Promoting clinical research excellence for the health and wealth of Lothian and Scotland

January 2020
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Introduction

Welcome to the 2018-19 brochure from the Academic and Clinical Central Office for Research and Development (ACCORD).

Sitting firmly at the heart of clinical research activity in Lothian, ACCORD draws together research management teams from NHS Lothian and the University of Edinburgh. Together these staff provide a joint research office that offers central access to professional advice, expert regulatory support and clinical research infrastructure for every stage of the research pathway.

2019 proved to be an extremely busy year for us, with significant changes to national R&D approval processes, a fast moving research transparency agenda and a GCP Systems Inspection by the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA inspection was conducted in two parts, between June and October, comprising an onsite review of our Sponsor systems and separate site inspections for selected clinical trials. Congratulations go to everyone in ACCORD for our most successful inspection outcome to date, and to the Cardiac Care and GaPP2 trial teams, who prepared for and participated in the site inspections. The very positive result highlights the excellent standard of regulatory support that ACCORD delivers for clinical researchers in Edinburgh and it affirms the commitment to quality and safety that underpins our growing trial portfolio.

In March 2019, we celebrated the wealth of clinical research that is led and undertaken in Edinburgh by holding our biennial NHS Lothian R&D Conference. This is a regular event in our calendar, which brings the local clinical research community together for an informative and enjoyable day of oral presentations, posters and networking. It is a very well attended meeting that is highly valued by our research teams, we hope you enjoy the article and accompanying photographs that illustrate the day.

Our brochure also highlights some of the significant developments, achievements and publications from the past twelve months. We are delighted to showcase our key operational partners and to feature prestigious research projects led by Professor Rustam Al-Shahi Salman (RESTART) and Professor Stuart Forbes (MATCH).
In addition, we have pleasure in introducing the newly formed SE Scotland Innovation Team that supports NHS Lothian, NHS Fife and NHS Borders. The innovation team has a key role in delivering innovative solutions to health and social care challenges, we look forward to working in close collaboration with our new colleagues.

As we enter a new decade, we pause to reflect on the successes of 2019 and to consider the challenges ahead. The portfolio of trials undertaken by our research teams continues to expand and flourish, as evidenced by our healthy performance metrics. Meanwhile, the regulatory and funding environment around clinical research has evolved significantly in recent years. Against this backdrop, NHS Lothian and the University of Edinburgh aim to provide the most efficient pathway in support of world leading clinical trials delivery. To inform our ongoing development, the institutions have jointly commissioned an external review of our structures, processes and ways of working.

At the end of January 2020, an expert review panel will visit our centres to assess our clinical research support systems. We very much look forward to hearing the observations, views and recommendations of the panel, which will support our teams in planning for the future. Whatever 2020 brings, we undoubtedly have another busy and exciting year ahead, helping our researchers make optimal use of Edinburgh’s world class clinical research infrastructure. We welcome the chance to present a flavour of our activities, facilities and research opportunities within this report. This is a time of great innovation and development and ACCORD will continue to support researchers in achieving their potential to deliver clinical research excellence.

We hope you enjoy our brochure!
ACCORD Metrics

Number of Studies by Year

Study Recruitment by Year

Distribution of NHS Lothian’s NRS Funding Allocation 2019/20
## ACCORD Services

### FUNDING PROPOSALS

| ACCORD NHS Lothian R&D Finance Team UoE Research Support Team | Working closely with the UoE Research Support Office and NHS Lothian Finance team, ACCORD reviews funding applications to identify important costs e.g. regulatory fees, monitoring, drug and labelling, database, archiving, NHS resources and facilities. |

### SPONSORSHIP

| Research Governance Team | The role of “Sponsor” is defined in the UK policy framework for health and social care research and in the UK clinical trials regulations as an organisation responsible for ensuring arrangements to initiate, manage, finance and indemnify a study. ACCORD reviews all clinical research led from Edinburgh that involves people, their tissues or data and identifies if single or co-sponsorship is appropriate. A lead Sponsor Representative is assigned to review the protocol, study documents e.g. participant information sheets/consent forms and the IRAS application for ethics and R&D submissions. The Representative provides advice and document templates to help ensure successful submissions. Throughout the research study, the Representative is available for advice, and to review Amendments for submission as they arise. |
| Facilitation Team | Clinical research that is regulated under the clinical trials or device regulations or that is considered to be complex or high risk is assigned a Clinical Research Facilitator. Facilitators provide support with the protocol, study documents and IRAS application for ethics, R&D and regulatory submissions. Facilitators also help with sourcing investigational supplies and work closely with the ACCORD Monitoring team to hand over for trial set up. Regulated and more complex research undergoes an ACCORD risk assessment to identify any risks and ensure appropriate measures are in place for mitigation. The risk assessment feeds into a risk based monitoring and audit plan for the ACCORD Monitoring and QA teams. |
| Contracts Teams | Legally binding agreements are often required between organisations participating in clinical research to set down arrangements for e.g. collaboration, finance, insurance, publication and intellectual property, regulatory compliance, provision of drugs or equipment, human tissue transfer, data sharing etc. Sponsor Representatives work closely with the University and NHS Lothian Legal and Contracts teams to identify agreements that are required for clinical research. The Legal and Contracts teams fulfill drafting, review, negotiating and signing of these agreements. |
| Quality Assurance Team | The QA team provides regulatory support and resources for researchers and independent oversight of trial related activities. QA manages a library of ACCORD Standard Operating Procedures (SOPs) and policies, which are designed to provide clear written instructions to help researchers. The team also manage an audit programme to ensure ongoing compliance of facilities involved in clinical research and of specific research studies that may have been identified as high risk. |
| Monitoring Team | Monitoring of clinical trials is performed on a risk-based approach to ensure that the rights and well-being of participants are protected; reported data are accurate, complete and verifiable from source documents and the conduct of the research is in compliance with the approved protocol, amendments, SOPs, Good Clinical Practice (GCP) and regulatory requirements. Clinical Research Monitors support researchers with trial set up and help to ensure compliance throughout the life of the trial to closure. |
| Pharmacovigilance Team | ACCORD takes on Pharmacovigilance responsibilities for regulated trials, receiving reports of Serious Adverse Events (SAEs), Serious Adverse Reactions (SARs) and Suspected Unexpected Serious Adverse Reactions (SUSARs), maintaining a safety database and onward reporting all SUSARs to ethics committees and regulatory authorities. The Pharmacovigilance team prepare SAE listings, fulfil MedDRA coding for annual Data Safety Update Reports (DSURs) for all regulated trials and provide safety line listing reports to Data Monitoring Committees. Pharmacovigilance also involves a regular review of the Reference Safety Information (RSI) for regulated trials to ensure participant safety and quarterly reviews of all SAEs to perform trend analysis on clinical research. |

### R&D MANAGEMENT PERMISSIONS

| NHS Lothian Research Governance Team | For research involving the NHS to begin in Scotland, the relevant NHS organisation(s) must issue NHS R&D permission. Permissions are obtained in Scotland via a national R&D process. HRA approval is required for research involving the NHS in England. ACCORD Sponsor Representatives advise on R&D submissions to all NHS organisations that may be involved in the research study. They also help with other requirements such as Research Passports or Caldicott Guardian approvals. Although many checks for NHS Lothian R&D Permission will already have been made at the Sponsor review stage, an R&D review is still required. |

### TRAINING

ACCORD Governance, Facilitation, QA, Monitoring and Pharmacovigilance teams deliver training courses in many areas of clinical research and are happy to discuss research team requirements for training and refresher courses. The Wellcome Trust Clinical Research Facility Education Programme also delivers a variety of courses relevant to researchers in Edinburgh.
ACCORD Update Events 2019

Dr Heather Charles, Head of Research Governance (NHS Lothian)

As the Head of Research Governance for Lothian Health Board, one of my key responsibilities is monitoring changes to the national legislative and regulatory framework for research governance and ensuring, as part of the ACCORD team, that we provide information and support for researchers wishing to do research within NHS Lothian.

There has been much focus in recent years on improving compatibility for cross-border research within the UK, led by the Four Nations NHS/HSC Compatibility Programme (www.nhsresearchscotland.org.uk/services/uk-wide-working). In 2018-2019 this resulted in changes to regulatory procedures with the implementation of the UK-wide Local Information Pack, introduction of new processes and guidance around the use of the Schedule of Events Cost Attribution Tool (SoECAT), and initiation of pilot projects asking for Sponsors, R&D departments, Research Ethics Services and research teams to get involved e.g. Combined Ways of Working (CWOW) and the process for review of study amendments. These UK changes are in addition to the forthcoming implementation of new European legislation on how clinical trials and clinical investigations of medical devices are run from 2020 onwards.

As such, in late 2018, the ACCORD team agreed that it was important for us to update the research community in Lothian on these changes by hosting regulatory update events. This also provided an opportunity to deliver some other training sessions on specific areas of research governance that raise a lot of questions from local researchers and their teams.

In the first half of 2019 (February, March and April), we hosted 3 ACCORD Update Events. Two of which took place in the Queens Medical Research Institute (QMRI) at the Royal Infirmary of Edinburgh, and one in the Wellcome Trust Clinical Research Facility (WTCRF) at the Western General Hospital. We advertised these events through various means including the ACCORD website (www.accord.scot) and our e-mail distribution list, as well as via our Twitter feed EdinburghACCORD.

The half day events, which included sessions on Sponsorship versus R&D review and approval, use of data in research, a review of common Medicines and Healthcare products Regulatory Agency (MHRA) inspection findings as well as an update on regulatory changes, were well received. Over the 3 dates and 2 locations, approximately 150 staff from NHS Lothian and the University of Edinburgh attended the events. As anticipated, the sessions sparked questions from the audience and provided an opportunity to share experiences and expertise. Attendees were asked to complete and return a short questionnaire, primarily to help ACCORD to develop future events and ensure that we are communicating effectively with the local research community. We were delighted that approximately 55% of the audience completed and returned the survey to us. Based on the feedback received, we have identified a number of key areas for further training events and we are aiming to deliver the next set of ACCORD Update Events in early 2020.

