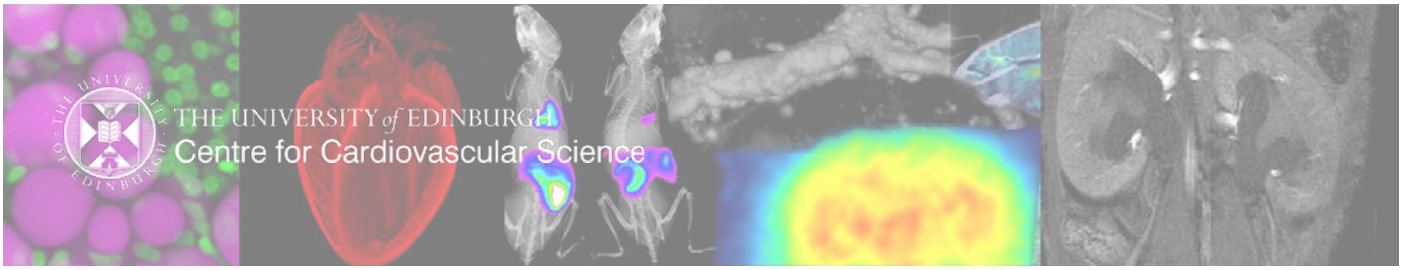
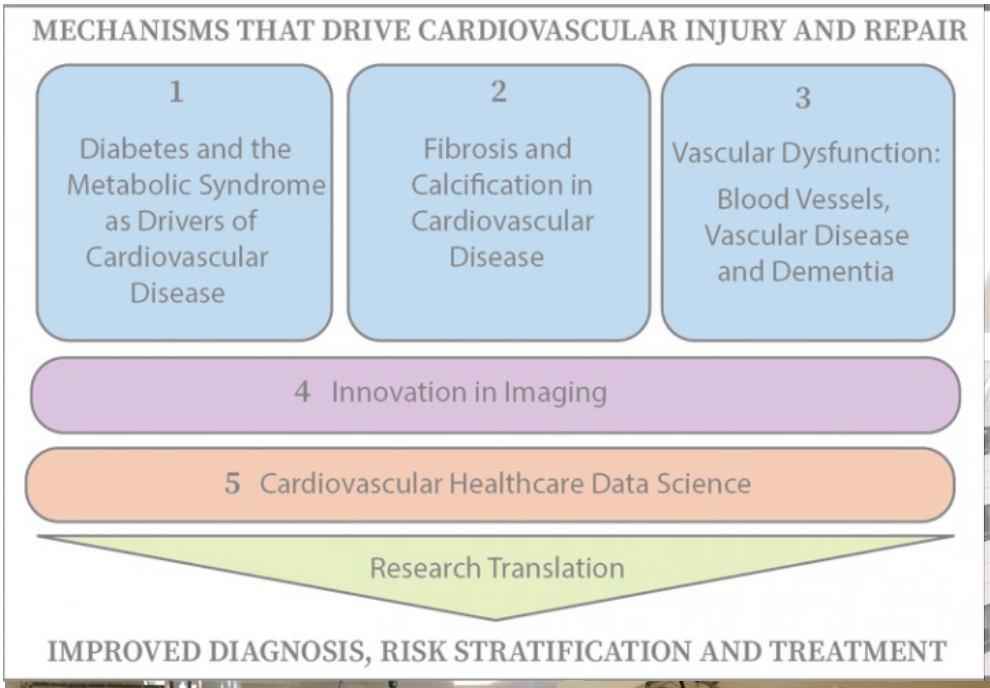
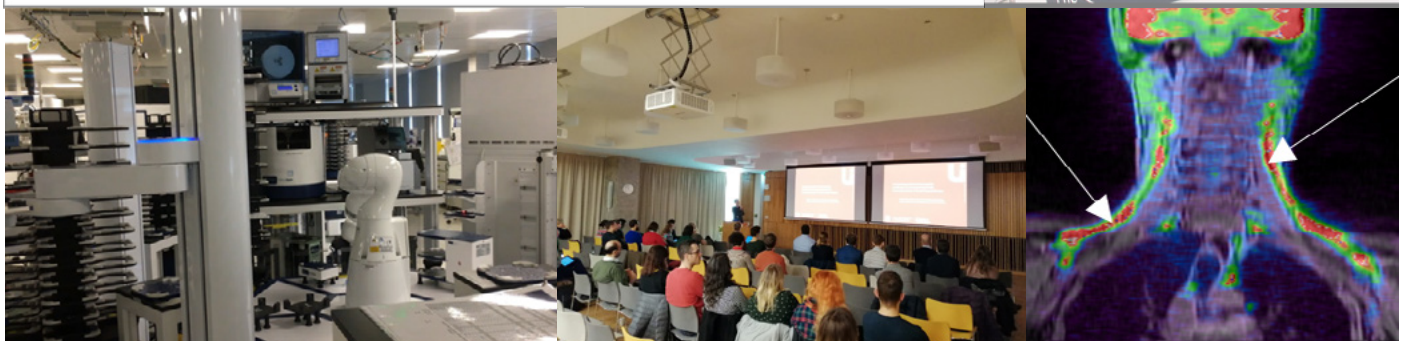
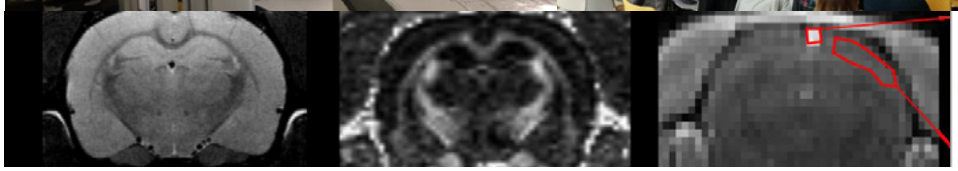


