NHS
King's College Hospital
NHS Foundation Trust

Research & Innovation Strategy:
Two years on

Excellence in patient care underpinned by research and innovation

Welcome

It is our pleasure to welcome you all to the Annual Research and Innovation Strategy meeting. We are so pleased to be able to hold this meeting face to face, at a time when so many of our events, seminars and meetings have been either postponed or held virtually. Research & Innovation (R&I) is one of King's College Hospital's (KCH's) defining characteristics. It is a central part of the offer of research that underpins quality care, a core principle of the NHS, that we make to our patients and their families and our staff.

Due to the COVID-19 pandemic, the last 18 months have represented unprecedented challenges for all staff across the Trust; from clinical staff dealing with an influx of patients with complex needs, to hospital porters and administrative staff who have been dedicated to keeping the regular functions of the Trust ticking over during this time.

In particular, we, the directors of R&I at the Trust, would like to say a huge THANK YOU to those who were clinically redeployed to support the huge influx of COVID-19 patients on the wards or in Critical Care, and those who have been involved in the delivery of research studies. We are so proud of our research teams who have quickly dealt with the government-ordered immediate pausing of all research studies and gone on to work round-the-clock to rapidly set up and deliver both Urgent and Non-Urgent Public Health Studies that aim to prevent, treat and understand the Sars-CoV-2 virus and the disease it causes, COVID-19.

Furthermore, the way that research staff across the Trust have worked together, with many being redeployed into new teams, to deliver this ground-breaking research while providing gold-standard patient care has made us honoured to be leaders of the research community. It is thanks to all of your hard work that we now have effective vaccines and treatments that have saved thousands of lives across the UK and around the world.

We are also immensely impressed by those who also managed to continue non-COVID-19-related studies and adapt to pandemic restrictions to ensure that participants already on clinical trials and studies were cared for in the best possible way.

Today, at our Annual Research and Innovation Strategy meeting, two years on from the launch of the Research and Innovation Five Year Strategy, we review and celebrate the fantastic achievements made since March 2020, which were only possible due to the hard work and dedication of our research staff.

With warm regards,

Professor K. Ray Chaudhuri
Director of Research & Innovation

Ann-Marie Murtagh
Director of Research & Innovation, Head of Nursing (Research)

Professor Anil Dhawan
Director of Research & Innovation

King's College Hospital
NHS Foundation Trust

Research and Innovation Annual Research Meeting

Fetal Medicine Research Institute Lecture Theatre, Windsor Walk

15th October 2021, 12-5pm

Agenda

12.00 - 13.00	**Registration, Lunch and poster viewing**
13.00 - 13.15	Welcome address (R&I Directors: Ann-Marie Murtagh, K Ray Chaudhuri, Anil Dhawan)
13.15 - 13.30	R&I Directors' Annual Review (Ann-Marie Murtagh)

Session 1 - COVID Research at KCH

Chaired by Prof K Ray Chaudhuri

13.30 - 14.00	COVID Research at KCH: Dr Piers Patten
14.00 - 14.25	COVID Vaccine Research: Dr James Galloway
14.25 - 14.45	SIREN, Long COVID and diversity: Prof K Ray Chaudhuri/Jon Breeze
14.45 - 15.15	**Coffee Break & Poster Viewing (Presenters stand by posters)**

Session 2

Chaired by Prof Anil Dhawan

15.15 - 15.45	SL CRN - Priorities and Performance: Dr Kosh Agarwal
15.45 - 16.15	Showcase - nurse and AHP led Research: Dr Sharlene Greenwood/Dan Hadfield
16.15 - 16.30	Showcase - Advanced Therapies Studies: Dr Phil Hopkins/Dr Celine Filippi
16.30 - 16.45	Showcase - Device Study – DBS: Prof Keyoumars Ashkan
16.45 - 17.00	Vote of Thanks, poster competition outcome and closing remarks

Contents

A year of research in unprecedented times

The start of Financial Year 2020/2021 (FY20/21) began just days after the UK entered its first national lockdown due to what was to become the global COVID-19 pandemic.

A respiratory infection caused by the coronavirus Sars-CoV-2, COVID-19 in many people resulted in flu-like symptoms, with key signs of infection being a dry cough, fever and changes to the senses of smell and taste. While many could fight off the infection and recover at home, it quickly became evident that a significant number of people - in particular older people and those with underlying health conditions - became seriously unwell, requiring hospital treatment. Rough estimates suggest that around 1% of people testing positive for the Sars-CoV-2 virus would die due to COVID-19.