Finally I would like to thank all those who contributed to these events, not only the speakers but those who took time out of their busy working days to attend, ask questions and also to complete the survey.
## ACCORD Update Events 2019

### Four Nations NHS/HSC Compatibility Programme

26 February 2019 (14:00 - 17:00) Queens Medical Research Institute Wellcome Auditorium

<table>
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<tr>
<th>TIME</th>
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| 14:00 | Welcome & ACCORD Overview | Fiona McArdle  
Deputy R&D Director |
| 14:15 | Sponsorship and R&D Approval | Raymond French  
Research Governance Manager &  
Kenny Scott  
NRS Generic Review Manager |
| 14:45 | Safe Use of Data in Clinical Research | Carol MacKenzie  
Project Manager, IG &  
Pamela Linksted  
eResearch Lead |
| 15:15 | Break | |
| 15:45 | The Changing Research Landscape | Heather Charles  
Head of Research Governance, NHSL |
| 16:15 | Preparation for an MHRA Inspection & Common Findings | Lorn MacKenzie  
ACCORD QA Manager |
| 16:45 | Close with survey | |
Research Transparency

In October 2018, the House of Commons Science & Technology Committee published a report on research integrity: clinical trials transparency, highlighting a shortfall on ‘clinical trials transparency’ through failure to publish clinical trials results.

The report was based on evidence given by the AllTrials Campaign and metrics drawn from their EU Trials Tracker, which tracks compliance of reporting into the European Union Drug Regulating Authorities Clinical Trials Database (EudraCT).

The Committee was particularly concerned that many trials are funded with public money and indicated that failing to publish clinical trials results “presents risks to human health, contributes to research wastage and means that clinical decisions are made without access to all the available evidence”.

The Rt Hon Norman Lamb MP, Chair of the Committee wrote to UK Universities asking for verification of systems to ensure adherence to transparency rules and legislation. The response from Edinburgh and NHS Lothian acknowledged we ourselves had a number of trials not uploaded to the EudraCT database and that steps would be taken to improve performance.

While the majority of our ‘unreported’ trials have journal publications, this is not recognised because the database does not allow upload of publications for trials completed after July 2013. Under EU rules, all regulated trials on the European Union Clinical Trials Register (EUCTR) should post results within 12 months of completion, which means our unreported trials are in breach of the clinical trials regulations.

The Committee report also called upon the Health Research Authority (HRA) to publish a detailed strategy for achieving full clinical trials transparency.

"The research community needs to be clearer and more distinct about what health research is taking place into things that matter to patients and the public."

MakeltPublic

Transparency and openness in health and social care research

The Committee report also called upon the Health Research Authority (HRA) to publish a detailed strategy for achieving full clinical trials transparency.
Research Transparency

Throughout 2019, the #MakeItPublic strategy was developed in partnership with a Research Transparency Strategy Group, made up of patients and professionals including Marise Bucukoglu, Head of Research Governance in the College of Medicine. A 12 week consultation on the draft strategy was launched in June 2019 and over 700 patients, research participants, researchers, funders and sponsors gave their views and described their experiences through a survey and public workshops held around the UK.

The final strategy will be published in 2020 to provide clear direction on how to make sure that patients, the public and professionals can easily access useful information about health and care research studies. The focus will be on making it easier to achieve three key areas of transparency – registering research projects, making research findings public and letting participants have access to findings from research which they have taken part in.

To improve Edinburgh’s performance, it is important for Investigators to plan adequate resource to complete EudraCT uploads, while ACCORD provides support and advice to overcome the challenges of the process.

Follow University of Edinburgh and NHS Lothian reporting at: eu.trialstracker.net

Please do your bit to improve our performance and keep transparency standards high.
Meeting NHS Priorities through Research and Innovation

On Thursday the 28th March 2019, we presented NHS Lothian’s R&D Conference ‘Meeting NHS priorities through Research and Innovation’.

Professor Tim Walsh (Director of Research, Development and Innovation) opened the conference, welcoming delegates and speakers from across Lothian. The event provided an ideal opportunity to celebrate the wealth of world class clinical research taking place in Edinburgh.

Tim Davison, Chief Executive for NHS Lothian, opened the programme with an inspiring and thought provoking presentation about the big strategic challenges facing NHS Lothian. He shared his thoughts on how Research, Development and Innovation can help to address these challenges now and for the future. Following Tim Davison’s session, we were delighted to welcome Ricky Verrall, then Head of the Chief Scientist Office (CSO), to present an overview of the role of the CSO, NHS Research Scotland (NRS) and the Health Innovation Network in supporting R&D and Innovation in health and care. Ricky set the work in a wider UK context and outlined how R&D and Innovation contribute to the Scottish Government’s national outcomes for both health improvement and sustainable economic growth.

The opening session concluded with an excellent presentation of the FOCUS Trial by Professor Gillian Mead. FOCUS is a pragmatic, multicentre, parallel group, double-blind, randomised, placebo-controlled trial that was conducted in 103 hospitals in the UK. FOCUS investigated the effects of fluoxetine on functional outcomes after acute stroke and the results were published in The Lancet in December 2018. The researchers demonstrated that fluoxetine, despite early promise, had no effect on recovery after stroke.

Following a break for refreshments and poster viewing, delegates enjoyed a fascinating trio of talks that contributed to a world class programme of research from the University of Edinburgh.

In 2018, this body of work received the prestigious award of the Queen’s Anniversary Prize for Research to Improve Women’s Health. Chaired by Professor Alex McMahon (NHS Lothian’s Executive Director for Nursing, Midwifery and Allied Health Professionals), this session comprised compelling presentations by Professor Richard Anderson, Dr Sarah Stock and Professor Hilary Critchley. Their topics ranged from fertility preservation to reducing perinatal mortality and abnormal uterine bleeding respectively.

Over lunch, delegates were able to network and view an excellent selection of posters from multidisciplinary health care researchers. These represented a wide range of clinical specialties and topics. Prizes were awarded to Natalie Homer, Tom MacGillivray, Duncan Martin and Lee Murphy for their poster: Success of technology-based cores in Edinburgh Clinical Research Facility, and to Holly Ennis and Catriona Keerie for their poster entitled Lessons learned: evaluation of a centralised system of safety blood monitoring within a multicentre randomised placebo-controlled clinical trial.

Professor Alison McCallum (Director of Public Health & Health Policy) Chaired the first afternoon session: Research & Development - Improving Patient Care. Delegates enjoyed a variety of presentations covering the following areas: use of novel technology to monitor patients with palpitations, decision-making for discharging patients to care homes, embedding PPI in research and; a trial of hypertonic saline nasal irrigation and gargling for treating the common cold.
NHS Lothian R&D Conference 2019

“Overall, the conference was a resounding success, highlighting how research led from Edinburgh is improving patient care in Lothian and around the world.”

The final session of the day showcased a selection of innovative projects from Lothian’s growing cohort of NRS Clinicians. Chaired by Andy Peters (AHP Research & Development Facilitator), the session highlighted studies of: data informatics research in paediatric critical care, use of urine cytology in bladder cancer surveillance, supporting recovery from pelvic chemo-radiation in anal cancer and; the role of dynamic FDG PET imaging as a novel biomarker for lung inflammation in COPD.

Our NRS Clinicians are all past recipients of NRS Fellowships and we are delighted to see their individual research programmes develop and grow so successfully.

Overall, the conference was a resounding success, highlighting how research led from Edinburgh is improving patient care in Lothian and around the world. Our programme highlighted a variety of scientific achievements and exciting investigations into new treatments and ways of delivering care. Speakers demonstrated the benefits of partnership working and the importance of Patient and Public Involvement in research.

Please enjoy a selection of photographs taken on the day (Colin Hattersley Photography).

We would like to acknowledge the excellent event management service provided by the WTCRF Education Team who did a superb job of organising the conference for us.
NHS Lothian R&D Conference 2019

Professor Tim Walsh
Director of R&D and Innovation

Mr Tim Davison
Chief Executive, NHS Lothian

Professor Gillian Mead
Professor of Stroke and Elderly Care Medicine, University of Edinburgh

Professor Hilary Critchley
Professor of Reproductive Medicine, University of Edinburgh

Dr Sarah Stock
Wellcome Trust Clinical Career Development Fellow & Senior Clinical Lecturer / Honorary Consultant and Subspecialist in Maternal Fetal Medicine, University of Edinburgh / NHS Lothian

Professor Richard Anderson
Elsie Inglis Professor of Clinical Reproductive Science, University of Edinburgh

Poster viewing
NHS Lothian R&D Conference 2019

Professor Tim Walsh Director of R&D and Innovation, Professor Alison McCallum Director of Public Health & Health Policy, Mr Tim Davison CEO, NHS Lothian, Mr Brian Houston Chairman, NHS Lothian, Professor Alex McMahon Executive Director, Nursing, Midwifery & Allied Health Professions, NHS Lothian

Scottish Health Innovations Limited (SHIL) Exhibition Stand

Professor Walsh Director of R&D and Innovation with Dr Sandeep Ramalingam Consultant Virologist and NRS Clinician
Lothian NMAHP Research Strategy

There have been ongoing discussions with academic partners regarding the Lothian NMAHP Research Strategy. This includes Edinburgh Napier University, Queen Margaret University, University of Edinburgh and Stirling University. A new strategic group has been established, which has been expanded to include pharmacy, clinical psychology and health care science. This will be finalised in 2020 with a planned launch at a joint conference in May 2020.

NMAHP Research Capacity Building

Capacity building within the NMAHP professions continues to progress and NHS Lothian is recognised as leading the provision of research training opportunities in Scotland. One of the ongoing challenges is opportunities for post-doctoral clinical academic appointments, which often means that NMAHPs gaining their doctorate move into full time posts in higher education. They do, however, tend to continue their research links and activity in NHS Lothian.

All researchers, including those that are aspiring to undertake doctoral studies in the future, are supported by a quarterly NMAHP Doctoral Network meeting facilitated by Dr Juliet MacArthur, Chief Nurse Research and Andy Peters, AHP Research Facilitator.

