

Glasgow Clinical Research Facility: Annual Report 2018-19

Glasgow HSP Operational Group

April 2019



Foreword

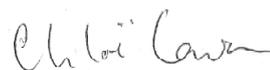
We continue to grow our busy research portfolio and have made novel therapies available to new patient groups with Motor Neurone Disease, Autism, Assisted Conception, Uro-surgery - and the spotlight from many research teams has been on the availability of research sessions and trained, skilled research staff to support this. Success of study delivery is reliant on a team with time designated to support the intervention, clinical assessments, safety reporting, data management and ability to respond to changes in the patient's condition, or study design. There have been real challenges this year where available resource has fallen short of the demand in some specialties. This report includes a focus on workforce movement in GCRF.

A more robust financial improvement plan in NHS GGC and a continually dynamic workforce has accelerated our need to maximise income from commercial studies. A Finance Working Group for research has been brought together to improve our tracking of items included in the budget. A summary of this work - which has greatly enhanced interdepartmental communication and transparency - is also included in our report.

Looking to next year, there are exciting opportunities to develop our expertise in and patient access to Advanced Cellular-based Therapies. All teams within the GCRF - the Project Management Unit, Education and Quality and Clinical Team - will be involved in improving and increasing our infrastructure to deliver these cutting-edge treatments across the spectrum of healthcare.



Professor Julie Brittenden
Clinical Director



Chloë Cowan
Clinical Research Manager

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GCRF Portfolio Performance 2018-19

Overall 2018/19 has seen an increase in recruitment to GCRF studies. Recruitment to academic studies has increased; three studies have really boosted these numbers

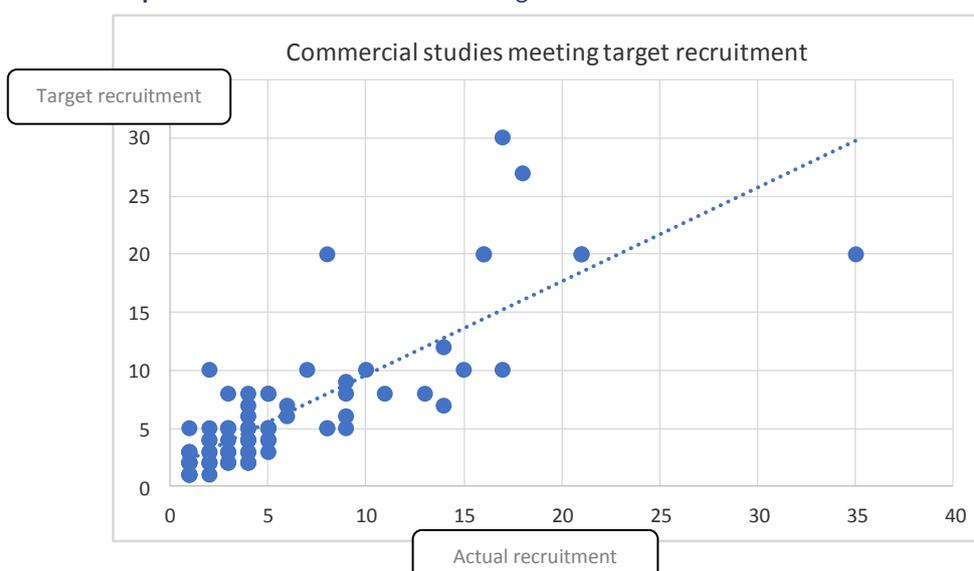
- Be on the Team – a vaccination study (Meningitis B)
- Minimum Unit Pricing - a survey of patients through the Emergency Department
- Airwaves – a 10 year follow up study of long term health effects of using the TETRA radio system

Commercial recruitment is lower this year largely because recruitment paused for three point-of-care device studies while newer prototypes were released.

Graph 1 GCRF Total recruitment by FY

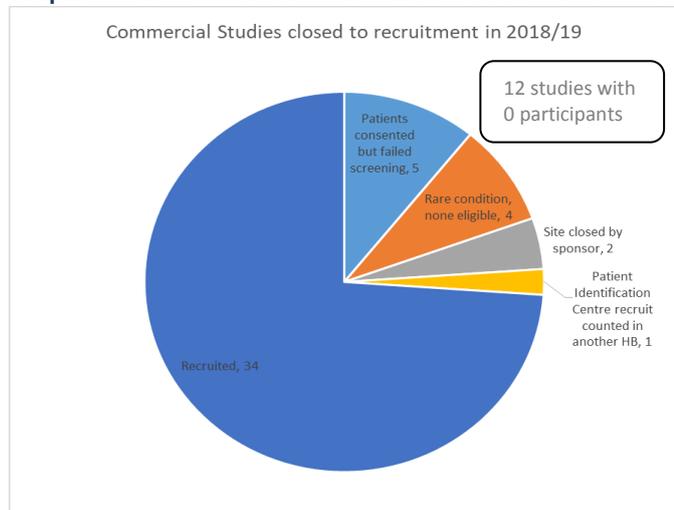


Graph 2 GCRF Commercial studies Target vs Actual



Over the last year 46 commercial studies have closed to recruitment. Recruiting to time and target for commercial studies is a Key Performance Indicator for the Healthboard to report to the Chief Scientist Office. The majority of GCRF commercial studies are Clinical Trials of Investigational Medicinal Products (CTIMPs) and have recruitment targets of <5. Improved ability to set an achievable target helps with financial planning and resource allocation, however attrition/retention data also needs to be included.

