Glasgow Clinical Research Facility: COVID-19 Response

GHSP Delivery Board Report

October 2021



Foreword

In the face of the worldwide crisis, healthcare research has been catapulted into the spotlight, and has been critical in the fight against COVID-19. Never before have we seen such a rapid, focussed national effort by researchers and as a consequence the outputs have been tremendous. In NHSGGC we mobilised our core research teams to the nationally agreed Urgent Public Health portfolio of studies – studies which included the generation of data to inform the SAGE and subsequent public health policy (ISARIC 4C, GenOMICC, HOCI COG UK, SIREN), COVID-19 treatments studies (RECOVERY, REMAP CAP), evaluating tests and diagnostics (FALCON) and the vaccination research programme directed by the UK Government Vaccine Taskforce (VTF).

The following report will provide examples of some key areas of COVID19 research which the Clinical Research Facility (GCRF) and wider Research and Innovation (R&I) team have supported over the last 18 months. In parallel, as patients have been able to attend hospital and reengage with different NHS services, so we have been able to restart studies that were paused to new recruitment, or suspended in the set-up phase. This demonstration of resilience in such a challenging time for the NHS is a real credit to our researchers and research teams.

Professor Julie Brittenden
Clinical Director

Chloë Cowan
Senior R&I Manager

Photos in the report were compliant with COVID 19 guidance at the time.

GCRF COVID-19 Response

Urgent action in March 2020 followed the chain of measures introduced to the Healthboard in response to the pandemic. New recruitment to clinical studies was paused, with the exception of studies which provided treatment for health conditions where none routinely available. Follow-up visits were rescheduled, conducted virtually, or took place in the patient's home (for instance Cystic Fibrosis patients, post-transplant patients). The new portfolio of COVID-19 studies underwent rapid, prioritised review for set up through the newly formed R&I COVID-19 Taskforce. GCRF staff were realigned from their specialty teams to form a red pathway team and a green pathway team, both meeting for daily huddles and informed by new COVID19 admission lists. A seven-day service at three hospitals was established to cover the urgent nature of admissions. A number of high impact trials are described below:

ISARIC 4C International Severe Acute Respiratory Infection Consortium Clinical Characterisation Led by Dr Toni Ho (Infectious Disease Consultant, Centre for Virus Research University of Glasgow) this study aimed to provide the clinical features of COVID19 and treatment response – the first NHS GGC participant was consented on 5th March 2020. The team rapidly adjusted to take written informed consent and blood samples in new and evolving infection control procedures. NHSGGC became the major contributor of samples of analysis for host/viral multiomics. Outputs included a risk stratification score, risk prediction models and data have been used to inform public policy as data feed directly to PHS, PHE and SAGE.

The ISARIC 4C sister study for genetic mechanisms of COVID-19 **GenOMICC** recruited critically ill patients from three ICUs in NHSGGC (GRI, QEUH and RAH). The data from this study have already identified DNA associations with determination of severe disease and this is now being used to predict the effects of new treatments, in collaboration with the RECOVERY Trial



Both ISARIC4C and GenOMICC include the ability to recruit paediatric patients inpatients with COVID-19. Dr Steve Foster, ED Paediatrician at the RHC led NHSGGC contribution to the **RAPID-19** study which measured antibodies of healthcare worker's children at three timepoints over the last year. Over 220 children - known as COVID WARRIORS - took part in NHSGGC.

Within weeks of the **RECOVERY** trial activating in the UK, NHSGGC had recruited patients at the GRI, QEUH, RAH and IRH. A pragmatic, dynamic, pre-ICU platform study, RECOVERY is now the world's largest clinical trial for COVID-19 treatments, and has already delivered results on nine treatments, most notably postive results for dexamethasone, Tocilizumab and Regeneron's monoclonal antibody combination.

NHSGGC is in the top 17 recruiting Healthboards/Trusts in the UK thanks to 567 of our COVID-19 positive hosptialised patients, and the collaborative efforts from medical, nursing and pharmacy teams across the city. (PIs Dr Kathryn Puxty, Prof Malcolm Sim, Dr alasdair Corfield and Dr Mohammed Azharuddin).