Doctoral Completions

There have been 4 doctoral completions in 2019

- Dr Katie McGoohan, Research Nurse Neurosciences (now Research Assistant King’s College, London) ‘Impact of cognitive impairment after stroke’.
- Dr Amy Ferry, Senior Research Nurse Cardiology ‘The role of high sensitivity cardiac troponin assays in the assessment and experience of patients presenting to the Emergency Department with suspected acute coronary syndrome’.
- Dr Sue Sloan, Organisational Development Consultant ‘Experiences of a Clinical Leadership Programme: A Constructivist Inquiry’
- Dr Karen Matthews, Liver Nurse Specialist (now Lecturer Queen Margaret University) ‘Advancing nursing practice in the field of Hepatology through a prospective observational research study implementing innovative screening for liver disease in a community alcohol service with a portable Fibroscan® device’

Doctoral Funding 2019

NHS Lothian continues to actively support capacity building with doctoral funding for academic fees from its Research Futures training fund. The doctoral student opportunities are open to NMAHPs working in NHS Lothian through open application guided by a series of agreed priority areas and interviews involving Professor Alex McMahon, Executive Nurse Director.
Lothian Nurses, Midwives and Allied Health Professionals (NMAHP)

Clinical Doctorate University of Stirling

This is the third year of offering jointly funded studentships with Stirling University

• Hilary Newey, Advanced Nurse Practitioner, Lothian Unscheduled Care Service who is undertaking a study examining clinical governance and benchmarking of advanced practice in out of hours services.

• Dawn Robertson, Senior Physiotherapist, REACT Team, St John’s Hospital who will be focusing her studies on multidisciplinary team working in health and social care to support people with frailty and complex needs.

• Judith Balfour, Advance Physiotherapy Practitioner, Midlothian who will be examining the role of advanced practice physiotherapists within general practice.

PhD Studentship Edinburgh Napier University

Hazel McPhillips, Advanced Nurse Practitioner, Hospital at Night, Western General Hospital was awarded a jointly funded studentship that will focus on factors influencing the success of nurses moving in to advanced practice roles.

RCN International Research Conference

There was good representation of early career nurse researchers from NHS Lothian at the annual Royal College of Nursing International Research Conference in Sheffield in September.

• Nicola Rea won the poster presentation award for her work on establishing a patient and public involvement group for critical care research.

• Gearoid Brennan presented his doctoral study on organisational and structural factors impacting on mental health nurses’ ability to provide physical health care. Gearoid was also awarded a Florence Nightingale Foundation Travel Scholarship to Australia to develop his research networks.

• Melanie Phillips presented a poster on the experience of working 24 hours on-call for the transplant team.

• Juliet MacArthur presented at two symposia; a Scotland-wide study on the experience of transition from paediatric to adult health services for young people with a complex learning disability and clinical academic career opportunities for clinical research nurses.

• Gemma Logan presented the findings of a qualitative research study on the stakeholder perspectives of the experience of discharge to care home from the acute hospital setting. She had previously presented this work at the NHS Lothian Research and Development Conference in March.
Mr Gabriel Oniscu was appointed as a consultant transplant surgeon at the Royal Infirmary of Edinburgh 10 years ago. He is an Honorary Reader with the University of Edinburgh and has been appointed as an NHS Research Scotland Fellow in 2012 and subsequently as an NRS clinician in 2016.

He is the Director of the Edinburgh Transplant Centre and the Chair of the Research, Innovation and Novel Technologies Advisory Group at NHS Blood and Transplant. He is also the Secretary of the European Society for Organ Transplantation. His research interests focus on organ perfusion technologies, transplant outcomes and organ assessment.

60 years ago, the first transplant in the UK was undertaken in Edinburgh. 60 years of clinical innovation and research excellence have made the Edinburgh Transplant Centre one of the leading transplant institutions in Europe. Hosting five national services (liver, pancreas, islets, kidney and organ procurement), the Centre provides the ideal clinical environment to foster innovative ideas. The close collaborations with the Centre for Inflammation Research and the Scottish Centre for Regenerative Medicine allow us to undertake world class research.

In many ways, transplantation is the victim of its own success. An increasing demand for organs combined with changes in the demographics of the donor population meant that innovative approaches were needed. In particular, ways to extend the organ preservation times combined with an ability to evaluate function prior to transplantation had to be developed.

Six years ago, supported by the NRS fellowship and together with a team of enthusiastic and like-minded colleagues, I established a new approach to organ recovery from donors after circulatory death. Instead of the standard approach of rapid recovery with cold perfusion, organs were perfused in-situ with normothermic oxygenated blood for a period of time which allowed an in-depth assessment of organ function.

Using this approach, we increased liver graft utilization from 27% to 63% whilst seeing a dramatic reduction in ischemic biliary complications from 27% to zero. This translated into better graft and patient survival, lower costs for the NHS and better resource utilization.

The use of this approach - normothermic regional perfusion (NRP), has been a real game changer in clinical practice and has led one of the most significant improvements in the outcome of the transplanted organs in recent years.

Using this approach, we increased liver graft utilization from 27% to 63% whilst seeing a dramatic reduction in ischemic biliary complications from 27% to zero. This translated in better graft and patient survival, lower costs for the NHS and better resource utilization. Using NRP we doubled the number of organs recovered from each DCD donor, and the utilization of individual organs increased.
Six years ago, very few thought that this was anything other than an experimental procedure. Now, we are ready to change clinical practice on a national scale...

between two and four fold. We also achieved a better kidney graft function which translated into four additional years of life for each patient. In fact, if NRP would have been used nationally for every single DCD donor, we could have halved the national liver transplant waiting list in one year.

Whilst pilot clinical data indicated a huge potential benefit, translating this into routine clinical practice needed additional evidence as well as discussions with regulatory bodies, commissioners, clinicians, ethicists and patient groups to define the elements needed to establish a sustainable clinical service.

Funded by NHS Blood and Transplant (£500,000) and supported by ACCORD, Edinburgh has been the lead Centre for the development of the NRP programme in the UK. From a practical point of view we undertook a major up-scale of the team and developed a robust and replicable training programme. This training programme has now been used to train NRP teams in Oxford, Royal Free, Birmingham but also, Leiden, Rotterdam, Gothenburg, Stockholm, Oslo, Prague and Denver.

Key to the success of the programme has been the strong support from the patient groups and the national transplant organization who lobbied for the wider introduction of the NRP service in the UK. A health economic analysis backed the clinical results and indicated that the use of NRP leads to a saving of £17,000 per every additional surviving patient, based on the liver transplant benefit alone. Furthermore, the cost per QALY was calculated at £16,000 per year, in the context of a £60,000 Willingness to Pay (WTP) which is the indicative cost that the health service is prepared to pay for any new intervention.

Supported by these figures, a UK wide business case was developed and approved by most health departments and will hopefully be implemented in 2020.

Six years ago, very few thought that this is anything other than an experimental procedure. Now, we are ready to change clinical practice on a national scale, a feat that illustrates the innovative drive of the transplant teams and the close relationship with our patients who have supported us all along.

Whilst the clinical programme is ready for implementation, we are turning back to the science, in order to understand the damage the organs suffer during the dying process, how this particular technology (and others alike) may change this and how we can modulate the damage by adding targeted therapies to the organs whilst being perfused.

It is without a doubt one of the most exciting teams to work in transplantation and I am really privileged to work with a superb team who put patients above anything else.
NRS Clinician: A simple intervention against common viral infections

Dr. Sandeep Ramalingam is a consultant virologist based at the Royal Infirmary of Edinburgh. He is interested in identifying innate immune mechanisms with which cells fight viral infections. The aim is to identify ways of augmenting these antiviral mechanisms to effectively treat viral infections without the need for antiviral drugs. He was an NRS fellow between 2015-2018. He has been an NRS clinician since.

A simple intervention against common viral infections: We are regularly infected by viruses. Vaccines and antiviral drugs are generally targeted against the more serious viral infections. However, we do not have an effective intervention against the vast majority of viral infections. For e.g. in our laboratory, we test routinely for 14 different respiratory viruses, all of which can cause the common cold. The only virus we have a vaccine for and would routinely treat with an antiviral is influenza. For the rest, we generally wait for the infection to run its course. This results in increased transmission within families and at work; days away from school/work, and thus a large economic burden both to the individual and the country. Hence we need an intervention that works against multiple viruses. Viruses can broadly be divided into enveloped/non-enveloped viruses based on whether they have an envelope covering it and DNA/RNA viruses based on their genetic material. An effective intervention should hence work against enveloped/non-enveloped, DNA/RNA viruses.

Ability of epithelial cells to fight viral infections: Parts of our body in contact with the external environment are covered by epithelial cells. Most viruses hence come in contact with epithelial cells and infect these cells first. Since viruses and cells have co-evolved over millions of years, it is likely that cells would have found a way of fighting common viral infections. We recently published evidence that epithelial cells use chloride ions to produce hypochlorous acid (HOCl) with which they fight viral infections. This mechanism has been known to occur within cells in the blood (macrophages, neutrophils). We have for the first time described this mechanism in other cell types. HOCl is the active ingredient in bleach (which we know kills viruses). We hence investigated if epithelial cells can fight viral infections if we supply the cells with salt (sodium chloride) as a source of chloride ions. We tested representative DNA/RNA, enveloped and non-enveloped viruses in cell culture (herpes simplex virus-1, respiratory syncytial virus, influenza A virus, coxackievirus B3, coronavirus 229E). All the viruses we tested were inhibited in the presence of salt while the cells were not significantly affected. You can see the effect of increasing salt concentration on herpes simplex virus-1 (HSV-1) and the viability of cells in Figure 1.

Figure 1: Dose dependent inhibition of HSV-1 by sodium chloride (a) and viability of HeLa cells in the presence of sodium chloride (b).

The manuscript can be found here https://rdcu.be/bYJWT. This has opened the possibility of using salt as an antiviral agent.
Does supplying salt locally reduce the duration of the common cold?