Graph 3 GCRF Commercial studies with 0 recruits at closeout



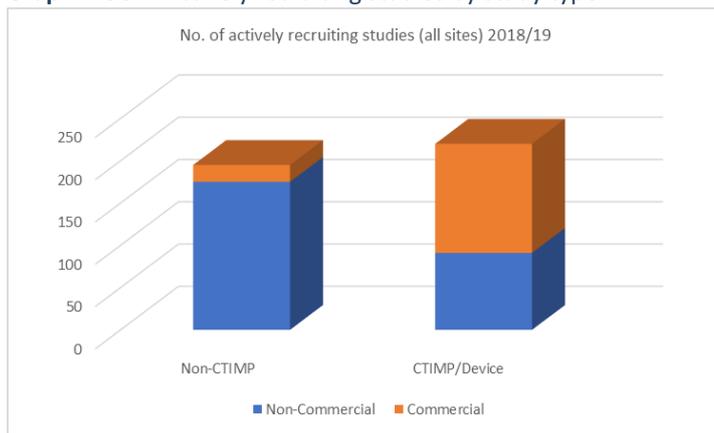
Another KPI is the number of studies closed to recruitment with 0 recruits. Twelve of the 46 studies closed to recruitment this year recorded 0 participants on study: 5 of these had recruited but the participants failed the screening procedures to go on to be randomised. For one of our early phase haemophilia studies, the participant is treated with a genetically modified therapy in London and will return to Glasgow for their long term follow up.

Of the academic studies supported by GCRF which have been actively recruiting over the last year, 23% are sponsored by NHS GGC and this proportion has increased over the last few years.

