Update in Intensive Care Medicine

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It has been a big year for evidence-based intensive care. We have seen a number of important advances in our understanding of the management of critically ill patients. For this year's AQUA ICU update I have put together my *'top 10 papers of the recent past for the occasional intensivist'.* These are papers that address fundamental issues in the management of critically ill patients that are likely to be encountered by anyone who looks after critically ill adults in the ICU. Some are practice-changing, others are practice-informing, and some contain paradigm shifting ideas for the present and the future. Here are some summaries:

These are papers that are practice-informing:

Arabi et al. N Engl J Med. 2015; 372:2398-408.	
Patient population	Adults enterally fed within 48 hrs of ICU admission and expected to stay in ICU at least 72 hours
Intervention	Permissive underfeeding (40-60% of calculated caloric requirements)
Comparator	Standard care (70-100% of calculated caloric requirements)
1° outcome	90-day mortality
2° outcomes	ICU, hospital, 28-day, and 180-day mortality
Key findings	Permissive underfeeding patients received 46% of goal calories; standard care patients received 71% of goal calories. There was no difference in 90-day mortality
Bottom Line	Permissive underfeeding resulted in similar outcomes to standard care *but* patients in both treatment arms received substantially less than their calculated caloric requirements

Frat et al. N Engl J Med. 2015; 372:2185-96.	
Patient population	Patients with acute type 1 respiratory failure excluding those with neutropaenia, asthma, cardiogenic pulmonary oedema, shock, and type 2 respiratory failure
Intervention	Humidified high flow nasal prongs (HFNP) (50L/min) [intervention 1] Non-invasive ventilation (NIV) [intervention 2]
Comparator	Standard oxygen therapy (O_2 via non-rebreather face mask)
1° outcome	Proportion of patients requiring intubation to day 28
2° outcomes	ICU and day 90 mortality, ventilator-free days, ICU LOS, dyspnoea and comfort
Key findings	Neither HFNP nor NIV reduced the rate of intubation compared with standard oxygen therapy. HFNP, as compared with standard oxygen therapy or NIV, was associated with reduced dyspnoea and respiratory discomfort as well as increased ventilator-free days, and reduced day 90 mortality.
Bottom Line	This study demonstrated no significant difference in the primary end point; however, secondary end points favoured HFNP over NIV or standard care. HFNP are in widespread use in NZ and these data suggest this therapeutic modality may be preferred to standard oxygen therapy or NIV in this patient population

Young et al. N Engl J Med. 2015; 373:2215-24.	
Patient population	Adults with fever and known (or suspected) infection
Intervention	1gm IV paracetamol Q6hrly until development of a contraindication, discharge from ICU, resolution of infection, or resolution of fever
Comparator	Placebo
1° outcome	Days alive and free from ICU (ICU-free days)
2° outcomes	Mortality at day 28 and day 90; body temperature; proportion of patients who discontinued study medication because of liver dysfunction
Key findings	No difference in ICU-free days or mortality. Paracetamol reduced body temperature by around 0.3°C. There was no difference in the number of patients who discontinued study treatment because of liver dysfunction.
Bottom Line	Using paracetamol to treat fever in patients with infections does not alter the number of days patients spend alive and outside ICU. Paracetamol is well tolerated in these patients but is only a weak antipyretic.

Young et al. JAMA. 2015; 314:1701-10.	
Patient population	Patients who required intravenous fluid therapy in ICU
Intervention	Plasma-Lyte® 148
Comparator	0.9% saline
1° outcome	Acute kidney injury or failure
2° outcomes	Proportion of patients who required RRT; serum creatinine levels in ICU; in-hospital mortality
Key findings	No difference in acute kidney injury or failure using Plasma-Lyte® instead of 0.9% saline. No difference in RRT requirements, serum creatinine, or in-hospital mortality
Bottom Line	For an all-comers ICU population saline and Plasma-Lyte® 148 result in similar renal outcomes.

These papers are game-changers:

Reade et al. JAMA. 2016; 315:1460-8.	
Patient population	Adults with agitated delirium that precludes extubation (excluding patients with traumatic brain injury or dementia)
Intervention	Dexmedetomidine by infusion at up to 1.5mcg/kg/hour
Comparator	Placebo
1° outcome	Dexmedetomidine increased ventilator-free time at 7 days by around a day compared with placebo
2° outcomes	Among the 21 a priori secondary outcomes, none were significantly worse with dexmedetomidine, and several showed statistically significant benefit, including reduced time to extubation and accelerated resolution of delirium.
Key findings	Dexmedetomidine lead to more rapid extubation and sped up resolution of delirium
Bottom Line	Dexmedetomidine is a highly effective treatment for agitated delirium. It is likely to be cost-effective.