**Adults:** We then carried out a pilot randomised controlled study of hypertonic saline nasal irrigation and gargling (HSNIG) versus usual care in adults with the common cold. The study was called the Edinburgh and Lothians Viral Intervention Study (ELVIS study) (www.elvisstudy.com). HSNIG was the way we applied salt to the epithelial cells of the nose and throat (Figure 2). The study videos are available here www.elvisstudy.com/nasal-irrigation-and-gargling.html. Participants had to start the study within 48 hours of getting a cold. Though a small study, those who did HSNIG (intervention arm) got better 2 days earlier than those who did not (control arm) (Figure 3). Fewer individuals in the intervention arm needed over-the-counter medication for the cold, or reported household contacts developing colds after them (i.e. transmission). These differences between arms were statistically significant. The manuscript can be found here https://rdcu.be/bYJWz.

**Children:** Since children have numerous colds, and there is no effective intervention, we are now conducting a large randomised controlled study of salt water nose drops versus usual care in children under the age of 7. The study is called the ELVIS Kids study and there is more information at www.elviskids.co.uk. Children can join the study at any time (i.e. they do not need to have a cold to join the study) and start the study when they have a cold. The intervention arm is taught how to safely make salt water nose drops and to apply it when the child gets a cold and the control arm deal with the cold as they normally do. Both arms collect nose swabs and post them back to the lab to measure viral shedding. We expect to complete the study in 2021.
Edinburgh Clinical Research Facility Education Core

The Education Core delivers a range of short courses, workshops and events for the local, national and international clinical research community.

Their aim is to provide easily accessible education to all involved in clinical research, promoting excellence and best practice. Delivered by academics, experienced clinicians and industry experts, their courses cover subjects from initial planning of clinical research through to the dissemination of results.

2019 saw the launch of the new Edinburgh Clinician Trialist Rounds (ECTR) network. Working alongside ECTU, ACCORD and motivated Chief Investigators, this network has been formed to support current and aspiring clinician RCT Chief Investigators across Lothian. The Education Core co-leads the co-ordination of the network and manages their monthly seminar programme. By recording the sessions, a resource bank is being developed to provide longevity of the series, with the hope to continue to inspire and support CIs in the future. Previous seminars can be accessed here: tinyurl.com/ECTRmedia

The Education Team have provided the event management for a number of large educational networking events and conferences in Scotland including: The Scottish Metabolomics Network Symposium, The Alzheimer’s Disease Summer School, Edinburgh Clinical Trials Management Course, The Scottish Research Nurse and Co-ordinator Network Conference and the NHS Lothian R&D Conference 2019. These events have not only attracted attendees from across the globe but have also provided opportunities to showcase Edinburgh’s significant contribution to clinical research.

The Education Core continue to be members of national education networks including the NRS Training Forum, UKCRF Education Work stream and the R&D Forum Training Working Group, to remain abreast of educational requirements and advances nationally. Collaboration with these groups and local key partners allows the programme to be adapted according to local need and, where relevant, in response to changes in legislation.

For more information on our courses, event management and other services please visit: www.wtcrf.ed.ac.uk
The Scale-Up BP team led by Brian McKinstry, with Elizabeth Payne (Telehealth Lead for NHS Lothian) and Mary Paterson (Project Manager) won the Clinical Improvement Award: Public Health and Prevention at the General Practice Awards in London on 29th November 2019.

The award was for the NHS Lothian project which integrates telemonitored BP readings texted from patients with the routine Docman reports sent directly to GP practices and has led to a high rate of take-up of telehealth in Lothian (78 practices and 3600 patients) and subsequent reductions in blood pressure and clinician-patient face-to-face time. The project was based on the Telescot programme of research led by Brian McKinstry [www.ed.ac.uk/usher/telescot](http://www.ed.ac.uk/usher/telescot)

Brian said “We are delighted that the hard work of everyone involved has been recognised by this award. It has been a fantastic collaboration of Universities, NHS and Scottish Government. Scale-Up BP has the potential to transform long term care management.”

The team acknowledge the funding support from the TEC programme and BHF.

“

We are delighted that the hard work of everyone involved has been recognised by this award. It has been a fantastic collaboration of Universities, NHS and Scottish Government. Scale-Up BP has the potential to transform long term care management.
The REstart or STop Antithrombotics Randomised Trial (RESTART)

Why did we do RESTART?
More than one-third of people who’ve survived brain haemorrhage stop taking oral anti-blood-clotting drugs, like aspirin. Normally taken to stop blood vessels getting blocked, so-called antiplatelet drugs increase the risk of bleeding in general. However, the randomised trials of antiplatelet therapy for secondary prevention of occlusive vascular disease showed they caused only a non-significant increase in the risk of brain haemorrhage. But in everyday clinical practice, survivors of brain haemorrhage often permanently stop these drugs because they’re widely believed to increase the risk of another brain haemorrhage. We wanted to see if this was true.

What was RESTART?
Led by Professor Rustam Al-Shahi Salman, RESTART was a randomised trial involving 537 survivors of brain haemorrhage, who were recruited in stroke services at 122 hospitals in the UK (see map). The trial was funded by the British Heart Foundation and sponsored by the Academic and Clinical Central Office for Research and Development (ACCORD). The trial would not have been possible without the trial management group based in the Centre for Clinical Brain Sciences, the Edinburgh Clinical Trials Unit and the Systematic Management, Archiving and Reviewing of Trial Images Service (SMARTIS) at the University of Edinburgh, the NIHR clinical research network, the National Health Service Research Scotland Scottish Stroke Research Network, clinicians, patients, and their carers.

What did RESTART find?
Those taking part were mostly men over the age of 70. They mostly had diseases that block blood flow due to clotting, but had then stopped taking antiplatelet drugs after their brain haemorrhage.

RESTART randomly split these people into two groups: half were encouraged to start antiplatelet drugs, and half were encouraged to stay off them. Over the course of 5 years, the trial management group kept track of those who had recurrent bleeding and any major event to do with blocked blood flow, including heart attack and stroke. We achieved a satisfying >99% completeness of follow-up.
The REstart or STop Antithrombotics Randomised Trial (RESTART)

Overall, fewer people who started antiplatelet drugs had another brain haemorrhage compared to those who kept off these drugs (see figure). The number whose blood vessels became seriously blocked was about the same in both groups. It looks like antiplatelet drugs for people with brain haemorrhage are safe, and any possible risk is small enough not to outweigh the established benefits of these drugs for stopping more heart attacks and strokes.

You can get more information including links to the papers in The Lancet and The Lancet Neurology, as well as a 2-3 minute video summary, at www.RESTARTtrial.org.

What’s next?

Following the publication of the main results, we are following the participants in RESTART to monitor outcomes over another two years, and monitoring their use of antiplatelet therapy to see if practice changes. In our online survey at www.RESTARTtrial.org, 83% of the 114 doctors who had responded by 14 November 2019 indicated that the result would change their prescribing of antiplatelet drugs for survivors of intracerebral haemorrhage.

However, several uncertainties remain. The generalisability of RESTART’s findings in other populations is unknown. The unexpected apparent reduction of the risk of recurrent brain haemorrhage by antiplatelet therapy in RESTART – which suggests that thrombosis or inflammation may underlie recurrent brain haemorrhage – approached the conventional level of statistical significance, and requires further investigation. If confirmed, this could radically change the understanding of the cause of recurrent brain haemorrhage.

In our online survey at www.RESTARTtrial.org, 83% of the 114 doctors who had responded by 14 November 2019 indicated that the result would change their prescribing of antiplatelet drugs for survivors of intracerebral haemorrhage.
Professor Stuart Forbes and a team of researchers, based at the MRC Centre for Regenerative Medicine, are currently developing a new macrophage cell therapy for liver cirrhosis in collaboration with researchers from the Scottish National Blood Transfusion Service (SNBTS).

Background
Liver disease is the third leading cause of premature death in the UK, with deaths increasing by 400% since 1970. Liver cirrhosis is the end stage of chronic liver disease, a very common cause of death in Scotland.

Liver cirrhosis can be due to many causes, including alcohol, obesity, hepatitis viruses and auto immune disease. Transplantation is currently the only effective treatment for end-stage liver cirrhosis. However, this is severely limited by organ availability and so there is a desperate need for new treatments for people with established cirrhosis.

Macrophage cell therapy
Previous research, undertaken by Professor Forbes and his research team, has shown that macrophages (large white blood cells which have the ability to “eat” bacteria) can help to reduce scarring and stimulate regeneration of the liver. This research was pre-clinical, with tests performed on mice in the laboratory.

The new treatment being developed involves taking cells from the blood of patients and turning them into macrophages in the lab using chemical signals. This is done in partnership with SNBTS, who produce these cells to Good Manufacturing Practice (GMP) in the Cell Therapy Facility at the Centre for Regenerative Medicine. The new cells are then re-injected into the patient in the hope of rebuilding the damaged organ from within.

The treatment involves the patient being connected to a cell separation or Apheresis machine. The Apheresis machine separates the monocytes (macrophage precursors) from the rest of the blood. This takes two or three hours. Those monocytes are then taken to the GMP facility where the Scottish National Blood Transfusion Service differentiate them into regenerative macrophages.

One week later the patient attends the Royal Infirmary of Edinburgh Clinical Research Facility and the modified cells infused into their blood via a vein in their arm. The macrophages home to the liver, where it is hoped that they will help to repair the damage.

Macrophages (large white blood cells which have the ability to “eat” bacteria) can help to reduce scarring and stimulate regeneration of the liver.
Macrophage Cell Therapy for Liver Cirrhosis

Clinical trials

The MRC Centre for Regenerative Medicine is now part of the newly established Institute for Regeneration and Repair at the University of Edinburgh, which aims to bring more discoveries in basic stem cell science and tissue regeneration and repair to the clinic.

A phase one clinical trial has now been completed, with the new treatment tested on patients for the first time. This was developed with support from ACCORD, the Phase 1 Research Committee at the Royal Infirmary Edinburgh Clinical Research Facility and the Edinburgh Clinical Trials team. The work was funded by a Medical Research Council UK grant.