Despite the enormous pressure on Critical Care throughout the pandemic, NHSGGC has led the way in Scotland for contribution to the REMAP-CAP randomised, adaptive platform trial for COVID 19. Led by Dr Puxty (GRI), Prof Sim (QEUH and Prof Rooney (RAH), NHSGGC has recruited 175 patients. Earlier this year, the study results provided a clear indication for Tocilizumab and Sarilumab as equally effective for patients with severe COVID-19 and also the most effective treatments in this domain.

Table 1 Recruitment to UPH/RR funded COVID-19 Treatment studies

	Urgent Public Health Study							CSO Rapid Response call	
	REMAP CAP (Recruiting)	RECOVERY (Recruiting)	COVACTA (Closed)	REMDESIVIR (Closed)	TACTIC R (Closed)	SPRINTER (Recruiting)	HEAL COVID (Recruiting)	GETAFIX (Recruiting)	Total
GRI	*66*	*180*			30	*8*	*4*	*2*	**290**
QEUH	*33*	*192**	9	16			*5*	*82*	**337**
RAH	*76*	*183*					*3*		**262**
IRH		*13*							**13**
Total	**175**	**568**	**9**	**16**	**30**	**8**	**12**	**84**	**902**

*Including children from RHC

Table 1 shows all UPH treatment studies supported by the GCRF team in NHSGGC. In addition the Chief Scientist Office (CSO) put out a Rapid Response funding call for COVID-19 projects. The UoG bid lead by Professor Iain McInnes, was awarded over 1 million in funding for a variety of projects. This included the GETAFIX randomised placebo controlled trial of an antiviral (Favipiravir) as early treatment for COVID 19. Recruiting in a community setting required new and different approach for the GCRF team. Caldecott approval was received to enable recruitment via Test and Trace data for those who were happy to be contacted for research. This is overseen by the Safe Haven. This has transformed recruitment to the study, and provides a model for future research. In the last year GCRF have also directly appointed Clinical Research Fellows who have taken a leadership role in working with the Chief Investigator (Prof Kevin Blyth) in recruiting to GETAFIX. The role of the Clinical Research Fellows has also proved to be invaluable to supporting the vaccine research programme, particularly the symptomatic/surveillance review and safety assessments.

COVID-19 Vaccine Research

COVID-19 vaccine research has moved at breath-taking pace over the last 18 months, from first dose in human to regulatory approvals within 9 months. This has been achieved because of co-ordinated, collaborative global responses, and prioritisation of the UK research community to focus resource and expertise on this field.

NHSGGC has been at the heart of this response, delivering five of the UK Vaccines Taskforce studies. Expertise and rapid response has been required from across the R&I team – the approvals team to expedite initial set up and subsequent amendments, the Clinical Trial pharmacy team, GCRF medic, nurse and admin team with senior medic support from the Infectious diseases team plus NHSGGC Senior Research Fellows. The QEUH SATA and out-of-hours teams have supported the surveillance pathways for all of these studies. GCRF Education and Quality team have paused much of their core business to coordinate the vaccine programme and now have employed two new Project Site Manager posts to continue this work.

Table 2 Recruitment to Vaccine studies

	COV002 (ChAdOx) (Closed)	**NOVAVAX** (Matrix 1) (Closed)	**COV-COMPARE** (VLA001) (Closed)	**COV BOOST** (Recruiting*)	**OCTAVE** (Closed)	**OCTAVE DUO** (Recruiting)
NHS GGC	588	517	161	*125*	686	*151*

*recruitment will restart in January 2022 to the next cohort

Oxford Astra Zeneca COV002 Phase II/III study to determine the efficacy, safety and immunogenicity of the candidate Coronavirus Disease (COVID-19) vaccine ChAdOx1 nCoV-19.
Principal Investigator Prof. Emma Thomson (University of Glasgow CVR, Consultant Infectious Diseases)

KENSINGTON PALACE

24th August, 2021

To all Oxford-AZ Vaccine Volunteers and Staff,

I wanted to say a huge thank you to each and every one of you for your part in trialling and developing the Oxford-AstraZeneca vaccine.

As volunteers, you have stepped forward from all corners of the UK, and from across Brazil and South Africa, with a humbling sense of selfless duty to trial a new vaccine. As research staff, you found the determination and resilience to keep going through the lockdowns and endless hours of work to bring a remarkable new vaccine to the world.

Your collective efforts allowed the authorisation and distribution of the vaccine to over 175 countries and the production of a billion doses by July 2021. As a result, hundreds of thousands of lives around the world have already been saved.

You should all be tremendously proud of the part you have played in tackling the global COVID-19 pandemic. Thank you again for all that you have done.

