

**Trainee research achievements, studies and publications**

1. David Cosgrave was awarded his MD this month has completed recruitment into a double blind RCT testing naloxone infusion to reduce complications following IT opioids for major hepatobiliary surgery. This is a significant achievement and the first EU Drug trial completed in Anesthesia in Ireland, to our knowledge. The protocol paper has been published in *Trials* (below). David will present his results at grand rounds this year and there is a manuscript under review. David was supported by the SVAF.

[The NAPRESSIM trial: the use of low-dose, prophylactic naloxone infusion to prevent respiratory depression with intrathecally administered morphine in elective hepatobiliary surgery: a study protocol and statistical analysis plan for a randomised controlled trial.](#)

Cosgrave D, Galligan M, Soukhin E, McMullan V, McGuinness S, Puttappa A, Conlon N, Boylan J, Hussain R, Doran P, Nichol A.

*Trials*. 2017 Dec 29;18(1):633. PMID: 29284510

2. Laura Flood has had two review papers published in *Anaesthesia and intensive Care*.  
*Acute kidney injury and the critically ill*  
*Acute pancreatitis: an intensive care perspective*
3. Shri Nair- is recruiting into his study examining the effects of enteral versus parenteral nutrition on GLP-1 levels in the critically ill.
4. Stephen Duff was awarded a UCD Newman fellowship and is his second year of his PhD. He is examining the utility of biomarkers in AKI using a recently established biobank in SVUH. This national and international biobank of the TAEM study will be a future resource to SVUH trainees. Thanks to the SVAF for helping support his PhD program.
5. Laura Flood, Kathy Brickell and Dr Abigail Walsh (Thanks!) have helped us participate in POSE, a European observational study of postoperative mortality and outcome in the elderly surgical population. This should be published later this year
6. Laura Flood and Kathy Brickell have completed data collection into WEAN-SAFE a global observational study of weaning practices in ICU.

**Update on current SVUH research studies**

All these studies are supported by the Irish Critical Care- Clinical Trial Network located in SVUH. Kathy, Michelle and Leanne and all the ICU clinical staff deserve great credit for all their effort

1. SPICE- (Goal Directed Sedation versus standard sedation). The SVUH ICU recruited 128 Patients were enrolled and the results are due in Feb 2019. Outstanding effort this fastest recruiting centre in the world and overall 9<sup>th</sup> highest recruiter overall!!!! Yahya the PI for this study will visit SVUH in March and present the results.
2. *The TRANSFUSE Study* – (Age of Red Blood Cells in the critically ill) has completed and the main manuscript published *NEJM* 2017-[PMID: 25437218](#). In addition, we conducted an updated Systematic review, which includes these results and was published March 2018 [PMID: 29526337](#). Follow-up analysis with other major trials (INFORM, ABLE, RECESS etc.). National Institutes of Health grant submitted to assist support US data processing Minnesota, US patient recruitment. An erratum has been submitted to the *NEJM* describing a miss-reporting

of a subgroup finding. Fresher blood results increased blood stream infections not febrile non—haemolytic transfusion reactions.

3. *The PHARLAP Study*- (Open Lung ventilation versus standard ventilation in ARDS) has finished and the results were presented at the CCR meeting in Belfast. The Protocol Paper has been published- Critical Care and Resuscitation. The manuscript has been submitted to the AJRCCM- fingers crossed.
4. *The PEPTIC Study* – (Proton pump inhibitors versus H2 Receptor Blockers on gastric prophylaxis). Recruitment successfully completed in Ireland, Australia and New Zealand. Awaiting UK recruitment to complete prior to data lock, data follow-up, analysis and manuscript preparation in Q2 2019. Protocol Paper completed and published.
5. *The REST* (Extra-Corporeal CO<sub>2</sub> Removal in Acute Respiratory Failure)- Study- Successful completion of UK run in phase. Roll out of UK wide and ROI sites. Ethical and regulatory approval in (SVUH)-only ROI site to date. Protocol Paper Published. This has resulted in a significant investment, in equipment, training and consumables that all comes to the Department for free. It will establish us as an adult ECLS center (only the second in Ireland). Thanks to Donal and Michael for their support in this.
6. STARRT-AKI (accelerated versus standard initiation of CRRT). This Canadian Critical Care Clinical Trials Group RCT has to date enrolled in one Irish site – SVUH to date (Sean Bagshaw). It is due to stop in Q3 2019
7. *TEAM Study*: The aim of this study was to investigate the effect of early mobilization practice on, strength at ICU discharge and functional recovery at 6 months among mechanically ventilated ICU patients. SVUH is a lead recruiting site. This project is a collaboration with our Physio colleagues-Well done! Thanks to Michael for his leadership with this.
8. *REMAP-CAP* (NCT02735707). A platform Trial testing antibiotic regimens, steroid and mechanical ventilation strategies in ICU patients with CAP. Michael O'Dwyer will represent SVUH ICU in this study. In addition, SVUH will lead the global ventilation strategy and examine the acceptability of the consent processes we use etc. with an embedded study. This study is a collaboration of the Europeans, Australians, New Zealanders and the Canadians.
9. *TAME*- A phase III RCT (NCT03114033) to examine the effect of hypercapnia to improve outcome post cardiac arrest. Dr Andrew Westbrook is representing SVUH ICU in this project. Andrew has taken lead for this in the unit- many thanks! 1 patients so far.

