Issue 33

EMERGE Newsletter

January– March 2021

Emergency Medicine Research Group of Edinburgh & Resuscitation Research Group Newsletter

ABC Sepsis Opens for Recruitment

NHS Lothian is the lead site for ABC Sepsis which aims to compare two different fluids; 5% Human Albumin Solution (HAS) and Balanced Crystalloid, in patients with sepsis. This study plans to find out if there is evidence that one fluid is better overall to determine the need for a subsequent, definitive trial.
The trial intervention is delivered in the first hours of hospital treatment with the team recruiting participants from the ED who require intravenous fluid resuscitation). HAS is potentially an ideal resuscitation fluid for sepsis. However, there are several considerations that are the motivation for this trial:

- Current evidence for HAS is inconclusive.
- HAS is much more expensive than balanced crystalloid.
- HAS has not been studied in large sepsis resuscitation outside of critical care, where only a small portion of sepsis patients receive treatment.
- A survey of pharmacists has suggested that HAS use has been increasing in critical care, but use is still minimal in EDs.

Thanks to the many ED clinicians that have already completed training to support this local led study. For those that have not yet done any training **WE NEED YOUR SUPPORT!** Please complete your ABC sepsis training if you haven't already! Training videos have been sent out via email or see Julia or Alison Williams for on the spot training. Completing the training not only supports CPD it is vital for the success of this study.
Special mention to Rooz Rezai and Suzi MacKenzie for helping to enrol the first 4 participants!

EMBOL-1

The EMBOL-1 trial is part of the larger EMERGE-LumiraDx collaboration. Many of us have seen Lumira's point of care devices for COVID-19 testing in the Emergency Department, in this trial we are testing another of their point of care systems. The trial aims to evaluate the accuracy and precision of the Lumira D-dimer test with members of the research team operating the devices as they would ideally be used, at the patient bedside. The devices use Lumira's proprietary microfluidics system to determine concentrations of certain biomarkers in patient's blood from just a few drops and with results in only a few minutes. As well as the team testing the devices we are sending blood samples to the Lumira team so that they can check the results using their own reference device, to compare the results that are being collected in the clinical setting to what is seen in a laboratory setting.
The prospect of a rapid turnaround point of care blood testing device is an exciting one. For commonly used blood tests fast results could reduce delays in treatment as well as being a compact enough system to be used in settings other than the Emergency Department.

Quote of the Quarter

"Scientific research is one of the most exciting and rewarding of occupations. - Frederick Sanger (1980), two time Nobel Prize laureate.

COVID Study Spotlight

HEAL-COVID

HElping Alleviate the Longer-term consequences of COVID-19.
While the acute effects of COVID-19 are well described there is emerging evidence that there could be serious, longer-term complications that are seen in a significant proportion of patients. ~20% of patients develop a new or worsened cardiopulmonary symptoms at 40-60 days after hospital discharge. In COVID-19 there us a high incidence of these cardiovascular and pulmonary complications including persistent lung inflammation, thromboembolism, and pulmonary fibrosis. Interestingly it seems that these complications are not limited to the acute phase but may also occur during the convalescent phase. This could be the reason many of us have become familiar with the term 'Long COVID.'

HEAL-COVID is using drugs with well known safety profiles, repurposing them for the treatment of long covid. Patients can be randomised to standard care, the statin atorvastatin, or apixaban.

Apixaban has been chosen as a thrombosis-specific intervention, as COVID19 is associated with a multifactorial prothombotic state that persists after discharge.

Statins are most well known for their inhibition of the production of cholesterol in the body. Statins work by inhibiting a specific enzyme called HMG-CoA reductase. This enzyme is key for cholesterol production but also for producing many other non-steroidal chemicals in the body. As a result inhibiting the ability of HMG-CoA reductase can effect inflammation, thrombotic and endothelial regulation. Atorvastatin has been selected as the statin for this trial as it has seen extensive clinical use, is widely available.

Participants will be recruited when they are close to discharge post hospitalisation for COVID.

Researcher of the Quarter goes to...

Dr. Roozbeh Rezai!

EMERGE would like to say a big thank you to Rooz for helping us to get the ball rolling on the ABC Sepsis trial and helping us with eligibility for our very first participants!

ABC Sepsis is on of our most important trials as it is a locally led study, so we're delighted to have had Rooz helping out with patient eligibility and prescribing of the trial treatment. We hope that Rooz's involvement with the trial will set a good example for being research active.

EMERGE Study Information – HOW CAN YOU HELP?