In response to the soaring numbers of people being admitted to hospital with COVID-19, coupled with the urgent need to develop new treatments and preventative therapies to combat infection, the UK Government immediately paused all research taking place at NHS Foundation Trusts across the UK so that research staff could focus on the rapid set-up and delivery of large number of clinical trials and studies into the prevention of COVID-19 as well as the treatment and care for people affected.

In the 18 months (and counting) since, the Trust has been at the forefront of some of the key clinical trials and studies that have led to life-saving treatments for COVID-19. For example, Denmark Hill was the first site in the UK to recruit patients to global clinical trials of

remdesivir, an antiviral which became the first licensed treatment for COVID-19. The RECOVERY trial, which launched at the Trust in late March 2020, has already led to availability of the first life-saving drug for people hospitalised with COVID-19 - Dexamethasone, a widely available anti-inflammatory steroid. Observational studies such as the SIREN study - to which almost 500 of our staff were recruited - have provided valuable information about the immune response to Sars-CoV-2 and the efficacy of vaccines. Furthermore, clinical trials of Novavax's COVID-19 vaccine, which were quickly

delivered at the Trust, have found that the vaccine was able to prevent severe COVID-19 and is currently awaiting approval by UK regulatory bodies.

In the next two sections of this booklet, we highlight the clinical trials and studies undertaken by our research staff that have led and will continue to lead to life-saving discoveries and significant improvements to the lives of people affected by COVID-19 at our Trust, across the UK and around the world.

Urgent Public Health Studies

At the start of the COVID-19 pandemic, the Chief Medical Officer identified specific studies and trials to be prioritised over other research in order to inform national policy and discover new diagnostic tests, treatments and vaccines to tackle COVID-19. These are termed 'Urgent Public Health (UPH) Studies' and are supported by the NIHR Clinical Research Network (CRN).

As such, all CRN and NIHR infrastructure funded staff are prioritised to work on UPH-badged studies, with study set-up times advised to be within 9 days of being taken on by the Trust. In the first year of the pandemic, many non-COVID-19 studies were paused so that research staff could concentrate on delivering UPH-badged studies.

Many UPH studies are interventional clinical trials of new treatments, such as the high-profile RECOVERY trial and commercial trials of a COVID-19 vaccine, whereas others are important observational studies such as the SIREN study. Since their launch, many of these studies have resulted in the licensing of new and existing therapies for the treatment of COVID-19 as well as providing important information the nature of Sars-CoV-2 infection, how it spreads through the community and the impact of vaccination and natural immunity.

Delivering these studies required a huge amount of cross-departmental teamwork between Research Delivery Units (RDUs) at the Trust. As one of CRN South London's partner organisations, KCH continues to spearhead and be involved with a number of UPH studies.

Safety and Antiviral Activity of Remdesivir for severe COVID-19

Commercial Phase 3 interventional clinical trials funded and sponsored by Gilead Sciences Inc.

Led by Dr Mark McPhail at Denmark Hill

About
KCH was the first site in the UK to open and recruit patients to Gilead's international clinical trials of the antiviral drug remdesivir. Two studies were carried at Denmark Hill, with one testing the potential benefits of remdesivir in patients with severe COVID-19 infection and another testing its potential benefits in those with moderate COVID-19 infection. The research team, led by Dr Mark McPhail, recruited around 30% of the total UK cohort to both of these studies.

Rationale
Remdesivir is an antiviral drug which has been previously investigated as a treatment for Ebola. In the lab, remdesivir was shown to tackle animal infections related coronaviruses SARS and MERS, and so researchers hoped that the drug would be of benefit to patients with COVID-19 infection.

Outcome
Early data showed that remdesivir reduced the recovery time of those with severe COVID-19 by around four days. As a result, the drug was made available on the NHS to people with severe COVID-19 via the via the Medicine and Healthcare products Regulatory Agency (MHRA). Remdesivir was therefore the first drug made available for the treatment of COVID-19 infection and is currently used at KCH.

KCH was the first site in the UK to open and recruit patients to Gilead's international clinical trials of remdesivir

Remdesivir was the 1st drug available in UK to treat COVID-19

Novavax COVID vaccine study

Commercial Phase 3 interventional clinical trial funded and sponsored by Novavax

Led by Dr James Galloway at the NIHR Wellcome King's Clinical Research Facility

About
KCH was one of 35 sites across the UK that held Phase 3 clinical trials of Novavax's vaccine for COVID-19. Held at the NIHR Wellcome King's Clinical Research Facility (King's CRF) at KCH's Denmark Hill site, more than 220 people were enrolled in the study, which was above the recruitment target for the site.

Rationale
The Novavax NVX-CoV2373 COVID-19 vaccine consists of a recombinant version of parts of the Sars-CoV-2 spike protein, which the virus uses to infect human cells. Combined with their patented Matrix-M adjuvant, the study leads hoped that this vaccine would immunise participants against COVID-19 in the real world, reducing symptoms and preventing hospitalisation and death from the virus.