REA3 BIMONTHLY NEWSLETTER

November 2020

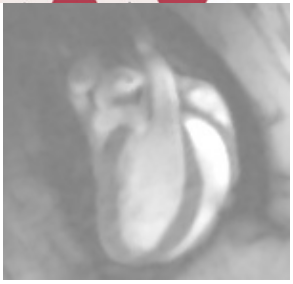


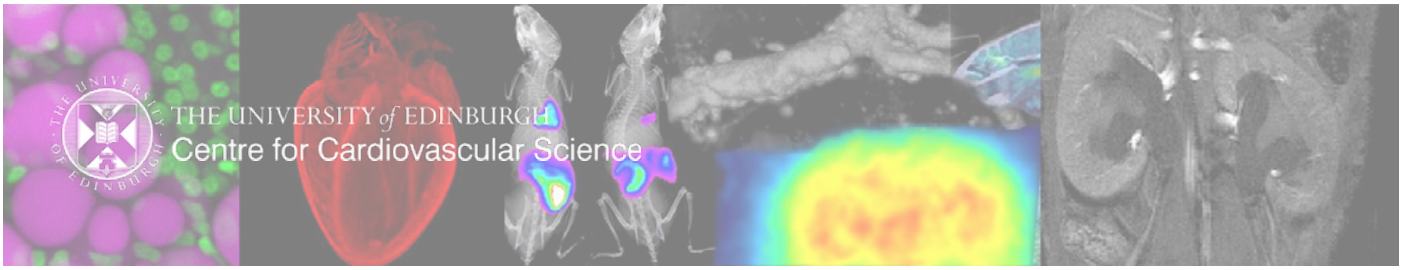




THE UNIVERSITY of EDINBURGH

BHF Research Excellence Award University of Edinburgh





INTRODUCTION

Welcome to our last edition of the REA3 newsletter for 2020.

How do we sum up the last year? For some of us it has been frustrating, sad, isolating, stressful, tiresome and monotonous. However, we are now ending this year perhaps with renewed optimism with the development of not one but three potential vaccines. We can envisage a 2021 that might allow for restrictions to be lifted and see the return of in-person meetings, seminars and conferences, which are so important to the research community, especially in encouraging networking links.

The pandemic has certainly created delays to some projects. But there is a sense that these setbacks have, thankfully, just been temporary and research that was suspended can now continue. It shows the resilience and tenacity of our researchers in ensuring the continued success of REA3 and CVS as a whole.

Dr Neshika Samarasekera

Within this issue, we have an introduction to Dr Neshika Samarasekera's Spring 2020 pump priming award, which looks at the association between swelling (peri-haematomal odema) after a brain haemorrhage and functional outcome.

Dr Peter Gallacher

We also made an award to Dr Peter Gallacher who has been able to continue his research into evaluating temporal trends and treatment gaps in cardiovascular disease in patients with kidney disease. He provides us with an overview of the first year of his PhD in clincial epidemiology.

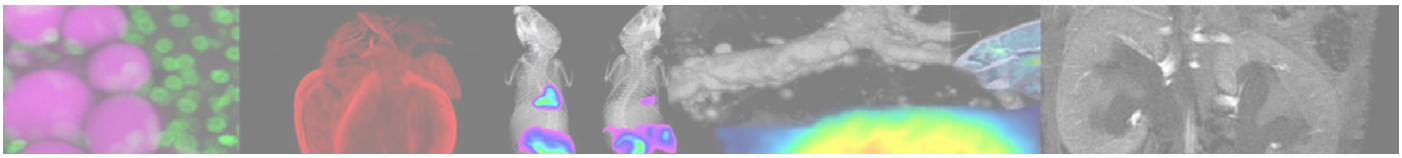
Dr Ellen Backhouse, R4VaD study manager, has provided an update and summary to the R4VaD study, which was awarded funding as part of the COVID-19 response and a COVID-19 sub-study has been established. In 2021 there will be further developments when they will implement a data linkage exercise to centralised hospital data, which we look forward to hearing about in a future edition.