Following an initial screening process, nine participants were enrolled in the trial and received a single infusion of macrophages. This was overseen by clinicians based at the Edinburgh Royal Infirmary, located in Edinburgh BioQuarter. Participants then completed a one year of follow-up.

This was a safety trial, and so it is not possible to draw any conclusions regarding the effectiveness of the new treatment, however results published in Nature Medicine in October 2019 have confirmed the safety and feasibility of a macrophage cell therapy for liver disease (Nature Medicine volume 25, pages 1560–1565(2019).

Professor Forbes and his team are now conducting a phase two clinical trial, to assess how well the new treatment works. During this phase, patients are randomised to either receive the macrophages or to receive the best standard care available. The team will measure whether the treatment helps to reduce scarring and improves liver function. Currently patients with established cirrhosis are signed up to the trial via clinicians within NHS Lothian, however soon this trial will be open to patients in Dundee and Glasgow.

The trials are carried out at Edinburgh BioQuarter, where there has been integration between basic researchers and clinicians. The BioQuarter has a cell separation unit and the Clinical Research Facility a few metres from the liver transplant unit and the liver wards. This integration has made it ideal to do this research at Edinburgh BioQuarter.
Selected Developments and Partners

Patient and Public Involvement in Research

The Patient and Public Involvement (PPI) Advisor works with a Patient Advisory Group to advise and support researchers and the public to ensure patient and public involvement is helpful and meaningful for everyone.

NHS Lothian is in a unique position in Scotland in having this service and Carol Porteous the new Patient and Public Involvement Advisor has been in post now for a year – which has focused on capacity building and growing PPI panels across NHS Lothian.

Our day-to-day work in supporting the research community includes advising on study methods, helping to write lay summaries and patient information sheets, reviewing grant applications and IRAS forms, training researchers and students for patient and public involvement. An example of this is Carol and the Patient Advisory Group in the CRF recently advising researchers at the Institute of Genetics & Molecular Medicine, who were preparing the now successful £4.9 million grant on the next phase of Generation Scotland co-hort. This study is a resource of human biological samples and data which are available for medical research, aiming to create more effective treatments based on gene knowledge for the medical, social and economic benefit of Scotland and its people.

Recent highlights from the Patient and Public Involvement Advisory Service work for 2019 include:

- Capacity Building to support researchers to set up their own Patient and Public Involvement groups.

  New training courses have been created to support capacity building with researchers and teams across Edinburgh and the Lothians (and beyond!). These include:
  - Creating and Running a PPI Group
  - PPI in Funding Applications and
  - PPI in Clinical Trials
  - PPI in Fellowship Applications and;
  - Bespoke training courses

  These complement the existing PPI Courses; ‘A Practical Guide to Patient and Public Involvement’ and ‘Writing in Plain English’. Additionally, 2019 saw the running of the first PPI Summer School, with delegates from all over the UK and from as far away as China attending. This year so far, we have trained over 140 people on our PPI training courses.

- Clinical Research Facility Patient Advisory Group

  The Clinical Research Facility Patient Advisory Group has been running for a number of years but due to increasing demand for support including input into the design and delivery of studies, the CRF Patient Advisory Group has recruited 20 new members this year. It is hoped that the large number of new members will help us continue to support and input to research studies and supporting successful grant applications for researchers in NHS Lothian.

The PPI Advisor’s focus is on capacity building and growing PPI panels across NHS Lothian.
Patient and Public Involvement in Research

• PPI Champions

In Spring 2018 we appointed eight people across NHS Lothian and Edinburgh Clinical Research Facility (ECRF) as PPI Champions. All PPI Champions roles have been completed and we have 5 new self-sustaining PPI groups up and running

- A Children and Family group supporting clinical research in the Children’s CRF
- A PPI in Research Group in the Centre for Dementia Prevention (CDP)
- A Colorectal PPI group which is currently preparing funding applications and ethics documentation for quality of life work
- A Cardiology Group in the Centre for Cardiovascular Sciences which has also been heavily involved in shaping research
- The WTCRF PPI Group has completed new patient information resources which will soon be available and these will be rolled out as information resources across all ECRF sites to improve participant experiences

• Conference and Invited speaker Presentations

Carol and members of the PAG have been invited speakers at a variety of conferences and workshops and courses, and advised on this area to the Chief Scientist’s Office Public Engagement work; and created and delivered a very popular workshop at the UK Clinical Research Facility (UKCRF) Conference in Nottingham, placing Scotland as visible leaders in PPI nationally.

• Visibility of Research

In 2019 we ran a successful exhibition on International Clinical Trials Day 2019 at the Royal Infirmary Edinburgh and have now been awarded a grant from the Institute of Academic Development to run a series of events as part of International Clinical Trials Day 2020, which will help us engage local communities in research activities.
Edinburgh Imaging Facilities

The University of Edinburgh supports world class medical imaging activity, via our Edinburgh Imaging Facilities, located at Edinburgh BioQuarter.

These facilities give clinicians and scientists access to our cutting-edge imaging modalities, key technical and specialist imaging staff, a comprehensive portfolio of supporting imaging resources and the potential to connect with academics who are experts within their chosen speciality.

Edinburgh Imaging Facility QMRI
Based in the University of Edinburgh’s Queen’s Medical Research Institute (QMRI) on the Edinburgh Bioquarter site, this state-of-the-art and world leading imaging facility houses our:

- Siemens Biograph mMR PET-MR scanner
- Siemens Skyrafit 3T MR scanner
- Siemens Biograph mCT PET-CT scanner
- GE Discovery PET-CT scanner
- PETtrace Cyclotron GE Healthcare
- Radiochemistry suite, MHRA licensed for Good Manufacturing Practice (GMP) activities plus support for R&D of novel radiotracers and labelled compounds
- Retinal Imaging facilities, including a standard fundus camera, a hand-held fundus camera and an ultra-widefield scanning laser ophthalmoscopy
- Image Analysis Laboratory
- Data Management infrastructure and software team

Edinburgh Imaging Facility RIE
Embedded in the Royal Infirmary of Edinburgh (RIE) hospital, based within Edinburgh’s Bioquarter site, this custom-built imaging facility houses our:

- Siemens Magnetom Prisma 3T MR scanner
- Retinal imaging facility, including a Heidelberg Spectralisc retinal camera
- Trials Image Management service (SMARTIS)

The Edinburgh Imaging Network
The Edinburgh Imaging Network is a virtual hub which promotes collaboration between clinicians, researchers and scientists working in departments across the University of Edinburgh, Heriot Watt University and NHS Lothian and local/locally based international commercial clinical imaging organisations by breaking down the barriers between disciplines and encouraging the sharing of data, knowledge, skills and facilities in order to advance healthcare through excellence in imaging science.

Through this collaborative work, all involved staff successfully draw on each other’s expertise, resulting in true multi-disciplinary teams of clinical and non-clinical researchers, physicists, image analysts, data managers and scientists working together for one common goal; improving patient health.

For further information, please visit www.ed.ac.uk/edinburgh-imaging or email Duncan.Martin@ed.ac.uk
Edinburgh Clinical Research Facility

Edinburgh Clinical Research Facility (CRF) operates as a partnership between NHS Lothian and the University of Edinburgh to provide state-of-the-art clinical facilities, training and support for clinical researchers.

Edinburgh was awarded Wellcome Trust Millennial funding in 1997 to establish the first Clinical Research Facility in Scotland and one of the first five Wellcome Trust CRFs funded in the UK. That commenced with three members of staff working in one section of a clinical ward and has now grown to over 150 clinical, scientific and support staff employed at four separate sites in Edinburgh.

In this period Edinburgh CRF has firmly established itself as a go-to place for innovation and best practice. Contributing to the clinical research landscape in the UK, influencing the development and acting as a blueprint for the CRFs that have followed and sharing the experience, study documentation and educational outputs, its influence and impact reaches well beyond the boundaries of NHS Lothian and the University of Edinburgh.

Clinical Facilities:

Edinburgh CRF’s clinical facilities provide researchers access to experienced research nurses and clinical support teams, dedicated clinical research space and equipment for the safe conduct of clinical studies. Putting patient safety and quality at the heart of activity, the CRF provides unparalleled support for the conduct of experimental medicine research in Lothian.

Our four clinical facilities are located across three hospital sites, Wellcome Trust CRF (WTCRF) at the Western General Hospital, Royal Infirmary of Edinburgh Clinical Research Facility (RIECRF), Centre for Dementia Prevention (CDPCRF) at Edinburgh Bio-quarter and the Children’s Clinical Research Facility (CCRF), at Royal Hospital for Sick Children.

Edinburgh CRF is unique across the 50+ CRFs that exist in the UK in having a Community Outreach team. Three highly experienced Community Research Nurses, lead on delivering Outreach visits in participants homes, ensuring that local investigators can run studies where home visits have been planned to reduce the burden on patients attending hospital sites. They have successfully supported their colleagues in the Children’s CRF to recruit and follow up over 200 babies in a large study into RSV in Children (RESCU study) with CRF.
Edinburgh Clinical Research Facility

Associate Director Prof Cunningham as Chief Investigator. Additionally they have supported new investigators in the Lauriston Building deliver trials in dermatology and ENT, where ACCORD have funded the redevelopment of an old lab room to a clinical research room helping increase research capacity in a stretched clinical environment.

**Early phase trials**

In 2011 Edinburgh CRF’s adult sites at RIE and WTCRF were the first non-commercial CRFs accredited under the Medicines & Healthcare products Regulatory Agency (MHRA) Phase I Accreditation Scheme. In July 2015 we were delighted to be the first paediatric facility awarded accreditation status in the UK. We have been inspected regularly for reaccreditation at all three facilities, most recently in May 2018 -and demonstrated our compliance with Good Clinical Practice and the Phase I accreditation standards consistently.

