) in 336 sedated, mechanically ventilated patients, the intervention was associated with more days breathing without assistance (14.7 vs 11.6 days; 95% CI 0.7 to 5.6; p=0.02), earlier discharge from both intensive care (median time in ICU 9.1 days vs 12.9 days; p=0.01) and the hospital (median time in the hospital 14.9 days vs 19.2 days; p=0.04), and reduced one-year mortality (HR 0.68; 95% CI 0.50 to 0.92; p=0.01; NNT 7.4, 95% CI 4.2 to 35.5). More patients in the intervention group self-extubated, but with similar rates for both reintubation after self-extubation and total reintubation.


For patients with severe traumatic brain injury, care focused on maintaining monitored intracranial pressure at 20 mm Hg or less was not shown to be superior to care based on imaging and clinical examination.


In patients with severe sepsis, albumin replacement in addition to crystalloids, as compared with crystalloids alone, did not improve the rate of survival at 28 and 90 days. It is important to note this is not a trial of albumin resuscitation, as the SAFE trial was, but rather a trial of continuous infusion of 20% albumin, and in a prespecified subgroup analysis patients with septic shock had improved mortality, warranting further investigation.


Intensive renal support in critically ill patients with acute kidney injury did not decrease mortality, improve recovery of kidney function, or reduce the rate of non-renal organ failure as compared with less-intensive therapy.
involving a defined dose of intermittent hemodialysis three times per week and continuous renal-replacement therapy at 20 ml per kilogram per hour.


In a single centre, randomized controlled trial comparing semirecumbent with supine body position in 86 mechanically ventilated medical patients, the semirecumbent group had a lower frequency of suspected nosocomial pneumonia (8% vs 34%; 95% CI for difference 10.0 to 42.0; P=0.003) and microbiologically confirmed pneumonia (5% vs 23%; 95% CI 4.2 to 31.8; p=0.018). Supine body position (odds ratio 6.8; 95% CI 1.7 – 26.7; P=0.006) and enteral nutrition (odds ratio 5.7; 95% CI 1.5 – 22.8; P=0.013) were independent risk factors for nosocomial pneumonia.


For mechanically ventilated adults managed with protocolized sedation, the addition of daily sedation interruption did not reduce the duration of mechanical ventilation or ICU stay.


In a multicentre, double-blind, randomized controlled trial comparing 48 hours of cisatracurium besylate with placebo in 340 patients with early severe ARDS, neuromuscular blockade was associated with a trend for reduced crude 90-day mortality {31.6% (95% CI 25.2 – 38.8) vs 40.7% (95% CI 33.5 – 48.4)} (P=0.08). After adjustment for baseline PaO2:FiO2, plateau pressure and Simplified Acute Physiology II scores, neuromuscular blockade reduced the adjusted hazard ratio for death at 90 days (HR 0.68, 95% CI 0.48 to 0.98; P=0.04). There was no difference in the rate of ICU-acquired paresis.

33. Jones. Lactate Clearance vs Central Venous Oxygen Saturation as Goals of Early Sepsis Therapy. JAMA 2010;303(8):739-746

Among patients with septic shock who were treated to normalize central venous and mean arterial pressure, additional management to normalize
lactate clearance compared with management to normalize ScvO\textsubscript{2} did not result in significantly different in-hospital mortality.


Compared with conventional insulin therapy, intensive insulin therapy did not improve in-hospital mortality among patients who were treated with hydrocortisone for septic shock. The addition of oral fludrocortisone did not result in a statistically significant improvement in in-hospital mortality.


Low-dose vasopressin did not reduce mortality rates as compared with norepinephrine among patients with septic shock who were treated with catecholamine vasopressors. However, in a subset of patients with less severe shock, vasopressin in addition to norepinephrine resulted in a reduced mortality rate compared to vasopressin alone.


In mechanically ventilated patients with mildly elevated gastric residual volumes and already receiving nasogastric nutrition, early nasojejunal nutrition did not increase energy delivery and did not appear to reduce the frequency of pneumonia. The rate of minor gastrointestinal hemorrhage was increased. Routine placement of a nasojejunal tube in such patients is not recommended.


Early provision of glutamine or antioxidants did not improve clinical outcomes, and glutamine was associated with an increase in mortality among critically ill patients with multiorgan failure.