Table 1 GCRF studies sponsored by NHS GGC

	2015/16	2016/17	2017/18	2018/19
GGC Sponsored Studies	52	51	59	63

Graph 4 GCRF Actively recruiting studies by study type

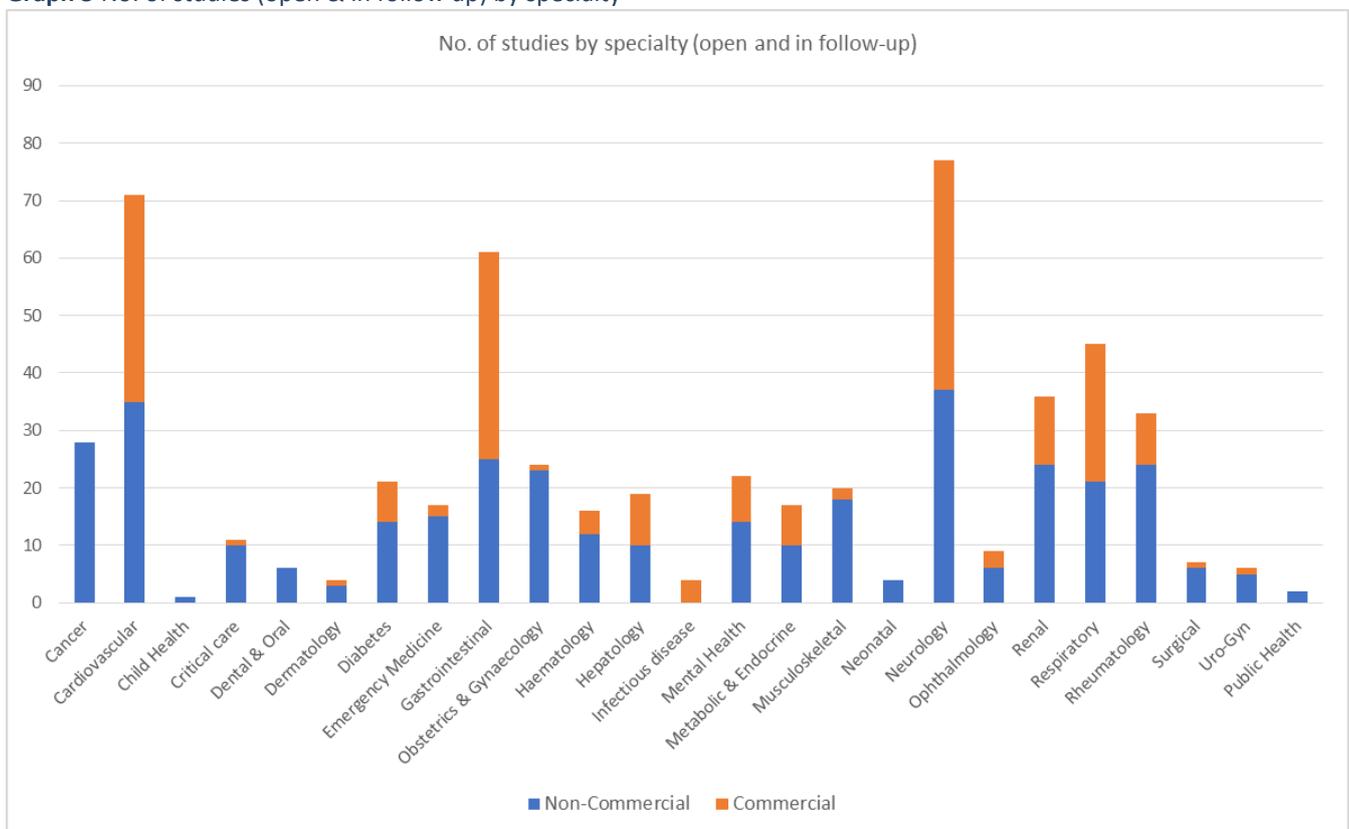


The number of actively recruiting studies has increased year on year in GCRF. We opened 57 new studies in the last year, and these include CTIMPs in new specialty areas including the Assisted Conception Service, Motor Neurone Disease, Autism and Cystic Fibrosis in children. Diabetes studies in Stobhill ACH are now supported by GCRF at the GRI, and the dementia research team work in the QEUH CRF.

Table 2 Total number of studies open to recruitment by FY

Recruiting Studies	Com	Non-com	Total
2016/17	126	228	354
2017/18	127	247	374
2018/19	153	266	419

Graph 5 No. of studies (open & in follow up) by specialty

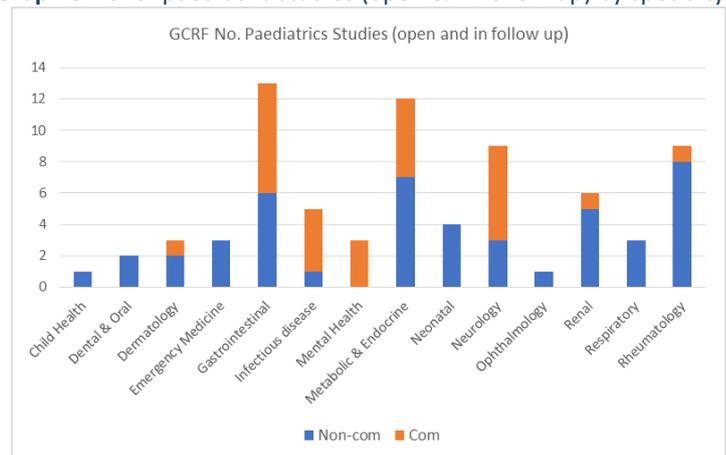


The number studies by specialty above includes each GGC study site where a different Principal Investigator and study team.

The most research active specialty areas are Cardiovascular, Gastrointestinal, Neurology, Renal, Respiratory and Rheumatology.