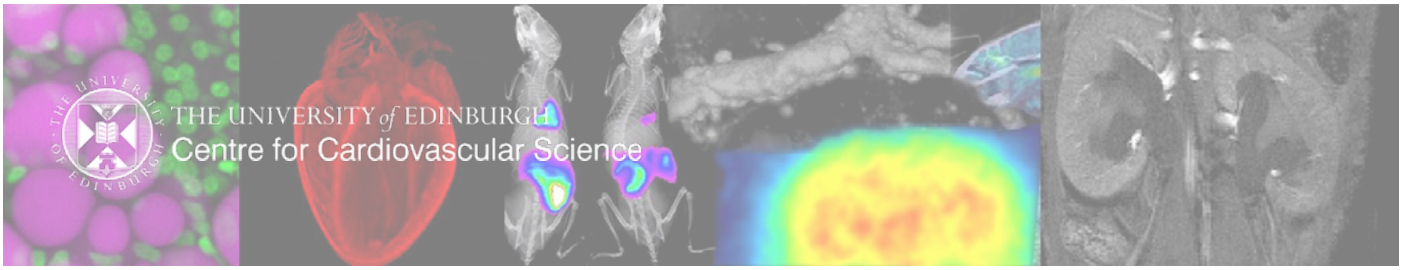
Finally on Monday 23 November, we hosted our first External Advisory Board (EAB) meeting to assess the progress of REA3. The REA3 Executive are grateful to to the EAB members and also those that presented in making the afternoon a success. A small summary is also within this issue.

We are always looking for stories and updates for the REA3 newsletter and if you have anything that you would like to highlight then do get in contact with Gillian Joyce: Gillian.Joyce@ed.ac.uk

Hopefully most of you will manage to have a break of some sort over the festive period, even if it's a couple of days away from the laptop. We would like to thank everyone for their hard work over 2020 and wish you well for 2021.

Professor Andrew H Baker, Director REA3
Professor David Newby, Deputy Director REA3





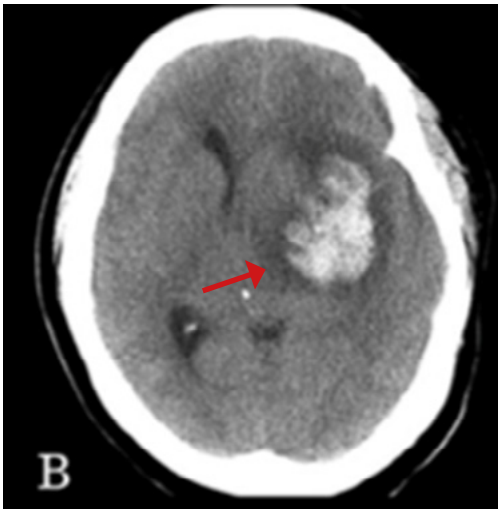
Dr Neshika Samarasekera- Individual patient data meta-analysis of the association between peri-haematomal oedema and outcome after spontaneous intracerebral haemorrhage

Amount awarded: £46,741

Co-applicants: Professor Rustam Salman, Dr Tom Moullaali, Dr Grant Mair, Dr Xia Wang, Professor Chris Weir and Dr Adrian Parry-Jones

I am extremely grateful to the BHF REA programme for awarding our team funding to look in more detail at the association between swelling (peri-haematomal oedema) after a brain haemorrhage and functional outcome.

Intracerebral haemorrhage (ICH) accounts for 10% of strokes in high income countries. About 40% patients die within the first month. There is no effective medical treatment.



Peri-haematomal oedema (marked with a red arrow in the picture opposite, which shows a computed tomography image of a left hemisphere intracerebral haemorrhage); is visible as a hypointense ring around the haemorrhage margin on brain imaging in most patients.

Oedema may well be associated with worse functional outcomes after a haemorrhage and it is a potential therapeutic target. However, we do not know enough about which factors can affect the relationship between peri-haematomal oedema and outcome.

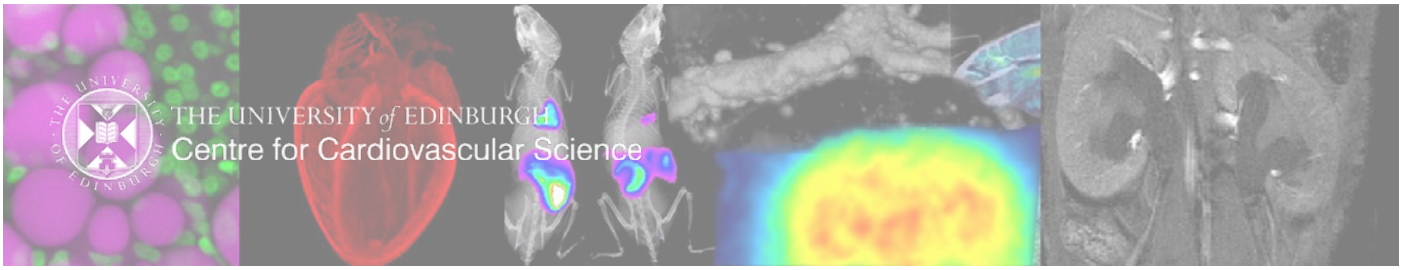
In a systematic review, we identified 28 studies of 6,142 participants, examining the association between oedema and functional outcome. A meta-analysis of studies that assessed outcome at 90 days did not find a definite association between oedema and outcome.