The use of intraaortic balloon counterpulsation did not significantly reduce 30-day mortality in patients with cardiogenic shock complicating acute myocardial infarction for whom an early revascularization strategy was planned.


The addition of nighttime intensivist staffing to a low-intensity daytime staffing model was associated with reduced mortality. However, a reduction in mortality was not seen in ICUs with high-intensity daytime staffing. High intensity staffing was defined as a mandatory ICU consult for all admissions, and the intensivist had primary responsibility for patient care.


The use of enoxaparin plus elastic stockings with graduated compression, as compared with elastic stockings with graduated compression alone, was not associated with a reduction in the rate of death from any cause among hospitalized, acutely ill medical patients.


Inappropriate initial antimicrobial therapy for septic shock occurs in about 20% of patients and is associated with a fivefold reduction in survival. Efforts to increase the frequency of the appropriateness of initial antimicrobial therapy must be central to efforts to reduce the mortality of patients with septic shock.

Effective antimicrobial administration within the first hour of documented hypotension was associated with increased survival to hospital discharge in adult patients with septic shock. Despite a progressive increase in mortality rate with increasing delays, only 50% of septic shock patients received effective antimicrobial therapy within 6 hrs of documented hypotension.

43. Chastre. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. JAMA 2003; 290: 2588-2598

Among patients who had received appropriate initial empirical therapy, with the possible exception of those developing nonfermenting gram-negative bacillus infections, comparable clinical effectiveness against VAP was obtained with the 8- and 15-day treatment regimens. The 8-day group had less antibiotic use.


In a multicentre, blinded, randomised, controlled trial comparing therapeutic hypothermia (33°C, achieved within 2 hours of ROSC and maintained for 12 hours) with normothermia in 77 comatose survivors of out-of-hospital VF cardiac arrest, hypothermia improved survival with a good outcome (49% versus 26%, p=0.046; odds ratio 5.25, 95% CI 1.47 to 18.76, p = 0.011). Hypothermia was associated with a lower cardiac index, higher systemic vascular resistance, hyperglycemia, with no difference in the frequency of adverse events.


In a multicentre, blinded, randomized, controlled trial comparing therapeutic hypothermia (32°C to 34°C for 24 hours) with normothermia in 273 comatose survivors of out-of-hospital VF/VT, hypothermia improved favourable neurological outcomes (55% vs 39%; RR 1.40, 95% CI 1.08 to 1.81) and 6 month mortality (41% vs 55%; RR 0.74, 95% CI 0.58 to 0.95). The complication rate did not differ significantly between the two groups.
46. Harris. Universal Glove and Gown Use and Acquisition of Antibiotic-Resistant Bacteria in the ICU: A Randomized Trial. JAMA 2013;epublished October 4th

The use of gloves and gowns for all patient contact compared with usual care among patients in medical and surgical ICUs did not result in a difference in the primary outcome of acquisition of MRSA or VRE. Although there was a lower risk of MRSA acquisition alone and no difference in adverse events, these secondary outcomes require replication before reaching definitive conclusions.


In routine ICU practice, universal decolonization was more effective than targeted decolonization or screening and isolation in reducing rates of MRSA clinical isolates and bloodstream infection from any pathogen. Universal decolonization required contact precautions for patients with a history of MRSA or a positive MRSA screen, then all patients received twice-daily intranasal mupirocin for 5 days, plus daily bathing with chlorhexidine-impregnated cloths for the entire ICU stay.

48. Mentzelopoulos. Vasopressin, Steroids, and Epinephrine and Neurologically Favorable Survival After In-Hospital Cardiac Arrest: A Randomized Clinical Trial. JAMA 2013;310(3):270

Among patients with cardiac arrest requiring vasopressors, combined vasopressin-epinephrine and methylprednisolone during CPR and stress-dose hydrocortisone in postresuscitation shock, compared with epinephrine/saline placebo, resulted in improved survival to hospital discharge with favorable neurological status.


No sedation of critically ill patients receiving mechanical ventilation is associated with an increase in days without ventilation. A multicentre study is needed to establish whether this effect can be reproduced in other facilities.

Among hospitalized patients with sudden clinical deterioration, we noted a significant association between the number of ICU beds available and ICU admission and patient goals of care but not hospital mortality.