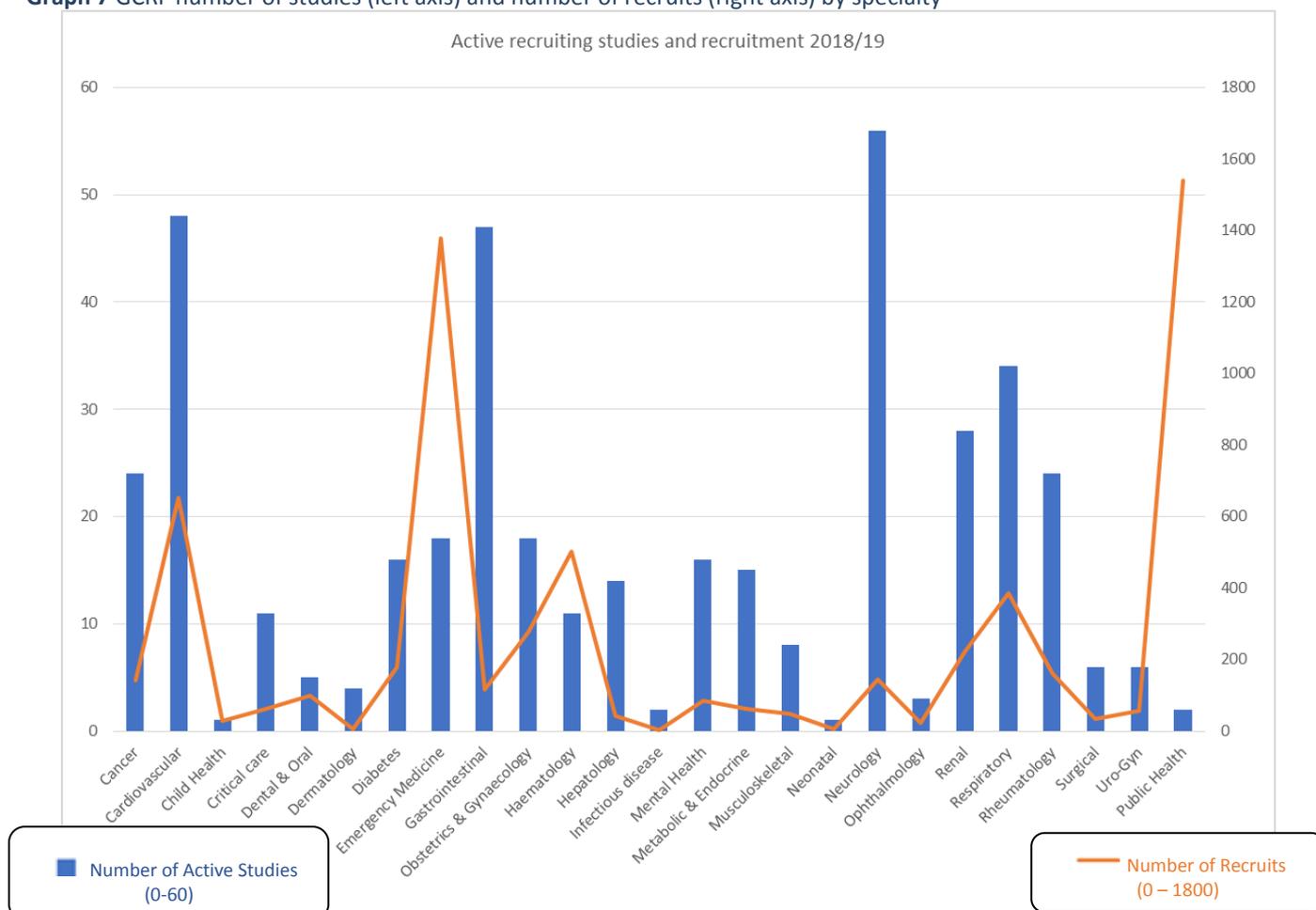
The graph above includes paediatric studies: the graph to the right is a subset, and shows metabolic and endocrine to be one of the most research active specialties in the Children's CRF.

Graph 6 No. of paediatric studies (open & in follow up) by specialty

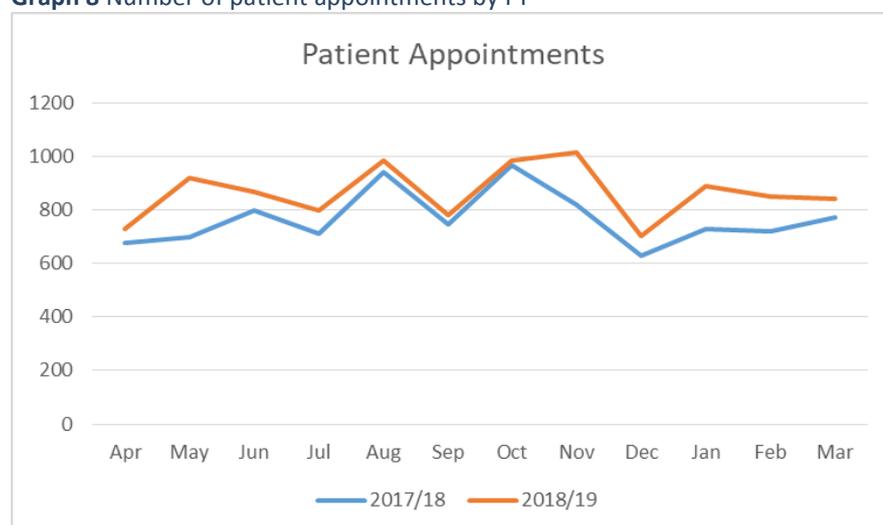


The specialties with the greatest number of early phase, complex CTIMP studies are Cardiovascular, Gastrointestinal, Neurology and Respiratory. The Neurprogressive Disease portfolio includes two phase one studies with an intrathecal investigational medicine for patients with Huntington’s Disease, and the first CTIMP in Scotland to be available for patients with Motor Neurone Disease. The Mental Health portfolio includes a phase 2 Boehringer Ingelheim study for patients with Schizophrenia and we are the top recruiting site in the UK. We have recruited our first participants to a bladder cancer surgical study comparing Intracorporeal Robot Assisted Radical Cystectomy with open radical cystectomy.