With gratitude,

NHS GGC had a fantastic response to the call for recruits to this study: over 580 healthcare workers and those from other high exposure/high risk groups took part. Study results demonstrated efficacy and by end of December 2020, the MHRA approved the vaccine for use. This, alongside the deployment of the Pfizer vaccine, required the research team to respond immediately to unblind participants as they were offered the deployed vaccine. This process has never been needed before but required a vital, rapid team effort to keep pace with the deployment programme, ensuring no disadvantage to those participating in the trial. A recent thank you event for participants and study teams included discussion from Professor Andy Pollard, and personal thank you from HRH Duke of Cambridge.

Participants are now coming to their final visits for the study, but will be invited to take part in a surveillance study **COV009** to measure ongoing levels of immunity.

NOVAVAX A Phase 3, Randomised, Observer-Blinded, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) with Matrix-M1™ Adjuvant in Adult Participants 18-84 Years of Age in the United Kingdom
Principal Investigator Prof. Emma Thomson

Over 15,000 participants were recruited in the UK; NHSGGC recruited over 500. This is the largest commercial Clinical Trial of an Investigational Medicinal Product ever conducted in NHSGGC. Participants were recruited and given two doses of the vaccine between November and mid-December 2020. The unblinding process also began in January 2021 with the deployment programme, however the trial design changed in March to include a crossover: those who remained blinded in the study would receive the opposite of their initial randomisation. Participants will attend their final follow up visit in November/December. Efficacy data was published in the NEJM in June 2021: 89.7% efficacy and low levels of reactogenicity. There has been a delay in the application to the MHRA for approval because of supply issues.

VALNEVA COV-COMPARE A randomised observer-blind, controlled, superiority study to compare the immunogenicity against COVID-19 of VLA2001 vaccine to AZD1222 vaccine in adults.
Principal Investigator Prof. Emma Thomson

Availability and rapid deployment of licensed COVID19 Vaccines required new trial design for VALNEVA: the control arm was the AZ vaccine for those over 30, but for those <30 new data looking at risk/benefit meant this age group would receive VLA2001. NHSGGC recruited over 160 to study. Initial results (via company press release 18/10/21) show low levels of reactogenecity and high functional antibody responses alongside broad T-cell responses. Valneva commenced rolling submission for initial approval with the UK's Medicines and Healthcare products Regulatory Agency (MHRA). A final assay validation required by the MHRA to verify the integrity of VLA2001-301 data remains ongoing and is a prerequisit for final submission of the clinical study report.

BBC Scotland

COV-BOOST A randomised phase II UK multi-centre study to determine reactogencity and immunogencity of booster vaccination against ancestral and novel variants of SARS-COV-2
Principal Investigator Prof. Emma Thomson

This study is looking at a booster dose of vaccine following the primary-boost doses; whether the type of vaccine is important and whether the strength of dose could be halved. The first phase of the the study has provided evidence to the Joint Committee on Vaccination and Immunication (JCVI) to inform the seasonal booster programme. NHSGGC recruited 125 participants for the first phase and will take part in the next phase later this year early 2022 and is expected to include vaccines redesigned for the new variants.

OCTAVE Observational Cohorts Trial - T-cells Antibodies and Vaccine Efficacy in SARS-CoV-2
Chief Investigator Prof. Iain McInnes **Principal Investigator** Prof. Stefan Siebert, Univeristy of Glasgow Dept of Infection, Immunity and Inflammation, Consultant Rheumatologist

Led by the University of Glasgow, the Octave study is looking at clinically at-risk patients with specific immunocompromised or immunosuppressed conditions, to identify those who mount a low or undetectable immune response after two doses of the same COVID-19 vaccine. Just under 700 patients with rheumatoid conditions have been recruited to this study in NHSGGC. The initial data (published on the Lancet pre-print site) show that 40% of people in the patient groups studied mounted a low serological immune response after two SARS-CoV-2 vaccines; approximately 11% of immunocompromised patients fail to generate any antibodies 4 weeks after two vaccines. Those who were in this group have been invited to take part in the Octave Duo Study.