Study	Clinical Presentation	Patient Group	How Can You Help?
ABC SEPSIS	Sepsis	• Patients aged 18 years old or over • Acute illness due to proven or suspected infection • NEWS/NEWS2 ≥5 • Clinician determined that IV fluid is needed within 1 hour of assessment.	Highlighting potential patients to the EMERGE team who will investigate further Ext 21315 or 21284
IONA	Suspected Recreational Drug Use	• Patients aged 16 years old or over • Suspicion of novel psychoactive substances	
KRAKIL	Acute Kidney Injury	• Patients aged 16 years old or over • Diagnosis of AKI	
lumiraDx NOVEL	D-DIMER or CRP required	• Patients aged over 16 years old • D-DIMER or CRP completed	
TARGET-CTCA	Suspected ACS	• Patients with troponin results between 5 and the 99th centile (Amber pathway)	Highlight potential patients to the research team and hand out the study postcards when the research team are unavailable

Research-focused Courses

Unfortunately at the moment the Wellcome Trust are unable to run research courses due to the COVID-19 pandemic however if you want to be research active and complete a Good Clinical Practice course, you can complete the free online RCEM or NIHR GCP courses (links below).

RCEM GCP Course: https://www.rcem.ac.uk/RCEM/Quality_Policy/Professional_Affairs/Research/RCEM/Quality-Policy/Professional_Affairs/Research.aspx?hkey=e822bd01-59ba-4003-9bdb-f9cc3e5a0474

NIHR ICH-GCP Course: https://www.nihr.ac.uk/health-and-care-professionals/learning-and-support/good-clinical-practice.htm

The Royal College of Emergency Medicine

AXIOMATIC-SSP

By Michelle Coakley

Antithrombotic treatment with factor XIa inhibition to Optimize Management of Acute Thromboembolic events in Secondary Stroke Prevention

AXIOMATIC-SSP is a global, phase 2, double-blinded, placebo-controlled, dose-ranging trial assessing the efficacy of an oral Factor Xia inhibitor in the prevention of new ischemic stroke or new convert brain infarct. The sponsor is Bristol-Myers-Squibb and our local PI is Dr. Neil Hunter.

The trial drug now has a name: **Milvexian**. "–xian" will be the new name stem for Factor Xia inhibitors.

AXIOMATIC-SSP is open and recruiting well. We have randomized 4 participants of our target of 10. The study will remain open until the 31st December 2021.

A brief reminder of the inclusion criteria:

- Adults over 40 who have had a mild stroke or high-risk TIA.
  - within 48 hours of symptom onset
  - with presence of atherosclerotic plaque in a relevant feeding artery
  - must be eligible for a study-specific MRI.

Eligible participants are randomised to Milvexian 25mg, 100mg or placebo for 90 days with dual antiplatelet therapy.

Care Trial

By Allan MacRaild

CareTrial
CAVERNOMAS: A RANDOMISED EFFECTIVENESS TRIAL

Cavernomas A Randomised Effectiveness (CARE) pilot trial, to address the effectiveness of active treatment (with neurosurgery or stereotactic radiosurgery) versus conservative management in people with symptomatic brain cavernoma

A cavernoma is a cluster of blood vessels that form blood-filled 'caverns' in the brain that look like a raspberry. Cavernomas can bleed into the brain and cause a stroke. Cavernomas can also cause a seizure or epilepsy. About 160 people in the UK each year are diagnosed with a cavernoma that has caused symptoms. Stroke and seizure may lead to disability, handicap and occasionally death. In standard practice in the UK, most people with cavernomas have medical management (which may involve scans, drugs, or rehabilitation) to manage these symptoms. About one fifth also have 'surgical management' with either brain surgery to remove a cavernoma or stereotactic radio surgery to stabilise it with radiation. Surgical management can cause death, disability, and handicap. The pros and cons of medical management versus medical and surgical management are finely balanced. The most reliable way of finding out which management is best is to do a randomised trial.

CARE is a feasibility study and pilot phase randomised trial investigating treatment with surgery vs. without surgery in patients with symptomatic brain cavernomas. CARE is a multicentre prospective randomised open blinded end-point randomised controlled trial at all neuroscience centres in the UK and Ireland. Funding is provided by the National Institute for Health Research Health Technology Assessment Programme following a James Lind Alliance Priority Setting Partnership. Patient and public involvement has been embedded from the outset and a QuinteT recruitment intervention (QRI) will evaluate screening logs and incorporate qualitative research to understand recruitment processes, facilitators and barriers, and identify actions to address barriers.