Graph 7 GCRF number of studies (left axis) and number of recruits (right axis) by specialty



Graph 8 Number of patient appointments by FY



Patient appointments are now captured on EDGE Research Management Application and this graph shows the number of participant visits has increased.

For future reporting the patient appointment report will be audited against patient recruitment for completeness – currently large recruiting studies with a single visit are **not** all included in this graph

- Be on the Team (Feb 2019, **550** participants),
- MUP (Feb/2018 **698** participants; Oct/2019 **619** participants; Feb/2019 690 participants)
- AIRWAVE (Jul-Dec/2019 **993** participants).

 **BE ON THE TEAM**
TEENAGERS AGAINST MENINGITIS

A NHS GGC collaboration between Health Protection Scotland, the school nurse team and GCRF, the *Be on the Team* study is a cohort study for 5th year school students testing a Meningitis B vaccine. Five hundred and fifty students were recruited and vaccinated from 5 Glasgow Schools. They'll all be followed up in September, and next March.





GCRF Workforce for a growing research portfolio

Clinical Fellows in GCRF This year Glasgow R&D welcomed its 50th medic to the NHS Research Scotland funded Career Researcher Fellowship. By providing funding for protected time to clinicians early in their substantive posts, the awards aim to strengthen the research culture in the NHS and to increase the capacity for clinical research.

After this initial funding, most clinical researchers seek to continue their activities and NHS Greater Glasgow & Clyde facilitates this with ongoing sessional support. These clinicians, by now Principal Investigators, often for multiple studies, carry the title “NRS Senior Research Fellow”.

Research activities cover the breadth of Medicine. Early stage research is always particularly exciting and recent highlights include a paediatric Phase I study in inflammatory bowel disease and a Phase I intrathecal administration of a study drug to volunteers with Huntington’s Disease.

We are delighted to have the help of several Junior Fellows in our CRFs, working across a range of disciplines and perhaps experiencing hands-on clinical research for the first time. These colleagues are at different stages of their careers: prior to taking up a training pathway, as a precursor to enrolment for a higher degree or as an opportunity to temporarily reduce their clinical commitment. Regardless of the entry point, the CRF experience aims to embed the doctor in research teams and activities and to support personal and academic development.

GCRF Research Staff

GCRF directly employs around 100 staff across disciplines including an education, training and quality team and a project management team though the majority of personnel form part of clinical study teams to deliver research projects. Roughly 45% of the workforce is funded directly by the recurrent funding from the Chief Scientist Office, the other 55% are funded on income generation from project grant awards and commercial income. Because of this mixed funding model, around 50% of staff have fixed term contracts and this means there is a constant progression of staff through the unit – on average two staff members leave a role in the GCRF every month, the majority to promoted posts within GCRF or within NHS GGC.

GCRF offers an exciting career path for registered nurses and midwives: placements are available for all specialty students so the role of Clinical Research Nurse is introduced pre-registration. Fifty percent of our Research Nurses progress within GCRF to Senior Research Nurse within two years. The majority of Clinical Research Nurses leaving GCRF for a new job in NHS GGC are successful in applications for Clinical Nurse Specialist posts or Senior Research Nurse posts in the cancer teams at the Beatson or RHC Schiehallion. Thirteen percent of the leavers over the last four years have retired, on average three staff members per year.

Every leaver is given the opportunity for an exit interview, and we use the feedback to improve. For instance, the introduction of team huddles to improve communication, summaries circulated from team meetings, a new SRN Induction and Guidance pack, introduction of reflective practice sessions.

“Running before walking” - more time for training and support

“Overwhelmed with workload from study perspective...”

“The CRF is an excellent facility for supporting research in NHS GGC. It is a great place for nurses to develop their career”

Replacing research staff takes around a year for them to be able to adopt a similar workload, and longer where there is a backlog of data capture and follow-up: the vacancy process from point of resignation to first day is now between 8-10 months and the greater the period of vacancy the lower the potential for the Healthboard to income generate through research activity either through CSO activity income to the Board, or through grant/commercial per patient fee. While we have a great opportunity to offer patients a wide spectrum of studies, and are the largest Board (patient population), there are many studies where we are outperformed by smaller Boards.

GCRF has a capable, ambitious staff, but increasingly are not able to meet all the expectations of study teams and maximise the opportunities for patients to access novel treatments or help develop new understanding about health conditions and healthcare.



GCRF Governance



Audit

In addition to the scheduled internal audits, GCRF had two external sponsor audits this year, neither with significant findings. Two routine GCP MHRA Sponsor Inspections have also fallen within this reporting year which has required significant input from the GCRF teams (Education & Quality, Project Management and Site study teams) in the preparation, hosting and acting on the findings to make improvements. The improvements are being taken forward through our MHRA taskforce meeting and the GCRF SOP committee and include improved documentation for tracking amendments and related versions, documented source data agreements (where not provided by sponsor), improved SOP documentation to evidence SOP training and ongoing compliance. The implementation of a quality application for document management – Q-Pulse – is being progressed through the R&D Governance team which will address findings related to SOP training.