This prospective, randomized study from a single institution clearly demonstrates that early intensive conservative treatment with late necrosectomy for selected cases is the current rationale approach for SNP.


Blockade of aldosterone receptors by spironolactone, in addition to standard therapy, substantially reduces the risk of both morbidity and death among patients with severe heart failure.


As compared with a liberal transfusion strategy (hgb < 9), a restrictive strategy (hgb < 7) significantly improved outcomes in patients with acute upper gastrointestinal bleeding.


In patients with intermediate-risk pulmonary embolism, fibrinolytic therapy prevented hemodynamic decompensation but increased the risk of major hemorrhage and stroke.

These results suggest that in patients with acute lung injury and ARDS who receive mechanical ventilation with a tidal-volume goal of 6 ml per kilogram of predicted body weight and an end-inspiratory plateau-pressure limit of 30 cm of water, clinical outcomes are similar whether lower or higher PEEP levels are used.

56. Jakob. Dexmedetomidine vs Midazolam or Propofol for Sedation During Prolonged Mechanical Ventilation: Two Randomized Controlled Trials. JAMA 2012;307(11):1151-1160

Among ICU patients receiving prolonged mechanical ventilation, dexmedetomidine was not inferior to midazolam and propofol in maintaining light to moderate sedation. Dexmedetomidine reduced duration of mechanical ventilation compared with midazolam and improved patients’ ability to communicate pain compared with midazolam and propofol. More adverse effects were associated with dexmedetomidine.


The incidence of sepsis and the number of sepsis-related deaths are increasing, although the overall mortality rate among patients with sepsis is declining. There are also disparities among races and between men and women in the incidence of sepsis. Gram-positive bacteria and fungal organisms are increasingly common causes of sepsis.

58. Annane. Corticosteroids in the Treatment of Severe Sepsis and Septic Shock in Adults. JAMA 2009;301(22):2362-2375

In this systematic review, Annane et al conclude that corticosteroid therapy has been used in varied doses for sepsis and related syndromes for more than 50 years, with no clear benefit on mortality. Since 1998, studies have consistently used prolonged low-dose corticosteroid therapy, and analysis of this subgroup suggests a beneficial drug effect on short-term


In adults with moderate-to-severe ARDS, early application of HFOV, as compared with a ventilation strategy of low tidal volume and high positive
end-expiratory pressure, does not reduce, and may increase, in-hospital mortality


In this multicenter study, adults were randomized for ARDS to undergo either HFOV with or usual ventilatory care. All the patients had a ratio of the partial pressure of arterial oxygen (Pao2) to the fraction of inspired oxygen (Fio2) of 200 mm Hg (26.7 kPa) or less and an expected duration of ventilation of at least 2 days. The use of HFOV had no significant effect on 30-day mortality in patients undergoing mechanical ventilation for ARDS


Fever control may improve vascular tone and decrease oxygen consumption, but fever may contribute to combat infection. A multi-center randomized trial was undertaken to determine whether fever control by external cooling diminishes vasopressor requirements in septic shock. In this study, fever control using external cooling was safe and decreased vasopressor requirements and early mortality in septic shock.

62. Young. Effect of Early vs Late Tracheostomy Placement on Survival in Patients Receiving Mechanical Ventilation: The TracMan Randomized Trial. JAMA 2013;309(20):2121

For patients breathing with the aid of mechanical ventilation treated in adult critical care units in the United Kingdom, tracheostomy within 4 days of critical care admission was not associated with an improvement in 30-day mortality or other important secondary outcomes. The ability of clinicians to predict which patients required extended ventilatory support was limited.


There have been conflicting reports on the efficacy of recombinant human activated protein C, or drotrecogin alfa (activated) (DrotAA), for the treatment of patients with septic shock. In this randomized, double-blind, placebo-controlled, multicenter trial. DrotAA did not significantly reduce
mortality at 28 or 90 days, as compared with placebo, in patients with septic shock.


Reduced duration of antibiotic treatment might contain the emergence of multidrug-resistant bacteria in intensive care units. In this multicentre, prospective, parallel-group, open-label trial, a procalcitonin-guided strategy to treat suspected bacterial infections in non-surgical patients in intensive care units could reduce antibiotic exposure and selective pressure with no apparent adverse outcomes.