Strategically placed and embedded within the acute hospital settings, being accredited under the MHRA Scheme means our adult and paediatric facilities are centres of excellence for the conduct of Phase I and First in Human research providing assurances that these early phase trials are as safe as possible for participants. Integral to ensuring the ongoing consistency in our quality and patient safety standards has been the appointment in early 2015 of a Lead Nurse for Phase I and Education and a robust Quality Assurance programme.

Oversight of trial design, planned conduct and clinical safety is managed by our Phase I Study Review Committee (PISRC). This committee includes experts in clinical pharmacology, toxicology, clinical research, pharmacy, clinical research management and quality assurance. This unique committee set up, designed in Edinburgh and adopted by the MHRA now facilitates local researchers to deliver challenging but essential early phase trials.

**CRF Cores:**

Edinburgh CRF’s Scientific Cores, led by expert scientists and academics provide specialist research support and expertise in Genetics, Mass Spectrometry, Epidemiology and Statistics and Imaging & Image Analysis.

The Epidemiology and Statistics Core aims to improve the methodological quality of clinical research through the provision of expert statistical input. The Core can provide valuable input to studies at all stages, from the initial design through to the final analysis and dissemination. By encouraging investigators to approach the Core as early as possible, we support the development of the highest quality study designs ready for grant funding bodies, regulators and ethics committees.

We are involved in a diverse range of projects drawn from the spectrum of clinical specialties and our team have a wealth of experience in the methodology of experimental medicine research with key staff involved in national collaborations.

The Genetics Core specialises in providing a diversity of workflows, with the ability to take a sample from collection through processing, storage and on to analysis, all to the principles of Good Clinical Practice (GCP).

This year we expanded our sample processing to allow extraction of cell-free DNA. This can be an important biomarker in disease, such as in the analysis of circulating DNA derived from tumours in patients with cancer. To support this work we purchased a Qiagen QiaCube to help automate the cell-free DNA extractions. We also purchased a digital PCR platform (Stilla Naica) to support the analysis and detection of somatic mutations present in circulating tumour-derived DNA. By combining these two methods we are helping investigate the genetic basis of an individual’s cancer, guiding therapeutic decisions by giving information on chemosensitivity and giving insights into tumour pathogenesis and evolution.
Another exciting area of development has been our work on single-cell sequencing. We have collaborated with the IGMM FACS team to provide a comprehensive workflow for single-cell gene expression and ATAC sequencing utilising the 10x Genomics Chromium system. By investigating biology at the level of the single-cell we hope to be able to better understand human disease.

Our reason for existing is to provide our researchers with the best genomics support we can for their clinical studies. We were delighted when two of our early career researchers, Drs Charlie Lees and Joe Rainger secured prestigious UKRI Future Leaders Fellowships and we look forward to continuing to support their programme of work.

In 2019 seven members of the Genetics team completed professional registration with the Science Council. This scheme provides independent recognition of the high level of knowledge and is testament to the high level of experience of the Genetics staff and commitment to professional development. Registration was supported by the University of Edinburgh’s Technician Commitment, a national initiative to support technical careers.

The Mass Spectrometry Core is a bioanalytical core with expertise in clinical sample analysis using state of the art separation and mass spectrometry instrumentation. We have many years of experience with small molecule biomarker quantitation, such as steroids and drugs. We also quantify other molecules along metabolic pathways, applying European Medicines Agency (EMA) bioanalytical guidelines to our analytical method development.

We offer a complete service from sample receipt, storage and processing to instrument analysis and reporting tabulated data. Our team advise, train and support investigators from PhD students to post-doctoral researchers, to become expert users of the analytical instruments in the Mass Spectrometry Core.

Edinburgh CRF Imaging and Image Analysis Core are part of Edinburgh Imaging, where members come from a broad range of scientific specialisms, who strongly believe that breaking down barriers between disciplines and encouraging cross-collaboration between academic and clinical work will benefit the patients. Our expert team in Image Analysis advise, guide and equip researchers with the skills necessary to perform image analysis on their own data in an appropriate and informed manner. They are also available to undertake analysis of image data acting as a central analysis facility for clinical trials or to develop state-of-the-art methodologies for new studies.

This type of environment that hubs specialist knowledge of medical physics, computer science and artificial intelligence embedded within clinically focused research infrastructure enables the Image Analysis Core to deliver innovative software solutions.

With a grant award from the Alzheimer’s Drug Development Foundation, the Core is leading on a collaboration with Duke University to quantify candidate biomarkers for the early stages of Alzheimer’s disease.
in standard ophthalmic images of the retina. In collaboration with the Centre for Cardiovascular Science in Edinburgh and with an award from the MRC, the Core is employing artificial intelligence to analyse images the data in the UK Biobank and assess bone marrow fat associations with common conditions such as diabetes and heart disease. The Core also supported the Proteus Group in the Centre of Inflammation Research in Edinburgh providing bespoke image analysis software as they translated their novel molecular imaging technology for identifying bacteria in the lungs from the laboratory to the clinic.

The CRF IT Core also provides invaluable support to the operational function of CRFs through the ongoing development of the CRFManager® system. Designed by Edinburgh CRF’s IT Team, CRFManager® supports over 50 CRFs across the UK and Ireland to manage their day to day operations. It is also proving fundamental to sites aiming to streamline their activity and key for many CRFs looking to become paperless. In addition this year the IT team have been developing Locus®, our latest web application designed to facilitate clinical sample management as well as supporting the ACCORD pharmacovigilance database.

In addition to our Scientific Cores we have a robust and highly successful Education Core Programme delivering research training for new and experienced researchers. This includes Scotland’s national education programme – Clinical Research Training for Scotland (CRTS). The content and delivery of these courses remains at the forefront of research training needs ensuring the programme delivers relevance and value in its courses.

For further information on any of the services offered by the CRF please contact:
Steven McSwiggan, CRF Deputy Director. Tel: 0131 537 3358.
Steve.McSwiggan@nhslothian.scot.nhs.uk
Health Innovation South East Scotland

Aligned to ACCORD and funded through the Chief Scientist's Office, Health Innovation South East Scotland (HISES) forms part of a national network created to deliver the Scottish Government's vision to utilise the innovation process to deliver a healthier and wealthier nation for the future.

Formed through a collaboration of three NHS Boards – Borders, Fife and Lothian, with the latter taking on the role of lead host Board, HISES has a pivotal role in delivering innovative solutions to the health and social challenges, both regionally and nationally.

At the core of our approach to developing innovative solutions is doing this in collaboration with our staff, academia, industry partners and the third sector. In this way we seek to collectively identify the problems faced by patients, staff and citizens in receiving/delivering high quality, effective and efficient health and care services – whilst also maximizing opportunities for individuals to better self-manage existing conditions as well as preventing their occurrence.

Our mission is to support and enable the future delivery of health and care services that when compared to current provision, are more effective, more efficient, of a higher quality (including more equitable access) and affordable within available resources.

From having developed, tested and then evaluated these new innovative solutions within the East Region health and care services in collaboration with our stakeholders, including our staff, we are confident that these will then have the potential for spread not just nationally but also globally.

Working to four key strategic priorities for innovation:

- Reducing the demand for health and care services
- Maximising the use of existing resources
- Delivering access targets
- Increasing income generated from the ideas of our staff

The immediate focus of our innovation activity is being directed towards:

- The better management of long term conditions, frailty and multi-morbidity.
- Enabling people to benefit from healthier living in their homes and communities.
Health Innovation South East Scotland

Our Key Measures for Success

- Providing “real world access” to services to develop and test innovative solutions with external partners.
- To run innovation challenges for problem solvers to respond to.
- To support funding applications to external organisations such as Innovate UK and CanDo.
- To support the evaluation of innovative ideas and products.
- Support the three local NHS Boards and six Health and Social Care Partnerships in adopting proven innovative solutions.

Key Projects Being Progressed in 2019 /2020

Developing a digital approach to rehabilitation prior to major surgery.
Looking for innovative ideas to develop into solutions that will create stronger more resilient communities.
Completing a systems analysis in the care home setting to identify with stakeholders future innovation opportunities.
Exploring the potential to gain new and better insights into how to better support patients with COPD through improved data analytics.
Identifying opportunities for new diagnostic tests in the emergency department setting to enhance and quicken decision making.
Searching for new ways to better maximize the health outcomes for patients with multimorbidity.
Scoping out how to improve the care for patients with a hip fracture – through enhanced data analytics and electronic prompts.

At the core of our approach to developing innovative solutions is doing this in collaboration with our staff, academia, industry partners and the third sector.

Meet the Team

Led by the Director for Research and Development, Prof. Tim Walsh and with oversight provided by the NHS Lothian Innovation Champion, Grahame Cumming, the East Region Innovation Office has now been set up, initially at Waverley Gate, Edinburgh.

Managed by Samantha Smith (the Innovation Project Team Manager), the other team members include two Innovation Project Managers Robin Scott & Veronica Arias, along with Gemma Campos the Innovation Project support Officer.

The team works across all of the East Region and in addition to supporting innovation projects, they are continually involved in developing further the networks of innovative solution providers, and identifying potential sources of external funding through which to form innovation collaborations.

The team will also be responsible for managing the new East Region innovation website to be located within the Edinburgh Bioquarter website.

Enquiries to the team can be made via the email address below:

Innovations@nhslothian.scot.nhs.uk
NHS Lothian Research Safe Haven

The Lothian Research Safe Haven (LRSH) provides support for researchers seeking to access data held within electronic health records of patients within NHS Lothian for use in health-related research while protecting patient privacy and confidentiality. Extracts of data are securely linked and de-identified within a secure environment before being made available through restricted access to named approved researchers for specific approved projects.

The LRSH secure environment comprises trained and approved staff working on a range of datasets held within dedicated secure servers within NHS Lothian. These staff curate hosted data and undertake data processing and linkage of extracts of data for specific projects. Named approved researchers are granted restricted remote-access to de-identified extracts of data on a secure analytic platform, within a safe haven environment, to carry out their analyses. Only aggregated data can be released from the safe haven after being assessed for risk of disclosure of any potentially identifiable information. Individual level data may be released if access to the data is consented and/or the appropriate additional approvals are in place.