Quality System We released a GCRF Brochure this year which we circulated to all Principal Investigators working with the GCRF, along with key SOPs for PIs to be familiar with. We have also released our Phase I SOPs and associated guides and forms.

This year all GCRF SOPs are undergoing the triennial periodic review. Two writing days have ensured this to be ahead of schedule.

Work to bring GCRF ready for Advanced Therapy delivery is described in the final section of this report and involves development of a new suite of SOPs.

Financial Governance Tracking research activity budgeted in commercial contracts was identified as an essential area for improvement last year. Traditionally, the R&D accounts team emailed various members of the study team to update milestone spreadsheets to inform invoicing. The milestone spreadsheets were frequently completed incorrectly, incompletely, or not at all. A multidisciplinary finance working group was brought together to explore how we could use EDGE - our Research Management Application - more effectively. The GCRF Information System developer built a macro to convert the NIHR costing template directly to the EDGE import template. This has allowed all NIHR template costs to be drawn directly over to EGDE without the risk of transcription error, or man-power to build the fields. Once tested, every active commercial study had the agreed costing templates uploaded to EDGE. The research teams including CT pharmacists, receptionists, HCSWs, research nurses, project assistant and team managers were then instructed to enter their research activity data in the relevant costing fields. GCRF team are now rolling this out to the Beatson CRF and designing a QC process with R&D Accounts team. Implemented in April 2018 and with several tweaks to processes since, this development has enhanced interdepartmental communication and improved financial transparency and budget accountability. Work now begins on building templates for the non-commercial studies.



This development work has brought about the development of an UK EDGE Super-User Network, led by Steven Barre GCRF IS Project Manager. Steven won an award at the EDGE Conference in Birmingham this year for his collaborative approach and willingness to share best practice.

GCRF Education & Training

NRS GCP Courses GCRF E&Q team continue their national coordination role and update and maintain all course materials, provide refresher training and QA assess all NRS GCP Trainers:

- 30 active trainers across all Boards (except Dumfries and Galloway)
- In November 2018 delivered half-day refresher training to 25 GCP Trainers from across all Healthboards

The MHRA Laboratory Inspection in June 2018 gave opportunity to establish a collaboration with MHRA GCP Inspector Jason Wakelin Smith to review the Introduction to GCP course content and materials – these are currently under review planned for release Summer 2019, and the GCP Update course to be reviewed by October 2019.



Shona McDermott was interviewed for Health Research Futures Podcast which was released in autumn 2018

GCP Awareness LearnPro module GCRF E&T team launched the GCP Awareness LearnPro Module in August 2018 – the module can be accessed by all Boards across Scotland (who have appropriate license).

Annual Skills Event This highly successful GCRF training and competency programme was held on 1st February 2019, with observers from our colleagues in the Aberdeen CRF team. The clinical staff had the core competencies covered for:

- Anaphylaxis
- ECG
- Informed consent
- Dangerous goods
- Sample processing
- Venepuncture & cannulation
- GCRF systems
- IV Medicines

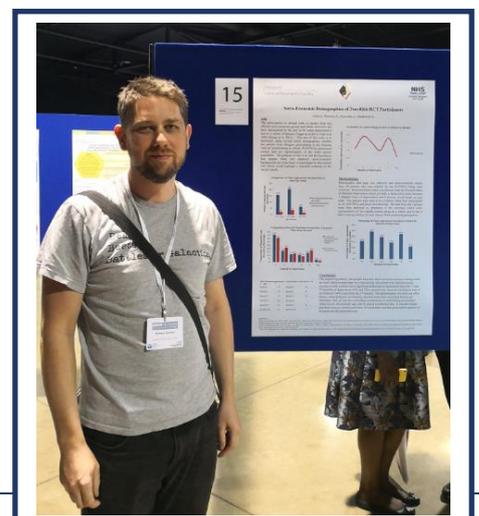
The programme for the admin team and project assistants which ran in parallel introduced them to new competency documents that had been developed by the GCRF team.

Student Placements We continue to have student nurses on placement in the GCRF throughout the year, and for the first time from the University of Glasgow School of Nursing, and in January 2019 had two 2nd year Medical students on a 6 week placement.