Our local PI for the study is Consultant Neurosurgeon Mr Ioannis Fouyas. The Chief Investigator in the UK is Prof Rustam Al-Shahi Salman. Edinburgh Clinical Trials Unit (ECTU) will manage the study and we are currently finalising the local approvals with a view to commence recruitment over the summer. More details are available at www.ed.ac.uk/care-study.

New Study– BRAIN MATRIX!

By Michelle Coakley

A BRitish feasibility study of molecular stratification and targeted therapy to optimize the clinical mAnagement of patIeNts with glioMA by enhancing clinical ouTcomes, Reducing avoidable toXicity, improving management of post-operative residual & recurrent disease and improving survivorship

The Tessa Jowell BRAIN MATRIX study will be the first collaboration between the EMERGE neurosurgery team and the oncology research nurses in the Western General Hospital. The central trial team are the Cancer Research UK Clinical Trials Unit at the University of Birmingham and the local PI in Edinburgh will be Mr. Paul Brennan, Consultant Neurosurgeon.

This is an observational study exploring biomarkers in patients undergoing neurosurgery for gliomas. It aims improve knowledge of gliomas and to optimise the clinical management and subsequent outcomes of these patients.

Along with cognitive testing and quality-of-life questionnaires, the study will involve the collection of blood and tumour samples and will follow participants from pre-operation throughout their oncology journey and up to subsequent surgeries if applicable.

While there is no definitive local target, we aim to recruit approximately 3 participants per week until the study closes in 2026. The study is in the process of obtaining local R&D approval and we hope to start recruiting soon!

Current Stroke Studies in the Emergency Department

Study	Clinical Presentation	Patient Group	How can you help?
ATTEST 2	Ischaemic Stroke	-Patients aged over 18 years old -Less than 4.5 hours after symptom onset -Male or non pregnant females	Highlighting potential patients to the EMERGE team who will investigate further Ext 21315 or 21284
BRAINED-TBI	Traumatic Head Injury	-Patients aged over 16 years old -Presenting to the ED having sustained a recent traumatic brain injury requiring CT imaging	
DASH	Intracerebral Haemorrhagic Stroke	-Patients aged over 18 years old - Confirmed intracerebral haemorrhagic - less than 12 hours onset	
INFERENCE	Head, chest, abdomen, pelvis-related presentation requiring radiological investigation	-Patients aged over 16 years old -Present to the hospital with a new onset symptoms related to their head, chest, abdomen or pelvis which requires radiological investigation	
LINCHPIN	Primary Spontaneous Intracerebral Haemorrhage (ICH)	-Patients aged over 16 years old - First ever ICH	
precious	Acute Stroke (Intracranial haemorrhage or ICH)	- Patients over 66 years old -Less than 24 hours after onset	

SAVE A LIFE FOR SCOTLAND

New Team Members!

The SALFS team is growing! We have two new interns joining the team for the next 6 months. Ally and Gary will be working remotely to help support the inequalities strand of the Out-of-Hospital Cardiac Arrest Strategy. They will be tasked with creating and promoting online resources for people with disabilities around CPR. They will be working closely with the Scottish Ambulance Service and their tailored CPR pilot training programme "CPR for people with disabilities". We feel so lucky to have them and if you would like to learn more about their work feel free to email hello@savealife.scot or join us for one of our 4pm catch up calls. We would love to hear from you.

Board Game to Learn about Out-of-hospital Cardiac Arrest

RRG is developing a board game to teach the public about 1) out-of-hospital cardiac arrest, 2) the Chain of Survival which is the sequence of events that need to happen in order to improve chances of survival and 3) the disparities that exist in OHCA survival outcomes such as those living in deprived areas are less likely to receive bystander CPR/defibrillation and also less likely to survive overall. RRG has recently secured a Graphic Designer from the Edinburgh School of Art to design both a physical board game and an online version available for download on the Save a Life for Scotland website. We look forward to sharing this with you!

Looking for Participants: Chest Compression Research Study

Liz Simpson, a long term supporter of Save a Life for Scotland is pursuing her PhD studies at Glasgow Caledonian University. She is looking for participants for her study about the physical demand on the rescuer when delivering high quality chest compressions (CPR). The aim of the study is to compare two methods of delivering chest compressions on a manikin, to find out more about the physical demand on the rescuer and effectiveness of each method. If you are interested in getting involved, get in contact with E.Simpson@gcu.ac.uk

For more information on EMERGE, RRG and our team, please visit www.emergeresearch.org

Or follow us on Twitter @emerge_research

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