However the strength, direction, and modifiers of an association are all uncertain, because of heterogeneity between studies, including the time of oedema assessment in relation to ICH onset.

Our project aims to (A): Determine the strength of the association between peri-haematomal oedema and outcome and (B): Identify variables which may modify the strength of the association of oedema with outcome.

The project is an individual patient data meta-analysis of observational studies or the placebo arm of interventional studies, measuring peri-haematomal oedema and functional outcome. We will use two data sources: firstly - data from studies identified by our systematic review of oedema and functional outcome; and secondly, data from our ongoing Stroke Association - funded prospective cohort study of oedema and ICH. We will add the data from this study to the data from published studies.

We hope that this work will increase our understanding of factors which affect oedema and will help to stratify patients according to their risk of oedema, to help select patients for trials in which oedema is the treatment target.



Dr Peter Gallacher - Clinical Research Fellow

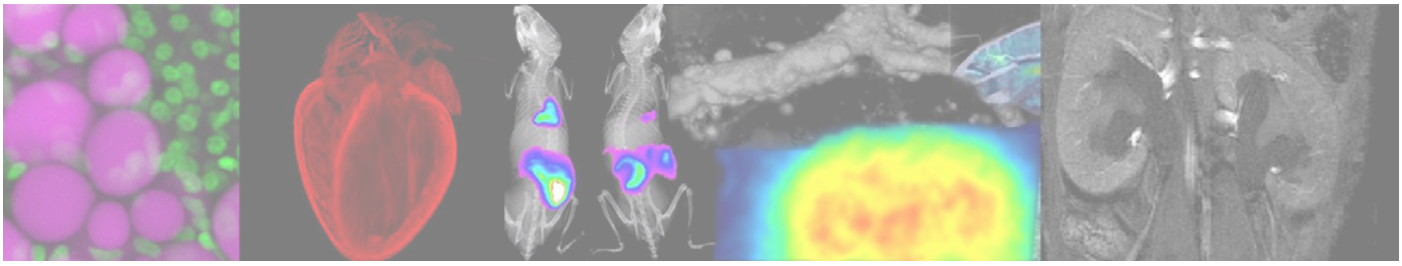
I am a General Practice trainee with a keen interest in clinical epidemiology and the analysis of routine healthcare data. I am coming to the end of the first year of my PhD in clinical epidemiology at the Centre for Cardiovascular Science, having been supported until now by a Mason Medical Research Trust clinical fellowship. This award from the BHF REA3 Executive will ensure that I am able to continue my research despite the ongoing COVID-19 pandemic. The primary focus of my PhD is to evaluate temporal trends and treatment gaps in cardiovascular disease in patients with kidney disease. The project is directly aligned with the 'Cardiovascular Healthcare Data Science' REA3 cross-cutting theme and will utilise high-fidelity linked healthcare data unique to Scotland.

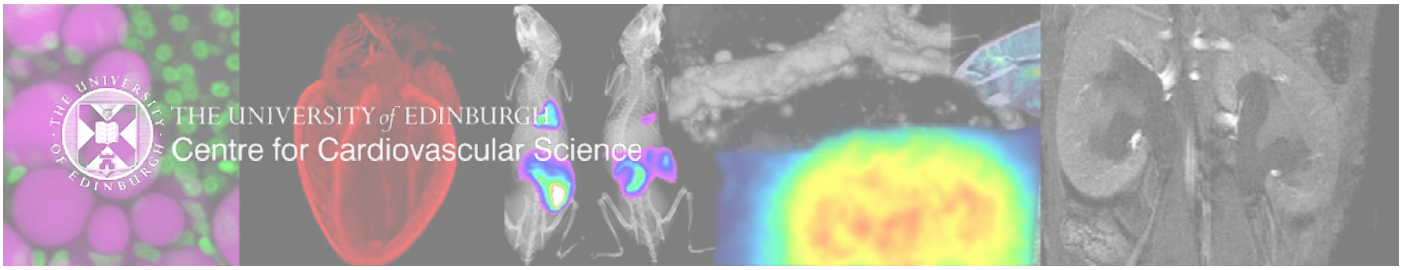
Chronic kidney disease (CKD) is an important global health problem whose prevalence increased by 30% and mortality by more than 40% worldwide between 1990 and 2017. CKD has a major effect on health, partly as a result of morbidity and mortality directly attributable to disease progression, but mostly as a consequence of its well-recognised association with cardiovascular disease. Cardiovascular risk is greatest in patients on dialysis, where cardiovascular mortality is 20-fold greater than in the general population; for a patient <45 years, it is 100-fold greater. Although renal transplantation is the best treatment for patients with end-stage renal disease, cardiovascular disease remains the commonest cause of death in transplant recipients. Despite all of this, more than half of cardiovascular trials in the last 30 years have excluded patients with any degree of renal impairment.