Outcome
Results from the trial found that two doses of the Novavax NVX-CoV2373 COVID-19 vaccine provided 89.7% protection against mild to moderate disease – regardless of whether this was caused by the original UK Sars-CoV-2 variant or the widespread 'Kent' variant which emerged in December 2020. There were also no instances of serious COVID-19 (hospitalisation or death) in those that received the vaccine and side effects were minimal. Novavax has been approved by the FDA and is in use across the United States, and is now awaiting regulatory guidance from the MHRA.

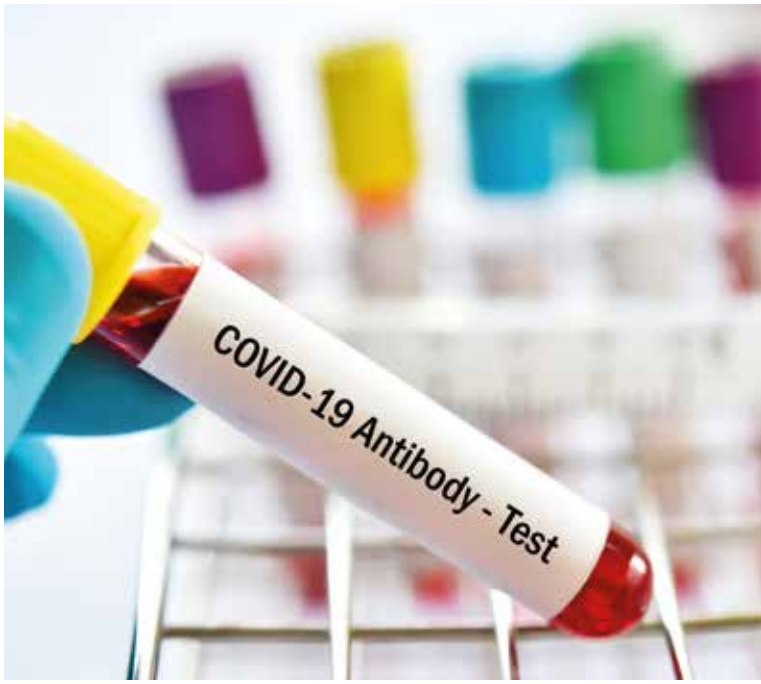
A trial participant receives a dose of either the Novavax NVX-CoV2373 vaccine or placebo at the King's CRF

SIREN

Non-commercial observational study funded and sponsored by Public Health England

Led by Professor K Ray Chaudhuri at Denmark Hill and the PRUH

About
The Sars-CoV-2 Immunity & REinfection EvaluatioN (SIREN) study was launched by Public Health England in healthcare settings across the UK, including the Denmark Hill and Princess Royal University Hospital (PRUH) sites of KCH. The study aims to determine whether the presence of Sars-CoV-2- specific antibodies can prevent people being infected with the virus, causing COVID-19 disease and so healthcare workers were selected due to their potentially frequent contact with those with COVID-19. Blood tests or nasal swabs were taken from participants every two weeks in order to detect antibodies for Sars-CoV-2 or viral genetic material.



Rationale
By carrying out either a blood test (to detect antibodies to Sars-CoV-2) or a PCR test (to detect viral genetic material), researchers are able to determine who has previously been exposed to Sars-CoV-2 and who is currently infected. By analysing information, researchers can determine whether the presence of antibodies can prevent reinfection - as well as determining how long the antibodies and/or the protection conferred by them lasts. Furthermore, following the introduction of COVID-19 vaccines to NHS staff at the beginning of 2021, researchers can also analyse their effects on the spread of Sars-CoV-2.

Outcome

4 in 5 people infected with Sars-CoV-2 were protected from reinfection for up to 9 months

A single dose of a COVID-19 vaccine made people 72% less likely to develop infection – rising to 86% after a 2nd dose

Vaccine protection started 2 weeks after the 1st dose - but protection was highest from 2 weeks after the 2nd dose

Platform trials

Platform trials are a new method of efficiently determining whether a number of different drugs are effective in a range of people. Unlike traditional clinical trials, which generally ask whether a particular drug is effective in a specific group of patients, platform studies allow for the evaluation of multiple drugs or other interventions simultaneously, with scope for the quick addition of new, promising drugs, or elimination of those that aren't effective. In a global COVID-19 pandemic, platform trials have allowed for the rapid discovery of effective treatments for COVID-19.