#### **Starting in 2019**

1. *TTM-2*- A Phase III RCT (NCT02908308) examine temperature management in ICU post cardiac arrest.
2. We are establishing a Critical Care biobank which will serve as a resource for our trainees and bench researchers going into the future. This has kindly been supported by the SAVF and Stephen Duff will be the first researcher to avail of it.

#### **Critical Care Reviews Meeting 2019.**

We held a CTN / CTG meeting in collaboration with the Critical Care Reviews (<http://www.criticalcarereviews.com>) meeting Jan 2019. This was a great success and was attended by Niklas Neilsen among others. There was lots of lively discussion and plans for new studies. The results of the PHARLAP study were presented to our group prior to its presentation at the main meeting. We were very appreciative to Rob McSweeney for his help with this meeting.

#### **Funding success and additional applications submitted**

We have been awarded a HRB DIFA awards, for a European study examining EPO in multi trauma. This was 1,000,000 Euro (UCD/SVUH Awarded >5 million Euro last 4 years)

### ***Future Meetings- (save the date)- May 19, June 19, Jan 20***

In collaboration with the ICSI Annual Scientific Meeting / COA symposium in May 2019 we will hold a CTG meeting on the Thursday afternoon. This will be followed by a TAME study investigator meeting. In addition, we will hold a joint CTN / Monash Clinical Trails Symposium in Prato, Italy, June 2019. If any of the Dept. would like to attend these meeting we can arrange to cover registration costs. Finally, we will hold a CTG / CTN meeting in Belfast at Critical Care Reviews meeting in Jan 2020. In addition, we will again sponsor 2 ICU nurses to attend the CCR meeting in Jan 2020.

### **SVUH Study of ethical and consent questions in the critically ill.**

We have just completed a survey of 6,000 members of the public, including 1,200 in Ireland. This has been submitted for publication and it inform on patients understanding of consent in the ICU- they are very supportive. This is embedded with a number of the SVUH trials and is examining patients and their family's understanding of the research processes (i.e. consent) in ICU.

### **Summary**

The year / quarter has been highly successful as measured by all research metrics relevant for our group. The next 12 months is expected to be highly productive as we oversee the completion of another 3 RCTs and start the development of new and stronger international collaborations and the roll out of new trials. In addition, we are undertaking more book chapters and articles with our trainees. It is an exciting time for our research group.

### **Publications in 2018 /2019 to date**

#### [Effect of Early Sustained Prophylactic Hypothermia on Neurologic Outcomes Among Patients With Severe Traumatic Brain Injury: The POLAR Randomized Clinical Trial.](#)

Cooper DJ, Nichol AD, Bailey M, Bernard S, Cameron PA, Pili-Floury S, Forbes A, Gantner D, Higgins AM, Huet O, Kasza J, Murray L, Newby L, Presneill JJ, Rashford S, Rosenfeld JV, Stephenson M, Vallance S, Varma D, Webb SAR, Trapani T, McArthur C; POLAR Trial Investigators and the ANZICS Clinical Trials Group.

JAMA. 2018 Dec 4;320(21):2211-2220. doi: 10.1001/jama.2018.17075.

#### [Priority Needs for Conducting Pandemic-Relevant Clinical Research With Children in Europe: A Consensus Study With Pediatric Clinician-Researchers.](#)

Gal M, Gobat N, Francis NA, Hood K, Butler CC, Bielicki J, Fraaij PL, Sharland M, Jarvis J, van Rossum AMC, Heikkinen T, Martinon-Torres F, Herberg J, Watkins A, Webb SAR, Moore R, Sukumar P, **Nichol A.**

Pediatr Infect Dis J. 2018 Sep 25. doi: 10.1097/INF.0000000000002204. [Epub ahead of print]

PMID: 30256315

#### [A cluster randomised, crossover, registry-embedded clinical trial of proton pump inhibitors versus histamine-2 receptor blockers for ulcer prophylaxis therapy in the intensive care unit \(PEPTIC study\): study protocol.](#)

Young PJ, Bagshaw SM, Forbes A, **Nichol A**, Wright SE, Bellomo R, Bailey MJ, Beasley RW, Eastwood GM, Festa M, Gattas D, van Haren F, Litton E, Mouncey PR, Navarra L, Pilcher D, Mackle DM, McArthur CJ, McGuinness SP, Saxena MK, Webb S, Rowan KM; Australian and New Zealand Intensive Care Society Clinical Trials Group on behalf of the PEPTIC investigators.