In the general population, recent advances in the diagnosis and management of cardiovascular disease, and a decline in smoking prevalence, have contributed to falling acute coronary syndrome rates and improved survival. However, few studies have reported acute coronary syndrome trends in consecutive dialysis and renal transplant patients, and in the contemporary era of sensitive cardiac biomarkers, effective pharmacotherapies and widespread coronary revascularisation.

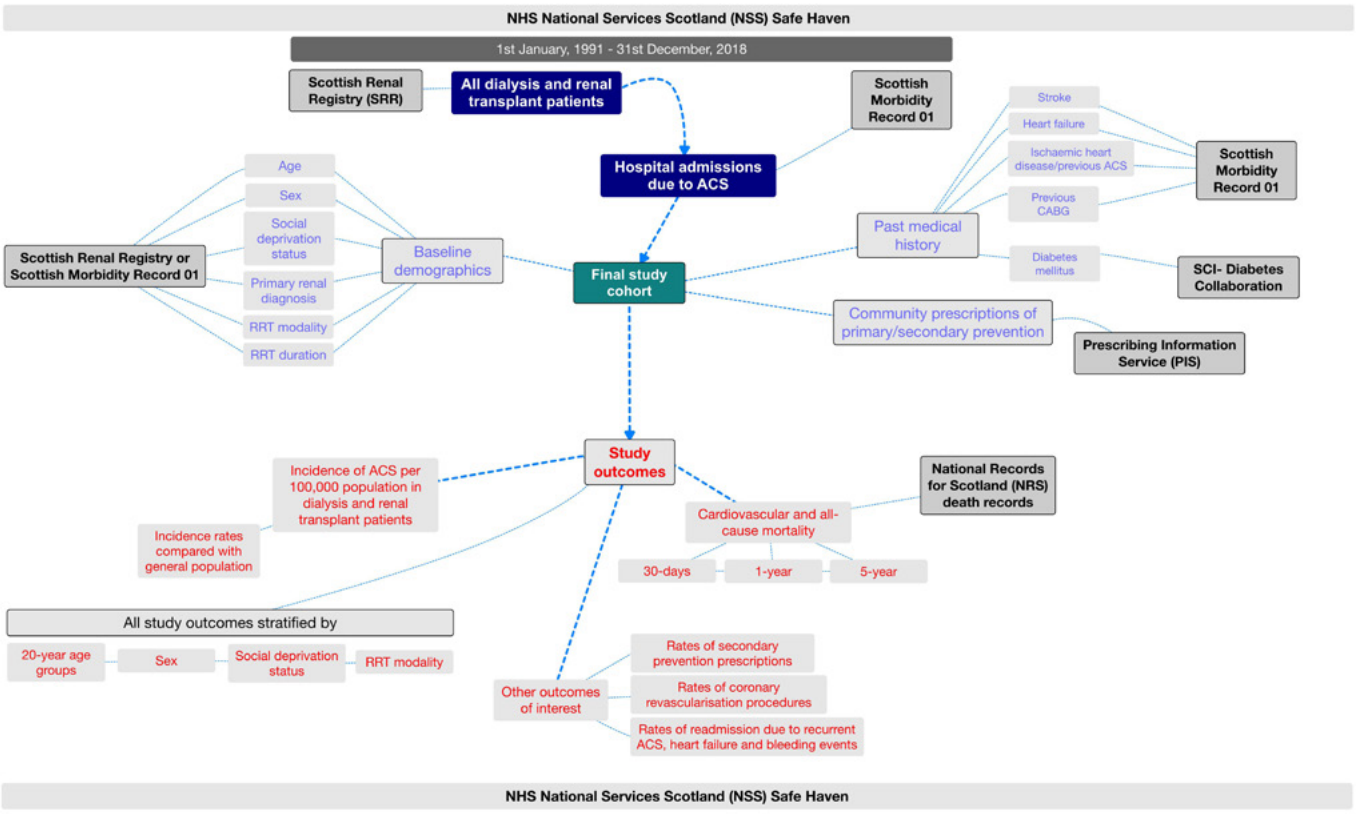
Utilising linked routine healthcare data from five national registries, I will perform a novel population-based epidemiological study to describe trends in the incidence of acute coronary syndrome in all patients on dialysis or with a renal transplant in Scotland between 1991 and 2018. I will evaluate outcomes including cardiovascular and all-cause mortality, rates of preventative therapy prescribing and readmission for recurrent acute coronary syndrome, stroke, heart failure or bleeding. These trends will be compared with pilot data describing the incidence and outcomes of acute coronary syndrome in the general population in order to identify modifiable factors, such as differences in preventative therapy prescribing rates. In summary, this study will help us identify important opportunities to improve outcomes for these high-risk patients.

Overleaf is a diagram showing an overview of the linked healthcare data for the five national registries.