REMAP-CAP

- **Non-commercial interventional platform trial funded by the European Commission and led by University Medical Centre Utrecht**
- **Led by Dr Phil Hopkins at the PRUH and Denmark Hill**

About
REMAP-CAP (A Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia) is a global platform trial that was launched in 2016 to find effective therapies and interventions for the treatment of community acquired pneumonia - with a focus on disease caused by pandemics. When the COVID-19 pandemic began at the end of 2019, the trial was adjusted to determine the best range of treatments for patients who became severely ill due to COVID-19. Since the start of the pandemic, REMAP-CAP has enrolled over 14,000 participants with suspected or confirmed COVID-19 at 330 sites around the world. At the Trust, the ACET research team, led by Dr Phil Hopkins, have enrolled 59 participants.

Rationale
Forty-eight interventions are currently or have completed being evaluated as treatments for COVID-19, and the variety of treatments reflects the multiple pathologies of the disease. At the Trust, 14 different drugs and therapies were or are currently being trialled can be roughly grouped into the following areas:

1) Immunomodulatory: these drugs work to dampen down or change the way the immune system responds to the infection as many cases of severe COVID-19 have been attributed to over-activation of the immune system.

2) Anti-replication: these drugs stop the replication of the virus, preventing further infection.

3) Anti-clotting: anti-clotting drugs prevent the formation of dangerous and sometimes fatal blood clots in patients with COVID-19.

4) Anti-bacterial: some patients with severe COVID-19 can have associated bacterial infections which may impede recovery. Furthermore, some licensed antibiotics have some antiviral properties.

Outcome
So far, the trial has found that immunomodulators tocilizumab and sarilumab, which block the action of pro-inflammatory cytokine IL-6, reduced the risk of death by 24% if given to people with severe COVID-19 within 24 hours of admission to ICU. Both drugs are now recommended by NICE for the treatment of selected patients with severe COVID-19.

The RECOVERY Trial

- **Non-commercial interventional platform trial funded by UK Research and Innovation and led by the University of Oxford**
- **Led by Dr Mark McPhail at Denmark Hill and the PRUH**

About
The RECOVERY (Randomised Evaluation of COVID-19 Therapy) trial is an international platform trial aimed at finding effective treatments for those hospitalised with confirmed or suspected COVID-19. Globally, there are 185 active sites and 41,529 participants. Researchers led by Dr Mark McPhail from the Liver RDU recruited 310 participants to the study across both the PRUH and Denmark Hill sites, more than tripling the recruitment target of 100. To date, 13 different drugs, treatments or interventions have been or are being trialled on people hospitalised with COVID-19.

Rationale
By testing a number of different types of drugs therapies and interventions simultaneously, the RECOVERY trial allowed for people hospitalised with COVID-19 to quickly access potentially life-saving drugs. The rationale for each drug differs depending on their mechanism of action. Most of the drugs trialled at KCH can be loosely grouped into four areas:

1) Anti-inflammatory: these drugs work to dampen down potentially harmful over-reactive inflammatory immune responses that are common in severe COVID-19 cases.

2) Anti-replication: these drugs prevent the virus from replicating in human cells, overall reducing viral load in the patient and preventing severe infection.

3) Anti-clotting: anti-clotting drugs prevent the formation of dangerous and sometimes fatal blood clots in patients with COVID-19.

4) Virus-neutralising: these therapies prevent the virus from attacking human cells and reduce infection.

Outcome
Since its launch in March 2020, the RECOVERY trial has had a number of impactful results that have changed the course of COVID-19 infection for tens of thousands of people around the world. In June 2020, researchers on the study found that low doses of the low-cost anti-inflammatory steroid dexamethasone could save the lives of up to a third of people in hospital with severe COVID-19. Since being licensed for use in these patients, it's been estimated that the drug has saved the lives of over a million people globally and over 22,000 in the UK alone. Next, immunotherapy tocilizumab, which is usually used to treat rheumatoid arthritis, was also found to save the life of one in 25 patients in hospital with severe COVID-19. It is now recommended for use in these patients by NICE.

The most recent findings from the study have revealed the REGENERON's lab-formulated cocktail of antibodies can prevent death from COVID-19 in those who haven't mounted an immune response. Importantly, the RECOVERY trial also identified treatments that did not help patients with COVID-19, such as the widely-publicised drug hydroxychloroquine.