LRSH hosts a range of datasets used to support health-related research, these include extracts of NHS Scotland national databases (e.g. births, deaths, prescribing, SMR) and clinical systems (e.g. TRAKCare) and comprise routinely collected data on individuals accessing the relevant service within NHS Lothian. LRSH is working closely with DataLoch™ to develop a repository of health and social care data for the Edinburgh and South East Scotland (ESES) region, through which access to more comprehensive data including from primary and social care is anticipated.

LRSH also hosts bespoke health or clinical collections, study data and registers. LRSH supports researchers seeking to curate and facilitate onward sharing, through controlled access, of their study data.

LRSH offers a range of services and support to the research community in facilitating access to data for use in health-related research. Researchers are encouraged to liaise with the

Datasets and Cohorts:
- Linkable routinely-collected health datasets
  - Vital statistics
  - Health data (e.g. TRAK, SMR, A&E)
  - Disease registries
  - Population surveys
- Local bespoke "specialist" datasets & cohorts
- Study/cohort data

Advice and support:
- Availability of data for research
- Project design & research methodology
- Advice on data management and linking datasets
- Data annotation of tissue studies
- Advise and support on the required approvals
- Links with analytical expertise/services
- Links with Researchers & Clinicians
- Provide cost estimates for the proposed activity
NHS Lothian Research Safe Haven

LRSH team at an early stage in developing their projects to ensure requirements can be met and to obtain an estimate of cost to write into grants.

Applications for access to data and data linkage activity are reviewed by the LRSH Project Review and Advisory Committee to ensure appropriate use of the data including whether it is suitably justified and within public interest. The Research Ethics Committee has granted generic Research Database approval to LRSH to process data for a range of health-related research that has been approved by this Committee.

A range of projects and activities can be supported by LRSH. The activities and outputs are developed to meet the needs of researchers and to address information governance and security requirements for handling patient data. Although supporting research is the focus of activity, audit and service evaluation is also supported.

LRSH works in collaboration with NHS Lothian Analytical Services, NHS Lothian eHealth, NHS Lothian BioResource, Edinburgh Clinical Trials Unit, the Usher Institute and DataLoch™.

LRSH is also part of the NHS Research Scotland (NRS) Network of Data Safe Havens established to promote sharing of expertise, working to common standards and support delivery of multi-centre projects. LRSH primarily engages with eDRIS to access the National Safe Haven analytic platform, however data for approved projects can also be transferred to other Safe Havens within the network.

Collaboration is invaluable in sourcing the right data and services to meet the needs of the research and technical solution required for hosting and analysing a range of data formats within an environment that maintains patient privacy and confidentiality.

LRSH is part of NHS Lothian R&D and receives funding from the Scottish Government Chief Scientist Office (CSO).

LRSH offers a range of services and support to the research community in facilitating access to data for use in health-related research.

Data Management/linkage:
• Dataset acquisition, hosting/curation
• Data linkage
• Vital status checking
• Data extraction, processing and anonymization
• Disclosure and Risk assessment
• Facilitating remote access to data via a Safe Haven analytic platform

Types of studies/activity
• Feasibility studies & cohort identification
• Linkage to study data (consented as part of research project) – SHARE register, CTs
• Data hosting for onward sharing
• Data linkage and annotation of tissue
• Real world studies

For further information contact LRSH@nhslothian.scot.nhs.uk
Web: www.accord.scot/researcher-access-research-data/nrs-safe-haven
The Healthcare Technology Accelerator Facility

The Healthcare Technology Accelerator Facility (HTAF), based at the Queen’s Medical Research Institute at the University of Edinburgh, is an initiative aimed at expediting the development and commercialisation of healthcare technology.

By integrating physical, biomedical scientists and clinicians into the same environment and providing the requisite infrastructure (in term of expertise and facilities), HTAF removes the barriers that frequently preclude the development and translation of new healthcare technology.

The Investigational Supplies Group (ISG) comprising of David Lyall and Mark Chapman has been under the management of the Healthcare Technology Accelerator Facility (HTAF) for over a year now and 2019 has been a busy one for the small team. 5 batches of investigational medicinal products (IMPs) for MHRA approved clinical trials have been supplied and 4 batches of clinical investigational agents supplied for other R & D studies.

Since 2013, ISG have been offering a repackaging, blind labelling and encapsulation service from their GMP licensed George Square facility to support local CTIMPs and other research investigations. In 2019 they had a couple of firsts; the scope of their manufacturing authorisation (MHRA licence) was extended to enable them to undertake the primary manufacture of a tubed gel product to support Professor Fallon’s MINT clinical trial and they have also undertaken their largest repackaging and blind labelling operation since their inception, involving some 600 bottles and in excess of 80,000 tablets to support Professor Norman’s PAPAGENO trial which are intended for export to Malawi before the end of the year. Their existing manufacturing authorisation permits exportation outside the UK.

Those challenging projects aside – a lot of their time has been spent in the planning, design and commissioning of a new sterile formulation suite on the top floor of the QMRI where an older Cat 3 lab has been reconfigured into a cleanroom facility.

Meet the team

QC/CP
David Lyall

Production Manager
Mark Chapman

QA Manager
Martin Pearson

Operations Manager
Emma Scholefield
Martin Pearson has joined the team as QA Manager to primarily set up the quality management system for this new sterile fill facility and to also provide QA support to ISG.

In the last quarter of 2019 this will undergo its formal validations before inviting the MHRA inspectorate in early 2020 as we seek to add the new sterile facility onto the University of Edinburgh’s existing manufacturing authorisations. This will be the third MHRA approved site on its licence joining ISG and the Edinburgh Imaging radiochemistry suite. This will enable the group to provide an additional small scale, in-house sterile product manufacturing option for the University of Edinburgh’s translational medicine platform to support the manufacture of his pipeline of probes as well as offering a sterile product finishing service to other investigators.

2020 is already throwing up some new interesting challenges. HTAF expertise has been called upon to assist in the build of detailed user requirement specification and outline layout for a new build translational medicine hub. The hub will incorporate a new GMP suite as an extension to the nearly completed Institute for Regeneration & Repair (IRR) building on the BioQuarter site where a section of a separate floor has been set aside. This will be needed as the current ISG base in 1 George Square is earmarked for demolition in 2022. This proposed new build will soon go forward for tendering, costing and final approval by the University.

We have also been approached to engage the importation category of our licence for the first time for the importation of a nutraceutical and placebo capsule product from a third country (New Zealand). This would involve a site audit by the ISG Qualified Person, report and EU GMP equivalence declaration to be completed for submission with the clinical trial application before any importation would be possible as the products will be IMP.

Contact for further information
HTAF@ed.ac.uk
Now entering its tenth year, the NRS Lothian Biorepository continues to be a key member of the NRS Biorepository Network, providing infrastructure and support for local and national projects that required access to patient samples and associated clinical data from Lothian.

Tissue samples are crucial in medical and scientific research enabling development of new medicines and treatments, improving detection of many different diseases, and advancing understanding of how and why they arise.

The NHS is a major source of tissue, such as surplus material from diagnostic specimens or surgical procedures, and the Biorepository provides managed access to this in accordance with the appropriate governance requirements.

The Lothian Biorepository provides an infrastructure to support tissue research either directly or indirectly. The management group can assist with legal, ethical and regulatory requirements, and also general project management of the procurement process. It can also offer pathology expertise, and technical and histological support as required. There is a dedicated research nurse who can provide a consenting service and assist the provision of clinical data. In addition to this we also have a close working relationship with the Lothian Research Safe Haven.

The Biorepository is a REC-approved Research Tissue Bank, which allows for the collection, storage, provision and use of material for research. The approval allows for the support of a broad and diverse range of studies and the provision of material locally, globally and to both academic researchers and commercial companies.

**Services**

- Expert advice
- Processing tissue
- Processing bloods into serum or plasma
- Slide or section preparation from paraffin/frozen blocks
- Hematoxylin and Eosin (H&E) and Immunohistochemistry (IHC) staining
- Specialist stains
- Slide Scanning
- DNA and RNA extraction
- Tissue homogenisation for protein extraction
- Production of tissue micro arrays (TMAs)
- Liquid biopsies via surplus bloods.
NRS Lothian Biorepository

The Biorepository also works closely with Laboratory Medicine to provide surplus diagnostic samples collected via the 4 main hospital sites in NHS Lothian. This close link not only allows access to the blood and fluid samples but also enables us to provide an additional blood sciences testing service for research purposes. The Research Project Lead, Lisa Wilson (lisa-mariewilson@nhslothian.scot.nhs.uk), can offer guidance on all aspects of laboratory tests available to researchers.

Expert clinical, pathological and scientific advice

The NRS Biorepository Network has created a streamlined pathway for researchers to obtain tissue samples and discuss the design and costing of projects across a range of clinical specialties.

- Autoimmune & Inflammation
- Cancer
- Cardiovascular
- Dermatology
- Diabetes
- Gastroenterology
- Haematology
- Hepatology
- Mental Health Studies
- Metabolic & Endocrine
- Microbiology
- Musculoskeletal
- Neurology
- Ophthalmology
- Oral & Dental
- Orthopedics
- Paediatrics
- Regenerative Medicine
- Renal
- Reproductive Health
- Respiratory

Material released by the BioResource to date has been used in a wide range of studies including: in vitro pharmacology, cell culture, digital imaging, proteomic studies, DNA analysis and genome wide sequencing.

Figure 1 – A typical TMA slide and an example of Quantitative immunofluorescence performed on a TMA constructed by Lothian Biorepository.
The network provides streamlined access to tissue from across Scotland - with a single point of contact, single application process and single approval process, as well as standardised cost recovery model and contracts - ending the need for researchers to approach multiple Board.

The Lothian Biorepository continues to work closely with colleagues in NHS Greater Glasgow & Clyde, Grampian and Tayside to develop the network and increase awareness, efficiency and engagement with the research community.