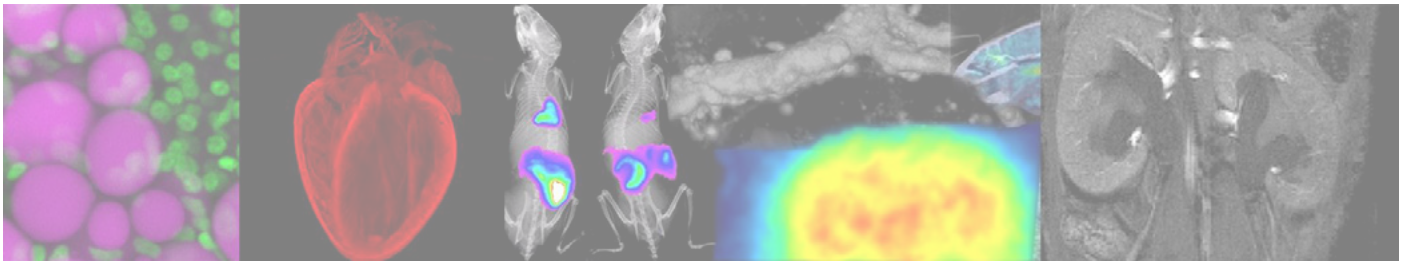


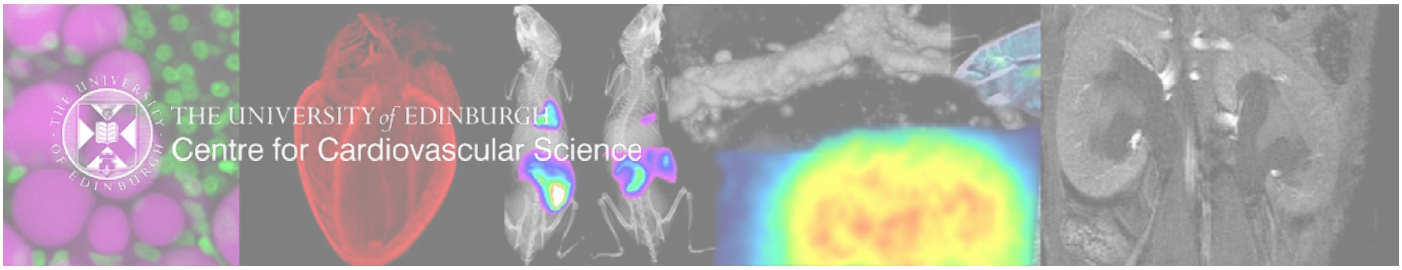


Dr Peter Gallacher - Clinical Research Fellow



ACS - Acute Coronary Syndrome





Dr Ellen Backhouse - Research Fellow in Cerebrovascular Disease & R4VaD Study Manager

Stroke and vascular dementia are closely related yet the aetiology, risk factors and prognosis of post-stroke cognitive impairment (PSCI) remain neglected areas of stroke research and are poorly understood, making it difficult to advise individuals, plan randomised clinical trials (RCTs) or develop clinical services. R4VaD aims to address these gaps in knowledge to determine the rates of cognitive impairment and dementia to at least two years after stroke across a wide range of patients, stroke severities and subtypes.

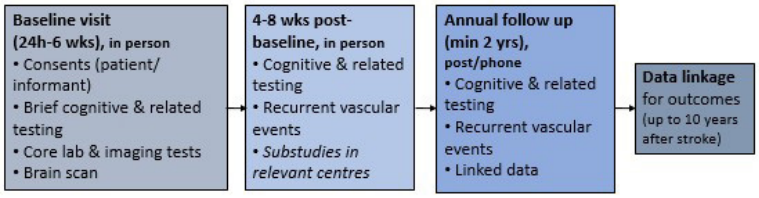


Figure 2: Flow chart of R4VaD assessments

Recruitment

We now have a total of 53 sites across the UK, including 8 applicant sites (Figure 1). We officially passed the halfway mark back in January and as of mid-November, we have recruited 1701 patients out of a target of 2000, including 423 recruited since the start of the COVIID-19 pandemic. Our annual follow-ups are about to start their second year coordinated by UCL, Glasgow and Leicester.

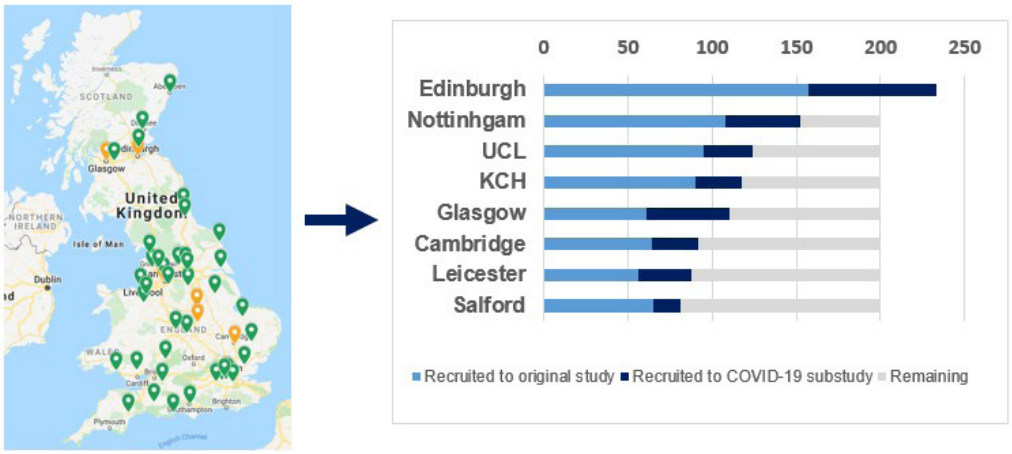
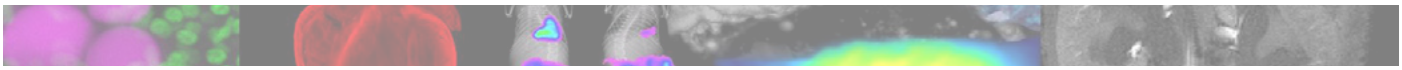