OCTAVE DUO A Phase III, Multicentre, Randomised Trial Comparing SARS-CoV-2 Re-Boost Vaccine Strategies in Immunocompromised Patients
Chief Investigator Prof Iain McInnes **Principal Investigator** Prof Stefan Siebert

NHSGGC are delivering most of the recruitment to the rheumatology cohort for this study with around 150 patients taking part: patients receive a re-boost of either Pfizer or Moderna vaccines and will be followed up to measure the impact of this revaccinatination on antibody reponse and any subsequent COVID19 infection.

COVID Surveillance

In November 2020 NHSGGC were tasked by PHS/PHE to support the SIREN study – the world's biggest real-world study of SARS-CoV-2 immunity and reinfection evaluation in Healthcare workers. Led by Dr Toni Ho and Research Nurse Manager Therese McSorley, NHSGGC went on to become the second highest recruiter to the study – 1253 healthcare workers have taken part and will be followed up for at least a year, and with their permission, for a second year. Participants are tested every 2-4 weeks using PCR and antibody test – thanks to the NHSGGC eHealth team a text message service for results was established which improve the efficiency of trial delivery.

SIREN
SARS-CoV2 Immunity & Reinfection Evaluation

Investigating and treating Long COVID

Another Urgent Public Health national collaboration and linked to the ISARIC programme is the Post-Hospitalisation (P-HOSP) research. Patients at the GRI and QEUH have agreed to take part in a series of assessments to better understand the long-term effects of COVID-19 and any ongoing medical, physiological and rehabilitation needs. PIs Dr Hannah Bayes (GRI) and Dr Dave Anderson (QEUH).

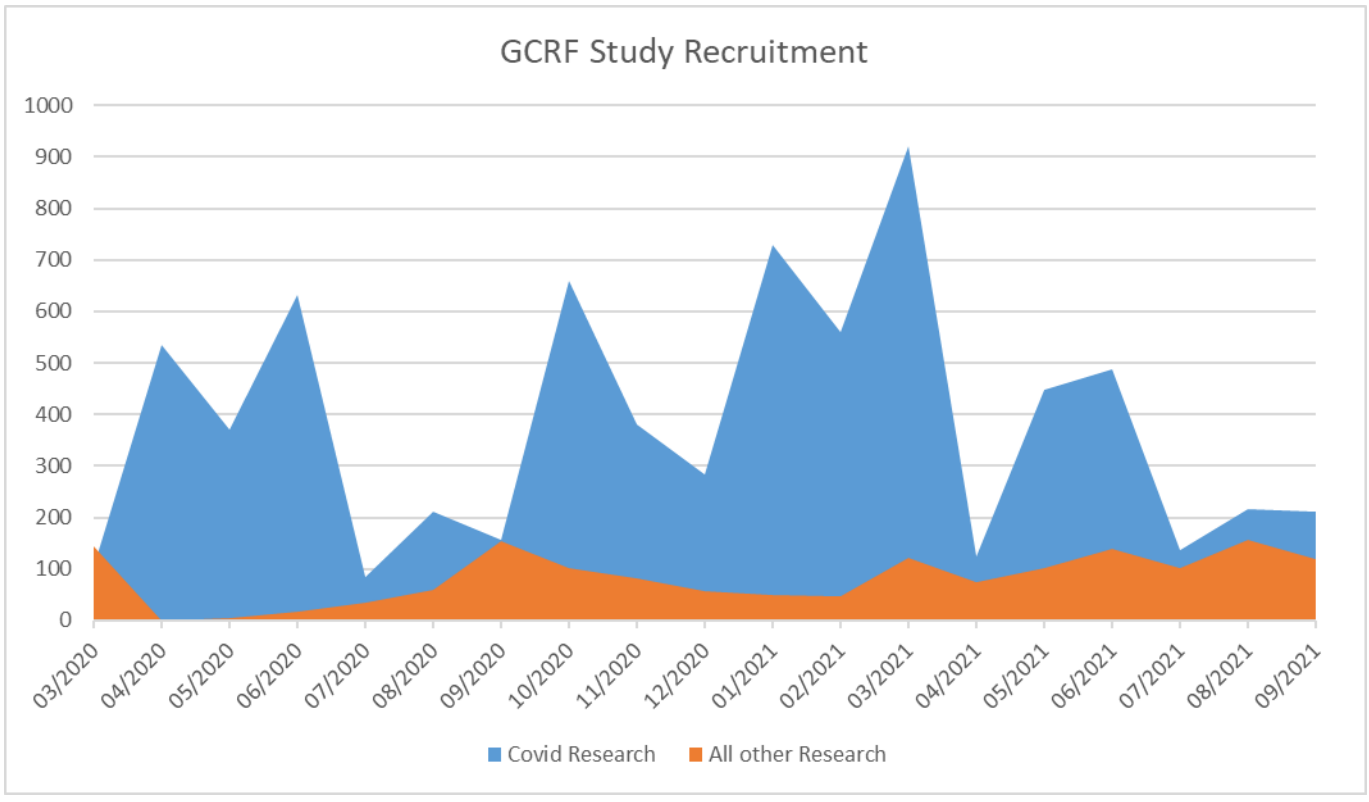
HEAL-COVID is also underway in GRI, QEUH and RAH– a trial aiming to identify treatments for patients who have been discharged from hospital after recovering from COVID-19 (PIs Dr Hannah Bayes, Prof Colin Berry and Dr James Hornsby)