125 patients were randomized in a double-blind placebo-controlled trial within 96 hours of their subarachnoid hemorrhage to determine whether the calcium channel blocker nimodipine would prevent or reduce the severity of ischemic neurologic deficit from arterial spasm. Nimodipine is recommended in patients who are neurologically normal after SAH to reduce neurologic deficit from arterial spasm.


In patients with cardiogenic shock, emergency revascularization did not significantly reduce overall mortality at 30 days. However, after six months there was a significant survival benefit. Early revascularization should be strongly considered for patients with acute myocardial infarction complicated by cardiogenic shock.


Among adults with out-of-hospital cardiac arrest, there was no significant difference in 4-hour survival between patients treated with the mechanical
CPR algorithm or those treated with guideline-adherent manual CPR. The vast majority of survivors in both groups had good neurological outcomes by 6 months. In clinical practice, mechanical CPR using the presented algorithm did not result in improved effectiveness compared with manual CPR.

68. Dieleman. Intraoperative High-Dose Dexamethasone for Cardiac Surgery - A Randomized Controlled Trial (Dexamethasone for Cardiac Surgery [DECS] Study). JAMA 2012;308(17):1761-1767

Prophylactic corticosteroids are often administered during cardiac surgery to attenuate the inflammatory response to cardiopulmonary bypass and surgical trauma; A multicenter, randomized, double-blind, placebo-controlled trial giving steroids intra-operatively failed to reduce the 30-day incidence of major adverse events compared with placebo.


Increasing numbers of intensive care units (ICUs) are adopting the practice of nighttime intensivist staffing despite the lack of experimental evidence of its effectiveness In an academic medical ICU in the United States, nighttime in-hospital intensivist staffing did not improve patient outcomes.


A strategy for whole-body rehabilitation—consisting of interruption of sedation and physical and occupational therapy in the earliest days of critical illness—was safe and well tolerated, and resulted in better functional outcomes at hospital discharge, a shorter duration of delirium, and more ventilator-free days compared with standard care.

71. Reignier. Effect of Not Monitoring Residual Gastric Volume on Risk of Ventilator-Associated Pneumonia in Adults Receiving Mechanical Ventilation and Early Enteral Feeding: A Randomized Controlled Trial. JAMA 2013;309(3):249

Randomized, noninferiority, open-label, multicenter trial conducted from May 2010 through March 2011 in adults requiringminvasive mechanical ventilation for more than 2 days and given enteral nutrition within 36 hours
after intubation at 9 French intensive care units (ICUs); Among adults requiring mechanical ventilation and receiving early enteral nutrition, the absence of gastric volume monitoring was inferior to routine residual gastric volume monitoring in terms of development of VAP.


A prospective randomised study on the impact different ultrafiltration doses in continuous renal replacement therapy on survival was undertaken. Mortality among these critically ill patients was high, but increase in the rate of ultrafiltration improved survival significantly. We recommend that ultrafiltration should be prescribed according to patient’s bodyweight and should reach at least 35 mL/kg/hr.


Infection is a major cause of morbidity and mortality in intensive care units (ICUs) worldwide. However, relatively little information is available about the global epidemiology of such infections. The authors concluded that infections are common in patients in contemporary ICUs, and risk of infection increases with duration of ICU stay. In this large cohort, infection was independently associated with an increased risk of hospital death.


Whether continuous renal replacement therapy is better than intermittent haemodialysis for the treatment of acute renal failure in critically ill patients is controversial. This study compares the effect of intermittent haemodialysis and continuous venovenous haemodiafiltration on survival rates in critically ill patients with acute renal failure as part of multiple-organ dysfunction syndrome. These data suggest that, provided strict guidelines to improve tolerance and metabolic control are used, almost all patients with acute renal failure as part of multiple-organ dysfunction syndrome can be treated with intermittent haemodialysis.

The use of intraaortic balloon counterpulsation did not significantly reduce 30-day mortality in patients with cardiogenic shock complicating acute myocardial infarction for whom an early revascularization strategy was planned.