IT IS ESTIMATED THAT DEXAMETHASONE HAS SAVED OVER 1,000,000 LIVES GLOBALLY & OVER 22,000 IN THE UK ALONE

TACTIC-R

- **Non-commercial interventional Phase 4 platform trial funded by Ely Lilly and Company and Alexion Pharmaceuticals, sponsored by Cambridge University**
- **Led by Dr James Galloway at the PRUH and Denmark Hill**

About
Early on in the pandemic, it was noted that aside from COVID-19 infection itself, overactivation of the immune system led to an inflammatory attack on patients' organs, leading to organ damage and frequently resulting in ICU admission and death. To tackle this, The TACTIC-R (Multiarm Therapeutic study in pre-ICU patients admitted with COVID-19 - Repurposed Drugs) trial was launched in the UK and at KCH in May 2020. The aim of the study was to test licensed immunomodulatory drugs baricitinib and ravulizumab for their ability to prevent organ damage and admission to ICU due to COVID-19. By testing licensed treatments, if proven to be effective these therapies could quickly be used in healthcare settings across the UK.

The study, led by Dr James Galloway, had three treatment arms; one testing the effects of immunotherapy baricitinib, a licensed drug for the treatment of rheumatoid arthritis, the other testing the effects of ravulizumab, a licensed therapy for the treatment of paroxysmal nocturnal haemoglobinuria, and a third arm for comparison, where participants received standard care. The study team at the Trust recruited more than ten times the initial target of ten participants, with 113 total participants enrolled.

ILIAD-7

- **Commercial Phase 2 interventional clinical trial funded and sponsored by Revimmune**
- **Led by Dr Georg Auzinger at Denmark Hill.**

About
T cells are a key immune cell that are central to antiviral immunity, however a lack of T cells is a common feature of COVID -19 infection and is associated with the development of severe infection. The cytokine molecule IL-7 is naturally produced in the body and kick-starts the growth and maturity of T cells. In the ILIAD-7 trial, researchers are testing test the safety and efficacy of lab-produced IL-7 in boosting T cell numbers in those with COVID-19 and low T cell numbers. Researchers will assess whether boosting T cell numbers in this way helps participants on the trial them fight off the infection and reducing patient mortality and morbidity. Led by Dr Georg Auzinger, Clinical Director for Critical Care, alongside the ACET research team, the study reached its recruitment target, treating five participants at the Trust.

REALIST

- **Non-commercial Phase 2 interventional clinical trial funded by the Public Health Agency for Northern Ireland and the Wellcome Trust, and sponsored by Belfast Health and Social Care Trust**
- **Led by Dr Phil Hopkins at Denmark Hill**

About
A life-threatening complication of COVID-19 is Acute Respiratory Distress Syndrome (ARDS), characterised by widespread inflammation in the lungs, leading to lung damage and failure. Umbilical cord-derived Mesenchymal Stem Cells (MSCs) are able to turn into many different types of cells and, due to this, have been previously investigated for their potential for tissue healing and regenerative abilities. In the REALIST (Repair of Acute Respiratory Distress Syndrome by Stromal Cell Administration) trial, researchers aimed to test whether an infusion of mesenchymal stem cells could assist in the repair of lung tissue, leading to the resolution of ARDS and reducing patient mortality and morbidity. This study, led by Dr Phil Hopkins alongside the Critical Care team, has so far recruited five out of its target of ten patients.

PHOSP-COVID

- **Non-commercial observational study funded by NIHR and UK Research and Innovation and sponsored University of Leicester**
- **Led by Professor Ajay Shah at Denmark Hill**

About
As a new virus, little is known about the long-term effects of Sars-CoV-2 infection and COVID-19, the symptomatic disease it causes. In particular, how these effects may differ between people of different age, race and sex as well as between people with different severity of COVID-19 infection is completely unknown. The PHOSP-COVID (Post-hospitalisation COVID-19) study aims to gain insight into the long-term physical and psychological effects of COVID-19 by recruiting COVID-19 patients following their discharge from hospital and studying the effects of the disease over the short-term (0-3 months), medium term (3-6 months) and long term (6-12 months). Using data from health and social care records alongside other metrics including those from biological samples, researchers hope to determine the impact COVID-19 has on health in the long-term.

The PHOSP-COVID study team at KCH, led by Professor Ajay Shah, have recruited 155 participants so far—over half of their target. Alongside colleagues from participating sites across the UK, the team have already found that seven in ten participants had not fully recovered from COVID-19 five months after discharge—and that those who were most likely to experience persistent symptoms were middle-aged white women with at least two co-morbidities. 'Brain fog' was also a common symptom experienced in older male participants and all but the most mild of post-hospital cases had elevated levels of C-Reactive Protein (CRP), a biomarker of inflammation.

RUX-COVID

- **Commercial interventional Phase 3 clinical trial funded and sponsored by Novartis**
- **Led by Dr Victoria Potter at Denmark Hill**

About
Infection with Sars-CoV-2 can result in overactivation of the immune system, leading to an influx of inflammatory immune cells to the lungs, resulting in fluid build-up and lung damage, also known as pneumonia. The most common cause of deterioration in COVID-19, pneumonia can put patients with COVID-19 at serious risk of requiring Intensive Care Unit (ICU) admission, mechanical ventilation or death.