Representing GCRF GCRF staff have delivered formal and poster presentations at a range of events, including:

Presentations:

- Paediatric Rare Disease Conference (May 2018)
- NRS Annual Conference (October 2018)
- Scottish Clinical Scientist Trainee Network (Nov 2018)
- SRNCN Conference (Dec 2018)
- MSc Nurses (UoG) (Dec 2018)



- MSc Pharmacology (UoG)(Feb 2019)

Posters:

- World Association for Infant Mental Health Conference – May 2018 (Rome)
- UKCRFN Conference (July 2018)

GCRF Membership on the following national Committees:

- Chair of the UKCRFN Education group – Shona McDermott
- Deputy Chair of the NRS Trainers Forum – Naomi Hickey.
- SRNCN (newly elected) Chair – Janet Johnstone
- Research Ethics Committee Member - Naomi Hickey, Janet Johnstone, Ammani Brown
- UKCRFN Manager’s Forum – Chloë Cowan
- UKCRFN Costing & Sustainability Forum – Chloë Cowan
- UKCRFN Quality Assurance Forum – Eilidh Wright
- Scottish CRF Collaboration (Chair) – Chloë Cowan
- EDGE UK SuperUser Forum (Chair) – Steven Barre

Nomination stage: UKCRC CTU Operational Group, Project Management Representation Jurgen Van Melckebeke

Nomination stage: UKCRFN Education Group Deputy Chair – Naomi Hickey



SRNCN Conference 2018



Scottish CRF Collaboration



ED Research Conference

GCRF Research Engagement

Patient Involvement & Engagement Networks GCRF work in collaboration with specialty-driven PPI initiatives coordinated by partnership groups, for instance at the University of Glasgow (Rheumatosphere), Research Networks such as the Primary Care group established by Glasgow’s Primary Care Team, Mental Health service user links with the MH Network, we access the support of the Young person’s panel with the Children’s Research Network. GCRF have established a Patient Panel for Cardiovascular Research: a recruitment day was held in December 2017, we’ve held subsequent information days, trial meetings and training days throughout the year and a research event is planned for 25th April 2019 where 170 patients have registered to hear about the latest research from



Patient Involvement & Engagement Events

The GCRF team supported the May Measurement day for Hypertension (May 2018) by inviting members of the public to have their blood pressure measured at various stations, and subsequent recruitment drive for two key Glasgow Hypertension studies: UMOD and Aim HY. In collaboration with the Diabetes Research Network the GCRF supported an event in Crieff for type 1 diabetes promoting participation in the study TrialNet. For one of Glasgow’s flagship mental health studies EMPOWER, GCRF employed two Service users in a Peer Support role for study participants.

The Chief Investigator for the NHS GGC sponsored REx study acknowledged the invaluable support of the patient representative by making her a co-author on her results publication. Our Cystic Fibrosis Trust Senior Research Nurse has been promoting the clinical trials available to CF patients in Glasgow through CFT supported initiatives including a newsletter article June 2018 and supporting a parent’s evening in March 2019).

At the ICAN (International Children’s Advisory Network) conference in Edinburgh (June 2018) hosted by the Children’s Research Network, one of our study participant’s mum’s was a keynote speaker describing her experience of attending our Children’s CRF, her child’s study participation and the positive experience of support she received throughout.

Engagement with schools and young people:

GCRF invited 40 school pupils and their teachers to visit the GCRF for our annual open day: there were 5 interactive workstations to demonstrate what we do and highlight career opportunities in clinical research. Now an annual event as part of National Science week GCRF had an interactive stand at Glasgow Science Museum describing placebo and randomisation using Tic Tacs.



GCRF Project Management Unit



MHRA Lab inspection 2018 and MHRA GCP inspection 2019: PMU lead studies were selected at the recent MHRA inspections in which the outcome was very positive with only some minor Project Management related findings. This evidences the excellent professionalism shown by the team and the sound project management processes in place whilst also highlighting the positive impact the PMU team can add to studies

T-TIME CI Prof. Colin Berry, Alteplase administration during PCI. Recruitment completed for the T-TIME study in December 2017 and the main paper arising from the study has now been published in JAMA. We are now working to lock the database and close out the participating sites.

January 1/8, 2019

Effect of Low-Dose Intracoronary Alteplase During Primary Percutaneous Coronary Intervention on Microvascular Obstruction in Patients With Acute Myocardial Infarction
A Randomized Clinical Trial

Peter J. McCartney, MBChB^{1,2}; Hany Eteiba, MD^{1,2}; Annette M. Maznycka, MBChB^{1,2}; et al
➤ Author Affiliations
JAMA. 2019;321(1):56-68. doi:10.1001/jama.2018.19802



XILO-FIST CI- Prof Jesse Dawson aims to investigate whether Allopurinol has any impact on preventing recurrence of stroke or a decline in brain function. This study is co-sponsored by NHS GGC & UoG. Target recruitment of 464 was achieved in November 2018 across 26 UK sites, Glasgow achieved the highest number of recruits with 184 – patients are currently in follow up.

Pontiac II UK CI Prof John Cleland aims to prove we will be able to detect risk for cardiac events in patients with diabetes using NT-proBNP. The Project Management Team are the UK coordinators for this study and currently have 6 UK sites with potential for another 2 coming on board. NHS GGC are the top recruiting site in the UK.