76. Jubran. Effect of Pressure Support vs Unassisted Breathing Through a Tracheostomy Collar on Weaning Duration in Patients Requiring Prolonged Mechanical Ventilation: A Randomized Trial. JAMA 2013;epublished January 22nd

Among patients requiring prolonged mechanical ventilation and treated at a single long-term care facility, unassisted breathing through a tracheostomy, compared with pressure support, resulted in shorter median weaning time, although weaning mode had no effect on survival at 6 and 12 months.

77. Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators. Extracorporeal membrane oxygenation for 2009 influenza A (H1N1) acute respiratory distress syndrome. JAMA 2009; 302 (17):1888-95

During June to August 2009 in Australia and New Zealand, the ICUs at regional referral centers provided mechanical ventilation for many patients with 2009 influenza A(H1N1)–associated respiratory failure, one-third of whom received ECMO. These ECMO-treated patients were often young adults with severe hypoxemia and had a 21% mortality rate at the end of the study period.


In this multicenter, randomized trial, we assigned patients with shock to receive either dopamine or norepinephrine as first-line vasopressor therapy to restore and maintain blood pressure. Although there was no significant difference in the rate of death between patients with shock who were treated with dopamine as the first-line vasopressor agent and those who were treated with norepinephrine, the use of dopamine was associated with a greater number of adverse events.

Among ICU patients receiving acute ventilatory support for respiratory failure, PDM (patient directed music intervention) resulted in greater reduction in anxiety compared with usual care, but not compared with NCH (noise cancelling headphones). Concurrently, PDM resulted in greater reduction in sedation frequency compared with usual care or NCH, and greater reduction in sedation intensity compared with usual care, but not compared with NCH.


In a randomized trial involving patients hospitalized for acute decompensated heart failure, worsened renal function, and persistent congestion, the use of a stepped pharmacologic-therapy algorithm was superior to a strategy of ultrafiltration for the preservation of renal function at 96 hours, with a similar amount of weight loss with the two approaches. Ultrafiltration was associated with a higher rate of adverse events.


In a previous randomised controlled phase 2 trial, intravenous infusion of salbutamol for up to 7 days in patients with acute respiratory distress syndrome (ARDS) reduced extravascular lung water and plateau airway pressure. The current study assessed the effects of this intervention on mortality in patients with ARDS. Treatment with intravenous salbutamol early in the course of ARDS was poorly tolerated. Treatment is unlikely to be beneficial, and could worsen outcomes. Routine use of β-2 agonist treatment in ventilated patients with this disorder cannot be recommended.

Magnesium sulphate is a neuroprotective agent that might improve outcome after aneurysmal subarachnoid haemorrhage by reducing the occurrence or improving the outcome of delayed cerebral ischaemia. We did a trial to test whether magnesium therapy improves outcome after aneurysmal subarachnoid haemorrhage. Intravenous magnesium sulphate does not improve clinical outcome after aneurysmal subarachnoid haemorrhage, therefore routine administration of magnesium cannot be recommended.


In critically ill patients in Australia and New Zealand with severe sepsis with and without shock, there was a decrease in mortality from 2000 to 2012. These findings were accompanied by changes in the patterns of discharge to home, rehabilitation, and other hospitals.


Despite advances in resuscitation care in recent years, it is not clear whether survival and neurologic function after in-hospital cardiac arrest have improved over time. This study shows both survival and neurologic outcomes after in-hospital cardiac arrest have improved during the past decade at hospitals participating in a large national quality improvement registry.


In this double-blind, placebo-controlled, randomized trial, the use of enoxaparin plus elastic stockings with graduated compression, as compared with elastic stockings with graduated compression alone, was not associated with a reduction in the rate of death from any cause among hospitalized, acutely ill medical patients.

86. Morelli. Effect of Heart Rate Control With Esmolol on Hemodynamic and Clinical Outcomes in Patients With Septic Shock. A Randomized Clinical Trial. JAMA 2013;310(16):1683-1691

For patients in septic shock, open-label use of esmolol vs standard care was associated with reductions in heart rates to achieve target levels, without
increased adverse events. The observed improvement in mortality and other secondary clinical outcomes warrants further investigation.


Twice-daily enteral supplementation of n-3 fatty acids, -linolenic acid, and antioxidants did not improve the primary end point of ventilator-free days or other clinical outcomes in patients with acute lung injury and may be harmful.