Doig et al. Lancet Respir Med. 2015; 3:943-52.	
Patient population	Adults with feeding-related hypophosphataemia (serum phosphate <0.65 mmol/L within 72 h of starting nutritional support not explain by another major cause of low phosphate)
Intervention	Thiamine and electrolyte replacement PLUS a protocolised reduction in calorie delivery to 20 kcal/h for at least 2 days, then a slow increase in rate by around 20kcal/h every 24 hours until goal rate achieved with the proviso that if the phosphate dropped below 0.71 mmol/L at any time calorie delivery was immediately dropped to 20kcal/h before being slowly increased
Comparator	Thiamine and electrolyte replacement PLUS standard calorie delivery
1° outcome	Number of days alive after ICU discharge within 60 day follow-up

2° outcomes	Day 60 mortality and survival time to day 60
Key findings	No difference in the number of days alive and free from hospital to day 60 BUT more patients were alive at day 60 and overall survival time was increased with protocolised energy restriction
Bottom Line	If you encounter a low phosphate you should reduce enteral calorie delivery

Baharoglu et al.	**Lancet. 2016 25; 387:2605-13.**
Patient population	Adults within 6 h or supratentorial intracerebral haemorrhage symptom onset who had used antiplatelet therapy within 7 days and had a CGS of ≥8
Intervention	Platelet transfusion
Comparator	Standard care
1° outcome	Proportion of patients with death or dependence at 3 months
2° outcomes	Survival to 3 months, haematoma expansion after 24 h, platelet transfusion complications
Key findings	Administering platelet transfusions to patients with ICH who are taking antiplatelet therapy increases the risk of death or dependence at 3 months, is associated with an increased risk of transfusion-related complications, and does not reduce haematoma expansion
Bottom Line	Platelet transfusion for patients on antiplatelet agents with ICH are a really bad idea

These papers contain bright ideas that may change practice in the future:

Eastwood et al.	**Resuscitation. 2016; 104:83-90.**
Patient population	Patients mechanically ventilated in ICU after non-traumatic cardiac arrest
Intervention	Mild therapeutic hypercapnia ($PaCO_2$ 50–55 mmHg) for 24 h during mechanical ventilation
Comparator	Normocapnia ($PaCO_2$ 35–45 mmHg)
1° outcome	Neurone specific enolase and S100B levels
2° outcomes	Glasgow Outcome Scale Extended (GOSE) at 6 months
Key findings	NSE levels were lower in patients allocated to therapeutic hypercapnia. S100b concentrations decreased over time in the therapeutic hypercapnia group but not in the normocapnia group.
Bottom Line	Mild therapeutic hypercapnia is a promising novel intervention for neuroprotection in patients with hypoxic ischaemic encephalopathy.

Hodgson et al.	**Crit Care Med. 2016;44:1145-52.**
Patient population	Mechanically ventilated adults expected to be ventilated the day after tomorrow
Intervention	Early goal directed mobilisation (active exercise at the highest level possible as soon as possible for 1 h per day)
Comparator	Standard Care
1° outcome	Highest maximal level of exercise achieved in ICU & increased duration of exercise in ICU
2° outcomes	Time from admission to first mobilisation, duration of MV, ICU and hospital LOS, adverse events, physical function
Key findings	Higher levels of activity and a longer duration of activity in ICU for intervention patients than control patients
Bottom Line	Active mobilisation of intubated and ventilated ICU patients can be done; at present we don't know if it should be done

Singer et al. Sepsis 3.0.	
Objective	To evaluate and update definitions for sepsis and septic shock
Process	Task force of 19 experts decided what sepsis should be and then sent their recommendations to 31 societies requesting peer review and endorsement
Identified limitations of previous definition	1. Inadequate specificity and sensitivity of the SIRS criteria. 2. The use of the various terms sepsis, septic shock, and organ dysfunction lead to discrepancies in reported incidence and observed mortality
Definitions & outcomes	*Sepsis* is now defined as 'life-threatening organ dysfunction caused by a dysregulated host response to infection' and is associated with an in-hospital mortality of >10%. *Septic shock* is now defined as 'a subset of sepsis with profound circulatory, cellular and metabolic abnormalities' and is associated with an in-hospital mortality >40%.
Diagnostic criteria	Life threatening organ dysfunction is formally defined as an increase in the sequential organ failure assessment (SOFA) score of 2 or more points. However, patients with suspected infection who are likely to have the poor outcomes typical of sepsis can by identified if they have at least 2 of the following quick SOFA (qSOFA) criteria: (i) RR≥22/min; (ii) altered mentation; or, (iii) SBP 100mmHg or less. Septic shock can be identified by a vasopressor requirement to maintain a MAP of 65mmHg or greater and a lactate >2mmol/L in the absence of hypovolaemia.
Bottom Line	These are the new sepsis and septic shock definitions (according to an all male panel with no representatives from any discipline other than critical care and no representatives from outside high income countries ☺)