Reduce Risk in CD. A paediatric study (UK CI: Prof Richard Russell) sponsored by PIBD Net in Paris aims to determine which treatment is more effective for high and low risk patients with Crohn's disease. We currently have 5 UK sites and the potential for another 3 sites.

The ICOSRA study, CI Prof Iain McInnes, an international collaboration, is now closed to recruitment: a precision medicine study for stratifying treatment for patients with Rheumatoid Arthritis. The study is now going into analysis phase and interest is high from the rheumatology society. Prof McInnes will present ICoSRA at both BSR; Eular and ACR events.

COLCOT: UK CI Prof Colin Berry, sponsored by the Montreal Heart Institute, aims to determine whether long-term treatment with colchicine reduces the rates of cardiovascular events in patients after myocardial infarction (MI). The Project Management Team are the UK coordinators for this study. Target recruitment for the UK was reached in July 2018; 156 participants over 11 sites. This trial predicts reaching the needed 301 reported events by summer this year at which point the trial will come to an end.



The LENS Study (Lowering Events in Non-proliferative retinopathy in Scotland) CI Dr David Preiss, has opened to recruitment across the 11 mainland Health Boards. Recruitment is ahead of schedule with over 280 randomised into the study and nearly 650 patients screened overall. NHS GGC is currently behind recruitment target owing to research nurse maternity leave and a vacancy in the Diabetes team, but has made some progress to catch up. The PM team organised a Research Nurse Meeting for the study in Stirling to feedback how well the study is progressing and projected targets and goals. The nurses had the chance to quiz the entire study team with questions and gave feedback to the study team. As an NIHR Efficient Design Trial, the plan is to draw down the first data linkage data sets from our collaborating agencies later in the year to update current study participants' records.

The project management team are working on the set up of a number of new studies including:

BenRex (Asthma Exacerbation Profile in patients on open label treatment with Benralizumab for severe eosinophilic asthma – an exploratory cohort study / CI Dr Rekha Chaudhuri). The primary objective of this study is to assess the inflammatory and physiological characteristics of an asthma exacerbation whilst on treatment with benralizumab for severe eosinophilic asthma. We aim to recruit 150 patients into the study from 14 participating sites, UK wide.

PRIZE A randomised, double-blind, placebo-controlled, cross-over trial of zibotentan in microvascular angina/ CI Professor Colin Berry). The study's primary objective is to gather evidence of efficacy for add-on treatment with zibotentan, an endothelin A receptor-selective antagonist (ERA), in patients with microvascular angina enrolled based on genotype. 8 sites have been identified to take part at present, and the trial aims to recruit 356 patients into the screening phase, with 100 patients minimum moving into the treatment phase.

TTT: Triple Therapy for Type 1 Diabetes with Insulin, Semaglutide and Dapagliflozin; CI is Prof Paresh Dandona (University of Buffalo). Prof John Petrie will be the lead within the UK for our Glasgow site. Recruitment Target is 114 participants across the two sites; Buffalo and Glasgow. The primary objective is to assess in people with type 1 diabetes whether triple therapy (dapagliflozin, semaglutide and insulin) reduces HbA1c by $\geq 0.5\%$ in comparison with dual therapy (semaglutide, insulin and placebo) and by $\geq 1.0\%$ compared with standard therapy (insulin only).



LENS pan-Scotland Study team meeting

Looking to 2019-20



The Northern Alliance Advanced Therapy Treatment Centre (NAATTC), is a consortium of twenty industry, NHS and academic organisations led by Newcastle Hospitals and the Scottish National Blood Transfusion Service (SNBTS). The purpose of the centre is to develop the systems and infrastructure required to support the delivery of cell and gene therapies with the ultimate aim of increasing patient access to advanced therapy medicinal products (ATMPs) on a national level.

In NHS GGC Dr Dave Irvine, Consultant Haematologist (Bone Marrow Transplant Unit) is the Lead Clinician for the network supported by Dr Samantha Carmichael, Lead R&D Pharmacist, and Jurgen Van-Melckebeke and Lisa Jolly from the GCRF PMU team.

The Innovate UK award and NATTC initiative will allow GCRF to further build expertise and infrastructure by developing a new Nurse Co-ordinator post. Key objectives will be to ensure our Quality System meets the needs for delivering Advanced Therapies of Investigational Medicinal Products (ATIMPs) and complements those of the Scottish Blood Transfusion Service and Bone Marrow Transplant Unit. Also in collaboration with the UKCRFN and NAATTC develop and share new training and education opportunities for staff delivering advanced therapies both within clinical trials or was part of standard care. With support from this coordinator, the Education and Quality team, the GCRF Lead Nurse and Beatson Senior Research Nurse team and BMT, CT Pharmacy and Apheresis, NHS GGC will be able to deliver our first CAR T-Cell pipeline study.