In a global Phase 3 clinical trial, licensed immunotherapy ruxolitinib was tested in patients with COVID-19 and pneumonia at KCH to see if the drug could safely prevent ICU progression, requiring mechanical ventilation or death.

Rationale
Developed by Novartis, ruxolitinib is an immunotherapy which interferes with upstream signalling pathways that lead to the expression of a number of pro-inflammatory cytokines, modulating and also suppressing inflammation. Researchers on the RUX-COVID trial hoped that it would reduce cytokine production and influx, in turn reducing immune-mediated lung damage and preventing further patient deterioration.

KCH was the first site in the UK to open both trials simultaneously

CANCOVID

- **Commercial interventional Phase 3 clinical trial funded and sponsored by Novartis**
- **Led by Dr Vishal Patel at Denmark Hill**

About
Cytokine Release Syndrome (CRS) is a life-threatening condition where a excessive number of pro-inflammatory cytokines are released from immune cells, causing the immune system to go into 'overdrive' and cause tissue damage and organ dysfunction and failure. Due to its inflammatory nature, CRS is often observed alongside pneumonia, with both conditions potentially leading to patients requiring mechanical ventilation in ICU and, in some cases, death.

In a global Phase 3 clinical trial, licensed immunotherapy canakinumab was given to patients at KCH with COVID-19-associated CRS and pneumonia to see if it could safely prevent ICU progression, mechanical ventilation or death.

Rationale
Canakinumab, developed by Novartis, is an immunotherapy which targets and blocks the action of the pro-inflammatory cytokine IL-1, suppressing inflammatory responses in immune cells. Researchers involved in the CANCOVID trial hoped that canakinumab would suppress inflammatory immune responses in COVID-19 patients with CRS and pneumonia, preventing further tissue and organ damage and halting deterioration.

Outcome
Neither canakinumab nor ruxolitinib made a difference in the severity of COVID-19, or reduced the number of patients who were admitted to ICU, mechanically ventilated or died. However, Novartis vow to keep working with the medical community to understand the pathology of COVID-19.

RECOVERY - Respiratory Support

- **Non-commercial interventional Phase 3 clinical trial funded by the Department of Health and sponsored by the University of Warwick**
- **Led by Dr Kai Lee at Denmark Hill and Dr Deepak Rao at the PRUH**

About
COVID-19 can cause serious breathing difficulties—in particular in those hospitalised with the disease. There are currently a number of breathing support methods in clinical practice, however it was important to determine which method resulted in the best outcome for patients with COVID-19. The RECOVERY Respiratory Support (Recovery RS) study recruited up to 4,000 patients from over 60 hospitals across the UK and compared the impact of either High Flow Nasal Oxygen (HFNO), Continuous Positive Airway Pressure (CPAP) or normal care involving standard oxygen therapy on patient survival and their need for mechanical ventilation. Across the Trust, 19 patients have been recruited so far.

Outcome
In August 2021, the NIHR announced that CPAP reduced the need for mechanical ventilation in patients with COVID-19, while HFNO and standard oxygen therapy made no difference. Following these important findings, the study researchers urged that. Following these important findings, study researchers urged that CPAP should be considered for hospitalised patients with COVID-19 needing increasing oxygen in order to reduce the need for invasive ventilation and relieve pressure on intensive care services.

GenOMICC

- **Non-commercial observational study funded by the Wellcome Trust and sponsored by NHS Lothian and the University of Edinburgh**
- **Led by Dr Mark McPhail at the PRUH and Denmark Hill**

About
The GenOMICC (Genetics of Susceptibility and Mortality in Critical Care) study launched at KCH in 2016 to gather information on the genetic profiles of people admitted to the Critical Care department in order to determine how a person's genetic make-up influences their susceptibility to certain infections and severe injury. As the COVID-19 pandemic swept the nation in March 2020, COVID-19 patients admitted to KCH were enrolled into GenOMICC, with all participants having blood taken for analysis.

Researchers can analyse and compare DNA and immune cells from these samples to those of healthy controls to see if any particular genetic or cellular markers make a person more or less likely to have severe COVID-19 infection. If found, these markers could help hospital staff to use and prioritise existing treatments better as well as helping to design new treatments to prevent or stop severe COVID-19.

Across the Trust, 257 participants have been enrolled in the GenOMICC study so far, with research staff from multiple teams pulling together to recruit patients during the pandemic.