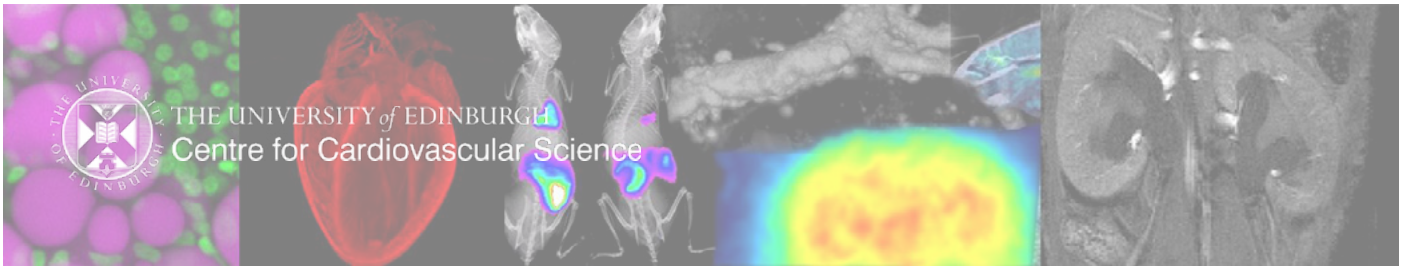
Figure 1: Our 53 sites (applicant sites in orange) and recruitment rates at the 8 applicant sites.

COVID-19 substudy

In April 2020, new recruitment to R4VaD was suspended due to the COVID-19 pandemic and all follow-up went remote so as to be able to continue to follow-up for participants already in the study. However, since we saw that study participants and patients with stroke were more generally experiencing many adverse impacts of the pandemic, including high levels of anxiety and major difficulties with social support during introduction of the UK social distancing measures, we obtained approval to continue recruitment to R4VaD at sites with capacity to do so.

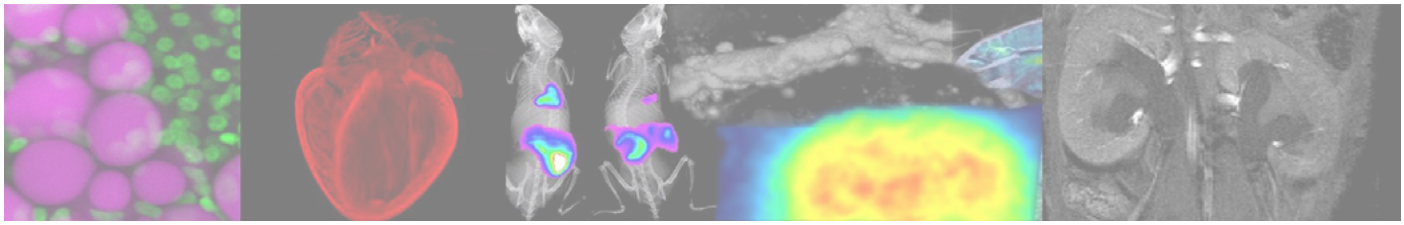
Continued Overleaf/

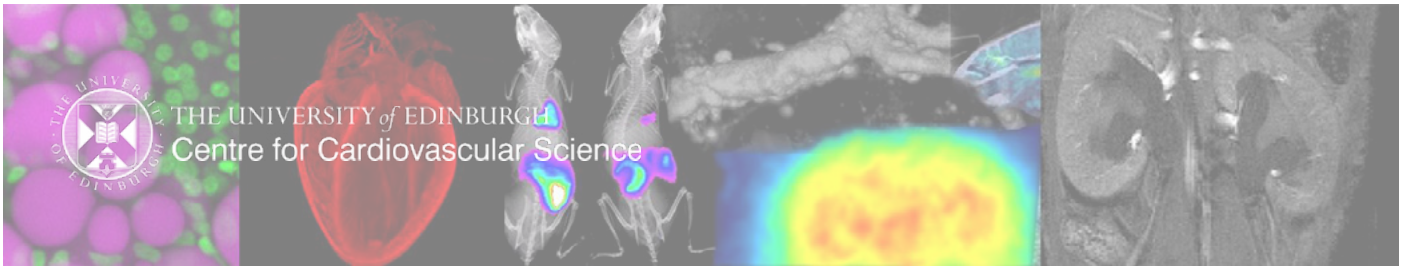




Dr Ellen Backhouse - Research Fellow in Cerebrovascular Disease & R4VaD Study Manager