In parallel, Prof Colin Berry has led cardiac and pulmonary imaging research in SARS Coronavirus Disease funded by the CSO. Over 200 patients with COVID19 consented to take part in the study (*Cardiovascular Research*, Volume 116, Issue 14, 1 December 2020, Pages 2185–2196, https://doi.org/10.1093/cvr/cvaa209). A great collaboration between the Clinical Research Imaging Facility (CRIF), cardiovascular research fellows and GCRF. Prof Berry is also investigating whether resistance exercise is of benefit in treating and preventing long Covid in the CISCO-21 study – also CSO funded. Recruitment is well underway at GRI and QEUH.

Glasgow is also leading projects in Diabetes with Dr Robbie Lindsay and Hypertension in Long Covid with Prof Sandosh Padmanabhan.

COVID Response Summary

In all, the GCRF team has supported over 40 different COVID-19 research projects and recruited over 7300 participants to COVID research in the last 18 months. This research will continue to evolve over the coming year. New members of the team have been enlisted including clinical fellows, research nurses, health care support workers and project site managers. As the new staff embed in the team, this will enable reassigned staff to re-establish pre-COVID research activity.



Restart and Recovery

Throughout the pandemic, the R&I taskforce for restarting research has reviewed the vast majority of studies supported by GCRF to assess the ability to reopen to recruitment. Around 26 of the 275 studies open to recruitment are flagged as part of the national Managed Recovery programme. Gradual re-introduction of GCRF Specialty Operational Groups is enabling further assessment of resource and capacity to re-establish research where activity paused. Over 1500 patients have been recruited to over 220 different clinical studies in the last 18 months.

Building back the diverse pre-COVID portfolio, in parallel with continued support of COVID-19 research is subject to many bumps in the road. Recruitment to studies is affected by pressures across the NHS, plus the reduction in face-to-face consultations has changed the recruitment strategies required for many studies. GCRF staffing has not been immune from the impact of COVID - either ill-health, social circumstances or requirement to isolate. The vaccine passport/certification programme has not had the inbuilt flexibility to accommodate clinical trial participants which the study teams continue to have to address urgently.

However, there have been some examples of advancement of GCRF service provision: the purchase of a new isolator hood for the GRI CRF has enabled the first GMO IV IMP to be delivered for the treatment of haemophilia (Dr Catherine Bagot, Principal Investigator). Commercial research will take time to recover but there are further novel studies on the brink of opening for instance the use of an implantable splenic nerve stimulation device for rheumatoid arthritis (Dr Duncan Porter and Mr Nigel Jamieson), testing a new lightweight, low cost inflatable incubator for premature babies (Dr Helen McDevitt), advanced novel (genetically modified) therapy for SCN1A-positive Dravet patients (Dr Andreas Brunklaus).

Other key developments over the last year - COVID19 presented the need to enable remote monitoring by external sponsors. This process developed by the GCRF Quality Lead Eilidh Wright was well-tested in a FDA inspection of a paediatric clinical trial which was all conducted remotely, including source data verification. The vaccine research programme has tested the use of a national opt-in registry hosted by NHS DIGITAL. The use of the Safe Haven to enhance patient identification for invitation to participate in research and forecast future cohort recruitment opportunity.

The opportunity to host medical and nursing student placements has continued throughout the pandemic and have provided a valuable contribution to the study teams. As well as presenting about Student Nurse placements at the International Association of Clinical Research Nurses ’21 Conference, Clinical Educator Naomi Hickey and the mentorship team have been nominated for the Nursing Times Student placement of the year.