Patients in medical and surgical ICUs are at high risk for long-term cognitive impairment. A longer duration of delirium in the hospital was associated with worse global cognition and executive function scores at 3 and 12 months.


Drotrecogin alfa (activated), or recombinant human activated protein C, has antithrombotic, anti-inflammatory, and profibrinolytic properties. In this randomized double-blind, placebo-controlled trial, treatment with drotrecogin alfa significantly reduces mortality in patients with severe sepsis and may be associated with an increased risk of bleeding.


Goal-directed therapy has been used for severe sepsis and septic shock in the intensive care unit. This approach involves adjustments of cardiac preload, afterload, and contractility to balance oxygen delivery with oxygen demand. The purpose of this study was to evaluate the efficacy of early goal-directed therapy before admission to the intensive care unit. Early goal-directed therapy provides significant benefits with respect to outcome in patients with severe sepsis and septic shock.

Hyperglycemia and insulin resistance are common in critically ill patients, even if they have not previously had diabetes. Whether the normalization of blood glucose levels with insulin therapy improves the prognosis for such patients is not known. Intensive insulin therapy to maintain blood glucose at or below 110 mg per deciliter reduces morbidity and mortality among critically ill patients in the surgical intensive care unit.


Placebo-controlled, randomized, double-blind, parallel-group trial performed in 19 intensive care units in France, a 7-day treatment with low doses of hydrocortisone and fludrocortisone significantly reduced the risk of death in patients with septic shock and relative adrenal insufficiency without increasing adverse events.


Intensive insulin therapy significantly reduced morbidity but not mortality among all patients in the medical ICU. Although the risk of subsequent death and disease was reduced in patients treated for three or more days, these patients could not be identified before therapy. Further studies are needed to confirm these preliminary data.


The role of intensive insulin therapy in patients with severe sepsis is uncertain. Fluid resuscitation improves survival among patients with septic shock, but evidence is lacking to support the choice of either crystalloids or colloids. The use of intensive insulin therapy placed critically ill patients with sepsis at increased risk for serious adverse events related to hypoglycemia. As used in this study, HES was harmful, and its toxicity increased with accumulating doses.

For patients with acute lung injury and acute respiratory distress syndrome, a multifaceted protocolized ventilation strategy designed to recruit and open the lung resulted in no significant difference in all-cause hospital mortality or barotrauma compared with an established low-tidal-volume protocolized ventilation strategy. This “open-lung” strategy did appear to improve secondary end points related to hypoxemia and use of rescue therapies.


Hemodynamic therapy to raise the cardiac index and oxygen delivery to supranormal levels may improve outcomes in critically ill patients. The authors studied whether increasing the cardiac index to a supranormal level (cardiac-index group) or increasing mixed venous oxygen saturation to a normal level would decrease morbidity and mortality among critically ill patients, as compared with a control group in which the target was a normal cardiac index. Hemodynamic therapy aimed at achieving supranormal values for the cardiac index or normal values for mixed venous oxygen saturation does not reduce morbidity or mortality among critically ill patients.


In patients with intracerebral hemorrhage, intensive lowering of blood pressure did not result in a significant reduction in the rate of the primary outcome of death or severe disability. An ordinal analysis of modified Rankin scores indicated improved functional outcomes with intensive lowering of blood pressure.


Histopathological findings were correlated to severity and duration of ARDS. Using clinical criteria, the revised Berlin definition for ARDS allowed the
identification of severe ARDS of more than 72 hours as a homogeneous group of patients characterized by a high proportion of diffuse alveolar damage.

99. He J. et al. Effects of Immediate Blood Pressure Reduction on Death and Major Disability in Patients With Acute Ischemic Stroke: The CATIS Randomized Clinical Trial. JAMA 2013; epublished November 17th

Among patients with acute ischemic stroke, blood pressure reduction with antihypertensive medications, compared with the absence of hypertensive medication, did not reduce the likelihood of death and major disability at 14 days or hospital discharge.

100. Santvoort et al. A Step Up Approach or Open Necrosectomy for Necrotizing Pancreatitis. NEJM 2010; 362: 1492-1502

A minimally invasive step-up approach, as compared with open necrosectomy, reduced the rate of the composite end point of major complications or death among patients with necrotizing pancreatitis and infected necrotic tissue.