Crit Care Resusc. 2018 Sep;20(3):182-189.

PMID: 30153780

[Erythropoietin in traumatic brain injury associated acute kidney injury: A randomized controlled trial.](#)

Skrifvars MB, Moore E, Mårtensson J, Bailey M, French C, Presneill J, **Nichol A**, Little L, Duranteau J, Huet O, Haddad S, Arabi Y, McArthur C, Cooper DJ, Bellomo R; EPO-TBI Investigators and the ANZICS Clinical Trials Group.

Acta Anaesthesiol Scand. 2019 Feb;63(2):200-207. doi: 10.1111/aas.13244. Epub 2018 Aug 21.

PMID: 30132785

[Changes in Temperature Management of Cardiac Arrest Patients Following Publication of the Target Temperature Management Trial.](#)

Salter R, Bailey M, Bellomo R, Eastwood G, Goodwin A, Nielsen N, Pilcher D, **Nichol A**, Saxena M, Shehabi Y, Young P; Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation (ANZICS-CORE).

Crit Care Med. 2018 Nov;46(11):1722-1730. doi: 10.1097/CCM.0000000000003339.

PMID: 30063490

[Permissive Hypercapnia, Alveolar Recruitment and Low Airway Pressure \(PHARLAP\): a protocol for a phase 2 trial in patients with acute respiratory distress syndrome.](#)

Hodgson C, Cooper DJ, Arabi Y, Bennett V, Bersten A, Brickell K, Davies A, Fahey C, Fraser J, McGuinness S, Murray L, Parke R, Tuxen D, Vallance S, Young M, Nichol AD; PHARLAP Study Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group.

Crit Care Resusc. 2018 Jun;20(2):139-149.

PMID:29852853

[The undiscovered country: therapeutic targeting of carbon dioxide levels in critically ill patients.](#)

Nichol AD.

Crit Care Resusc. 2018 Jun;20(2):81-82. No abstract available.

PMID: 29852844

[Pathophysiology of severe traumatic brain injury.](#)

O'leary RA, Nichol AD.

J Neurosurg Sci. 2018 Oct;62(5):542-548. doi: 10.23736/S0390-5616.18.04501-0. Epub 2018 May 22. Review.

PMID:29790727

[Statistical analysis plan for the POLAR-RCT: The Prophylactic hypOthermia trial to Lessen trAumatic bRain injury-Randomised Controlled Trial.](#)

Presneill J, Gantner D, **Nichol A**, McArthur C, Forbes A, Kasza J, Trapani T, Murray L, Bernard S, Cameron P, Capellier G, Huet O, Newby L, Rashford S, Rosenfeld JV, Smith T, Stephenson M, Varma D, Vallance S, Walker T, Webb S, James Cooper D; POLAR investigators and the ANZICS Clinical Trials Group.

Trials. 2018 Apr 27;19(1):259. doi: 10.1186/s13063-018-2610-y.

PMID:29703266

[Effect of age of red cells for transfusion on patient outcomes: a systematic review and meta-analysis.](#)

McQuilten ZK, French CJ, **Nichol A**, Higgins A, Cooper DJ.

Transfus Med Rev. 2018 Apr;32(2):77-88. doi: 10.1016/j.tmr.2018.02.002. Epub 2018 Feb 17.

PMID: 29526337

[Bending the Pandemic Curve: Improving Decision-Making With Clinical Research.](#)

Webb SA, Nichol AD.

Crit Care Med. 2018 Mar;46(3):442-446. doi: 10.1097/CCM.0000000000002912. No abstract available.

PMID: 29474325

[The NAPRESSIM trial: the use of low-dose, prophylactic naloxone infusion to prevent respiratory depression with intrathecally administered morphine in elective hepatobiliary surgery: a study protocol and statistical analysis plan for a randomised controlled trial.](#)

Cosgrave D, Galligan M, Soukhin E, McMullan V, McGuinness S, Puttappa A, Conlon N, Boylan J, Hussain R, Doran P, **Nichol A.**

Trials. 2017 Dec 29;18(1):633. doi: 10.1186/s13063-017-2370-0.

PMID: 29284510