Tissue Governance

The Biorepository also has the responsibility of providing a ‘tissue governance’ function for the health board. The remit of this is to help the board fulfil the role as ‘custodians’ and ensure that the collection, storage and use of tissue from NHS Lothian is governed appropriately and complies with all applicable regulatory, legal and ethical requirements.

Collections of patient samples held or stored for research purposes within NHS Lothian and the University of Edinburgh are required to register with the Biorepository, particularly where there is no current project-specific REC or R&D approval.

The Biorepository will be implementing a new electronic management system in 2020, as part of the successful national HDR-UK bid, which should streamline this process for all involved. This system will also provide a database of local collections that are available for use to other researchers.
NRS Lothian Biorepository

Accreditation

In 2011, the CSO announced the introduction of an external accreditation scheme for human tissue in Scotland, to demonstrate that Scotland operated to the highest possible professional governance standards in line with those for the rest of the UK.

This process was developed by Health Improvement Scotland (HIS) and is now overseen by NRS Central Management Team. This assesses the performance of NHS Boards rather than individual tissue banks or tissue collections. The accreditation standards address three key aspects of using human tissue for research: Consent and authorisation; Governance; and Premises. The Biorepository management fulfil this tissue governance function and are responsible for ensuring that collections within the board (and affiliated academic institutions) meet these standards.

The board successfully applied for and received accreditation in 2013 and again in 2016. At the time of publication, the outcome of the 2019 accreditation process is pending.

Any researchers interested in using patient samples from NHS Lothian should contact the Biorepository management team, Frances Rae (frances.rae@nhslothian.scot.nhs.uk) or Craig Marshall (craig.marshall@nhslothian.scot.nhs.uk) at the earliest opportunity to discuss the services and support the Biorepository can offer to facilitate their research.
Edinburgh Clinical Trials Unit – Doing the Trials that Matter…

Edinburgh Clinical Trials Unit (ECTU) has enjoyed another successful year, building on sustainable collaborations with NHS and University colleagues to undertake randomised controlled trials on a diverse range of clinical issues to make a difference to the lives of patients and their families.

ECTU continues to contribute to the Usher Institute’s mission to be the methodological heartbeat of the College of Medicine and Veterinary Medicine in the University of Edinburgh.

Building our research portfolio…

A. New grants awarded

ECTU has had another successful year in terms of major grants won competitively – including several NIHR/HTA funded studies (Dr Sarah Stock’s CHOICE study comparing in and out of hospital induction of labour; the CHAPS study comparing drugs & stockings in prevention of post thrombotic syndrome (PTS, Alun Davies, Imperial); and the MucAct COPD trial led by Professor Adam Hill on nebulised saline in COPD) and a BHF funded study on the use of Computed Tomography Coronary Angiography (CTCA) for coronary heart disease risk assessment and reduction (SCOTHEART-2, Professor Dave Newby).

ECTU also had notable success at the MRC, with Professor Yannick Crow’s inhibition of reverse transcriptase in type 1 interferon mediated neuropathology (the AGS study) funded, and likewise Dr Barry Laird’s ‘Be-Alpha’ phase II study of anti-IL1 alpha on muscle, physical function and appetite in lung pancreatic and ovarian cancer starting soon. We had great success this year at the JP Moulton Foundation – with three randomised trials gaining funding, including Professor Tim Walsh’s ABC post-ICU study on anaemia management with RBC transfusion to improve disability; Professor Alun Davies (Imperial) decellularized dermis allograft for the treatment of chronic venous leg ulceration (the DAVE study); and Gwo-Tzer Ho’s mitochondrial anti-oxidant therapy to resolve inflammation in ulcerative colitis (the MARVEL study).

We also continue to collaborate on earlier phase and pilot/feasibility studies, including Professor Andrew Horne’s ESPRIT study on laparoscopic treatment of isolated superficial peritoneal endometriosis for managing chronic pain; and also Tom Russ’ Playlist for Life using personalised music for dementia in care homes; and Reaching Consensus for core outcomes measures for end-of-life care after stroke (Professor Gillian Mead); and the SCARF project (Professor Tim Walsh) around supporting community recovery post-ICU – all funded by the CSO.

We have continued to collaborate on various Global Health Projects, including Professor Ewen Harrison’s CANut study looking at nutrition prior to cancer surgery in various lower and middle income settings; and various initiatives from Professor Fiona Denison around developing device infrastructure in Uganda, and projects around investigating the very high rates of caesarean section in Egypt (Professor Mohamed Abdel-Fattah, University of Aberdeen). ECTU are heavily involved in the delivery of several Edinburgh global health projects, including Professor Aziz Sheikh’s RESPIRE programme (respiratory health in India, Pakistan, Bangladesh and Malaysia), where ECTU’s activities have focussed this year on advancing data sharing across the 40 projects within RESPIRE; and Professor Jane Norman’s (now at Bristol) DIPLOMATIC project on premature birth in Malawi and Zambia.

B. Trials continuing recruitment

Several studies are continuing to recruit ECTU during 2019. These include (see www.ed.ac.uk/usher/edinburgh-clinical-trials/our-studies/ukcrc-studies for full details):

ALLEGRO - A placebo controlled randomised trial of intravenous lidocaine in accelerating gastrointestinal recovery after colorectal surgery. Funder: NIHR. Chief Investigator (CI): Dr Hugh Paterson
A2B - Alpha 2 Agonists For Sedation To Produce Better Outcomes From Critical Illness (A2B TRIAL): A Parallel Group Randomised Controlled Trial Comparing Clonidine, Dexmedetomidine And Current Usual Care. Funder: NIHR. CI: Professor Tim Walsh

EVOLVED AS - Myocardial Fibrosis And Left Ventricular Decompensation In Patients With Aortic Stenosis. Funder: Sir Jules Thorne Charitable Trust. CI: Dr Marc Dweck

LACI 2 - LACunar Intervention (LACI-2) Trial: Assessment Of Safety And Efficacy Of Cilostazol And Isosorbide Mononitrate To Prevent Recurrent Lacunar Stroke And Progression Of Cerebral Small Vessel Disease. Funder: BHF. CI: Professor Joanna Wardlaw

PIB CAP - Pneumonia Investigation Bundle To Guide Therapy For Hospitalised Community Acquired Pneumonia. Funder: NIHR. CI: Professor Adam Hill

Research Impact

A. Publications

ECTU is an academic unit and an essential part of collaborating on our trials is the dissemination of trials results, publication of protocols, and papers on methodological advances. Some highlights from the last year include:


**RESTART** RESTART collaboration 2019, ‘Effects of antiplatelet therapy after stroke due to intracerebral haemorrhage (RESTART): a randomised, open-label trial’ The Lancet. DOI: 10.1016/S0140-6736(19)30840-2

**RESTART** RESTART collaboration 2019, ‘Effects of antiplatelet therapy on stroke risk by brain...
imaging features of intracerebral haemorrhage and cerebral small vessel diseases: subgroup analyses of the RESTART randomised, open-label trial’ Lancet Neurology. DOI: 10.1016/S1474-4422(19)30184-X


ECTU’s Annual Meeting

ECTU continued its line of annual meetings, again in May, with presentations from Professor Nick Mills, Professor Lorna Marson, Dr Suvanka Pal, Professor Rustam Al-Shahi Salman and Dr Gwo-Tzer Ho on various clinical trials and collaborations with ECTU. Once again, senior members of ECTU took questions on how best to work with a CTU and what we can offer in collaboration. And we intend running this again on May next year.
Developing early phase trials

ECTU has the expertise and infrastructure to help develop and deliver early phase clinical trials. We have had important success gaining funding from MRC for two early phase trials (see above for details of Professor Yannick Crow’s AGS study, repurposing HIV drugs in a rare and devastating childhood disease, AGS syndrome; and Barry Laird’s Be-Alpha Phase II study looking at of anti-IL1 alpha on muscle, physical function and appetite in lung pancreatic and ovarian cancer. We successfully completed the phase I POP study (with commercial funding) led by James Dear on a novel treatment for paracetamol overdose. Professor Chris Weir has methodological expertise in the design of early phase studies, including interests in adaptive designs, and Professor John Norrie has recently taken over as Chair of the MRC/NIHR Efficacy and Mechanisms Evaluation (EME) Board, with a focus on phase II designs. Our trial management and business teams have worked hard to extend and validate new Standard Operating Procedures to work with these early phase designs, and we see these trials as a particular potential strength in Edinburgh, and will be very happy to discuss supporting both publically funded and commercial trial proposals.

Datasets & routine data in clinical research...

ECTU is continuing its work and collaborations around the exciting future in Data Science in Edinburgh, following the signing of the Edinburgh City Deal and Edinburgh’s aspirations to become a data force for the future.

We are delighted to be collaborating with Professor Aziz Sheikh and a UK-wide team on the recently awarded HDR UK ‘BREATHE’ digital innovation hub around curating and sharing respiratory datasets, and working on digitally-enabled respiratory randomised trials. We are also continuing to collaborate on Professors Aziz Sheikh and Harry Campbell’s RESPIRE programme (respiratory health in India, Pakistan, Bangladesh and Malaysia), where ECTU’s activities (led by Moni Choudhury) have focussed this year on advancing data sharing across the 40 projects within RESPIRE, working together with the Universities Research Data Services, and other NIHR Global Health partners (such as at York and Leicester universities). Our collaboration with Professor Bruce Guthrie on an observational study on understanding the link between depression and trajectories of physical multimorbidity using UK Biobank data was funded by the MRC further demonstrates our commitment to being involved in important data enabled initiatives.

Developing trials for the future...

An important aspect of the work of ECTU is developing innovative and efficient trial methodologies. All of our funders, and in particular the public funders such as NIHR/HTA and MRC, wish to see “efficient trials”, and recognise that innovation (for example, using adaptive type designs) is a promising way to delivery efficiency. However, innovative designs need to be thoroughly tested and are often hard work to implement. Our methodologists and trialists have had another busy year on this, and particularly grappling with the challenges of implementing these innovative designs. We very much welcome you bringing your trials to us!
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