ISARIC
Clinical Characterisation Protocol for Severe Emerging Infection

- **Non-commercial observational study funded by the Wellcome Trust and sponsored by the University of Oxford led by University Hospital Southampton NHS Foundation Trust**
- **Led by Professor Frank Post at the PRUH and Denmark Hill**

About
ISARIC (International Severe Acute Respiratory and emerging Infection Consortium) is a global federation of clinical research networks whose key aim is to provide a coordinated and agile research response to outbreak-prone infectious diseases such as COVID-19. While designed for any severe emerging infection, the Clinical Characterisation Protocol (CCP) is now being used at the Trust to gain an understanding of the pathology of COVID-19 in order to, ultimately, develop better treatments for the disease.

ISARIC involves recording patient data as well as taking medical and genetic samples in order to understand how the Sars-CoV-2 virus virus grows in the body, how the immune system responds to it and what, if any, genetic factors put people at risk for severe infection. Researchers hope that these data will then be used to inform treatment development programs as well as public health measures. So far, 199 people have been recruited to the study at the Trust.

The PRIEST study

- **Non-commercial observational study funded by the NIHR and sponsored by the Sheffield Teaching Hospitals NHS Foundation Trust**
- **Led by Dr Fleur Cantle at the PRUH and Denmark Hill**

About
The PRIEST study (Pandemic Respiratory Infection Emergency System Triage) was a national observational study that aimed to determine the best triage system for patients coming into hospitals with respiratory infections such as COVID-19. Led by Emergency Care Speciality Lead Dr Fleur Cantle, the PRIEST study enrolled patients using the emergency care system (111 and 999 calls), ambulance conveyance, or hospital emergency department) with suspected respiratory infections. The triage method used and the patients' medical data was used to determine the most accurate triage method for predicting severe illness, as well as identifying the optimal treatment pathways to use for the best patient outcomes. Now closed for recruitment, across the UK the PRIEST study recruited four times its recruitment target of 20,000, with over 80,000 people enrolled in the study.

OCTAVE

- **Non-commercial observational study sponsored by the University of Birmingham**
- **Led by Dr Robin Sanderson at Denmark Hill**

About
Since early 2021, COVID-19 vaccines have been made available to most of the adult population in the UK, and were particularly welcomed by those with chronic conditions that impair the immune system, such as cancer, inflammatory arthritis and kidney or liver disease, as there is thought to be a higher risk of severe COVID-19 in people in these groups. However, due to their general exclusion from vaccine studies, there is a lack of data to show how well vaccines immunise people in these groups and protect them against COVID-19.

The OCTAVE (Observational Cohort Trial -T-cells Antibodies and Vaccine Efficacy in SARS-CoV-2) study aimed to determine the impact of vaccination against COVID-19 on people with chronic conditions that impair immunity. Researchers across the UK analysed blood samples from up to 5,000 people with impaired immune systems before or after full COVID-19 vaccination. They found that 40% of people in the study mounted a low antibody response after two Sars-CoV-2 vaccines, and around 11% of immunocompromised patients failed to generate any antibodies at all.

Results from this study were used to inform a further trial, OCTAVE DUO, which aims to analyse the efficacy of a third, 'booster' vaccine dose in these groups and is currently being carried out at the Trust.

CLARITY

- **Non-commercial observational study funded by Roche and sponsored by the Royal Devon and Exeter NHS Foundation Trust**
- **Led by Dr Alexandra Kent at Denmark Hill**

About
Inflammatory bowel disease affects around 1% of the UK population and is generally treated with immunosuppressive drug, yet a common side effect is an increased risk of infection.

The UK-wide CLARITY (impaCt of bioLogic therApy on saRs-cov-2 Infection & immunity) study aimed to investigate the impact certain immunosuppressant drugs have on immune responses to Sars-CoV-2 infection or immunisation against the virus to help improve the relevant public health and vaccination strategies.

Researchers across the UK, led at Denmark Hill by Dr Alexandra Kent, measured antibody responses to either Sars-CoV-2 infection or COVID-19 vaccination in patients receiving the immunosuppressive drug infliximab, one in a family of anti-TNFα drugs, which is known to impair immune responses particularly to respiratory infections.

So far, researchers have found that fewer than half of those receiving infliximab had detectable antibodies following infection with the virus. Furthermore, around a third of people receiving infliximab made a robust antibody response to a single dose of a COVID-19 vaccine. However, a small number of people in this group who either had a Sars-CoV-2 infection or prior to vaccination or a second dose of the vaccine made a robust antibody response, suggesting that an effective booster strategy could enable people taking infliximab and related immunosuppressants to be fully immunised against COVID-19.