The objective of the ongoing COVID-19 substudy is to determine the prevalence of COVID-19 in patients with stroke, examine the relationship between the two illnesses including laboratory features, risk factors and phenotypes and to evaluate the clinical and neuropsychological impact of COVID-19 on these patients. Furthermore, in 2021 we will implement a data linkage exercise to centralised hospital data to ascertain the accuracy of our follow-up data, including COVID-19 infection, which will supplement the data collected directly in the study. By continuing to recruit through the pandemic, using a streamlined data collection form to reduce burden on patients and researchers, R4VaD aims to compare data collected before, during and after the pandemic, using existing funded infrastructure. It will be one of the few opportunities to obtain objective data on COVID-19 and stroke, including at late stages after stroke.





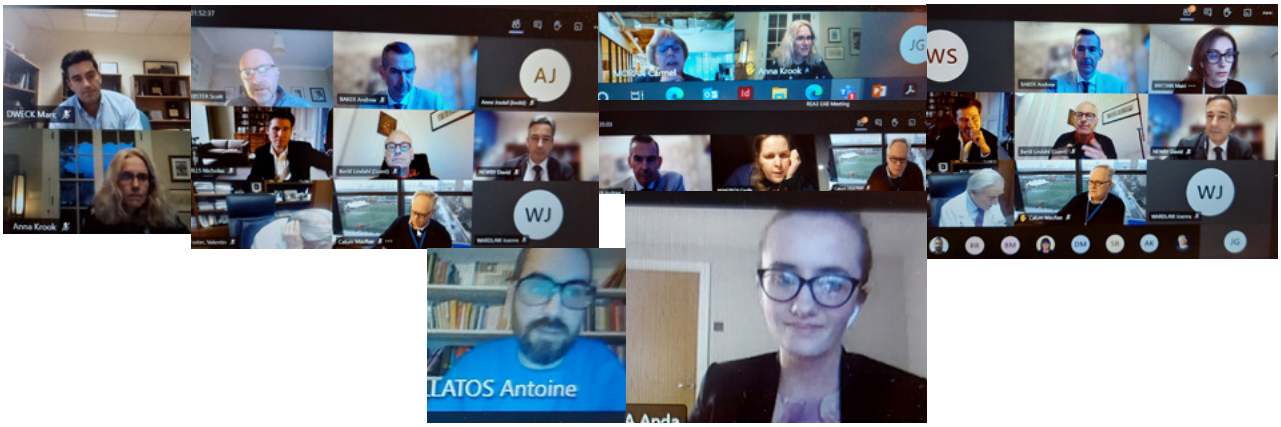
REA3 EAB MEETING - MONDAY 23 NOVEMBER 2020

We held our first EAB meeting to assess the productivity and progress of REA3. Unfortunately due to the current circumstances we were unable to have an in-person board meeting, which was our original plan. Luckily there were no issues regarding connectivity and everyone engaged effectively over the afternoon.

The EAB were particularly interested in hearing from some our pump priming awardees, who provided 5 minute presentations with an opportunity for questions and answers afterwards.

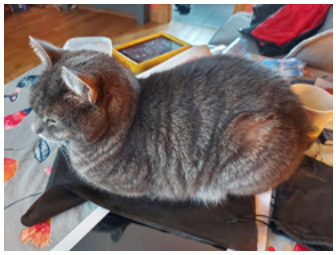
Overall we seem to be heading in the right direction, though there are some areas for improvement. The EAB will provide written feedback at the start of the new year, which we look forward to assessing.

The REA3 Executive would like to thank the EAB Board, Professor Valentine Fuster (Chair of the EAB), Professor Anne Joutel, Professor Anna Krook, Professor Bertil Lindahl and Professor Calum Macrae for giving up their time and providing external assessment of REA3

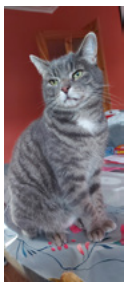


FINALLY....

Working from home has meant that Gillian Joyce has a new work colleague. They are quite lazy, expect to be fed on demand, interupt meetings by sitting on the laptop, contribute nothing and answers to none of their names, a selection of which are as follows: Furmonkey, Ratbeast, Weaselface, Ferretweasel, Fleasel, Monkeyrat, Horrorbeast, Grumpy McGrump Face and The Butcher of Ratsville. Hello to Sookie:



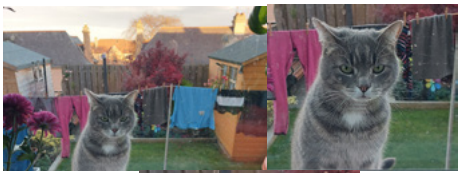
Do not move me

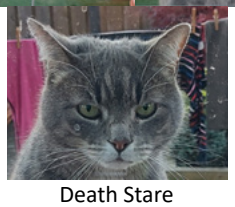


I am magnificient

Feed me

Do not disturb me





Death Stare