COVID-CNS

- **Non-commercial observational study funded by the NIHR and MRC's COVID-19 Rapid Response and sponsored by Cambridge University Hospitals NHS Foundation Trust**
- **Led by Dr Daniel van Wamelan at Denmark Hill**

About
Around 20-30% of patients hospitalised with COVID-19 suffer neurological and psychiatric problems, such as stroke, Parkinsonism, encephalitis and psychosis. Similar problems have been seen in previous pandemics, including Spanish influenza over 100 years ago, but how and why this occurs is poorly understood. The COVID-CNS study aims to collect and analyse various data from participants who have had COVID-19 and experienced neurological and psychiatric problems, ranging from clinical notes and electronic records to brain injury, virologic and immunological mechanisms in cerebral spinal fluid. By combining and understanding these factors, researchers on the COVID-CNS study should be able to stratify patients into clinical care pathways and trials using existing and novel therapies.

NHS-CHECK: Health & Experiences of staff working at NHS Trusts and Nightingale Hospitals

- **Non-commercial observational study funded by NIHR Health Protection Research Unit in Respiratory Infections at Imperial College and sponsored by King's College London**
- **Led by Professor K Ray Chaudhuri at Denmark Hill**

About
Pandemics expose healthcare workers to overwork and exhaustion, discrimination, isolation from friends, family and other support networks and an increased risk of developing mental health disorders. This has been confirmed by early evidence from Wuhan China, where the current COVID-19 pandemic initially took hold. Further data also showed that early signs of distress could lead to mental health disorders as well as impairing decision-making, attention and understanding that ultimately hindered initial control of the pandemic.

The NHS CHECK study aimed recruit around 60,000 NHS staff to investigate the short, medium and longer-term impact of the COVID-19 pandemic on staff performance and well-being. Data will be collected via an online survey at 3, 12 and 18 months from the start of the initial survey, and researchers plan to continue assessments until 18 months after the lifting of social distancing measures.

COVID-19 Vacc Maternal Immunisation

- **Commercial Phase 2/3 interventional clinical trial funded and sponsored by Pfizer Inc.**
- **Led by Dr Nick Kametas and Senior Research Midwife Katherine Clark at Denmark Hill**

About
Pregnant women, especially those at 28 weeks gestation or more, have an increased risk of developing severe COVID-19 and, as such, are classified as clinically vulnerable. Following the vaccination of around 90,000 pregnant women in the United States with no safety concerns raised, Joint Committee on Vaccination and Immunisation (JCVI) has recently stated that pregnant women should be offered the COVID-19 vaccine at the same time as the rest of the population, however its safety and efficacy has yet to be formally validated in pregnant women.

The Pfizer-sponsored COVID-19 Vacc Maternal Immunisation study launched at Denmark Hill and Orpington in June 2021. The Phase 2/3 trial aims to evaluate the safety and efficacy of Pfizer-BioNTech's Sars-CoV-2 mRNA vaccine in healthy pregnant women between 24 and 34 weeks' gestation. In the Phase 2 portion, 50 women were randomised to receive two doses of the Pfizer-BioNTEch Sars- CoV-2 mRNA vaccine and monitored for its safety for seven days after the second dose. If found safe, the remaining 350 women will receive either the vaccine or the placebo and this will be monitored for its safety and efficacy in preventing COVID-19 infection in vaccinated pregnant women.

PAN-COVID - Pregnancy and neonatal outcomes in COVID-19

- **Non-commercial observational study funded by the Medical Research Council and sponsored by Imperial College London**
- **Led by Research Midwife Hayley Martin at the PRUH and Denmark Hill**

About
As yet, there has been no evidence to suggest that pregnant women are at an increased risk of severe infection from Sars-CoV-2 and COVID-19. However, the fact that other related coronaviruses have been shown to cause severe infection in this group means that pregnant women are included on the list of 'clinically vulnerable' people. Due to this gap in evidence, maternity services are developing their guidance for pregnant women using current guidance for non-pregnant women.

The aim of the PAN-COVID study is to create a global registry of women with either suspected or confirmed Sars-CoV-2 infection during pregnancy as well as their new babies. Researchers will collect data regarding a number of outcomes, such as pregnancy complications, gestational age at delivery, stillbirth, miscarriage and death of the baby or mother. The data will then be used to better understand the impact of COVID-19 on mothers and their babies and guide improved treatment and prevention methods. So far, the study has vastly exceeded its recruitment target across the Trust, with 191 participants recruited so far – almost five times that of the original target of 40 participants.

Coronavirus infection in immunosuppressed children

- **Non-commercial study led by University Hospital Southampton NHS Foundation Trust**
- **Led by Dr Sanjay Bansal at Denmark Hill**

About
Immunosuppression is thought to be a risk factor for developing severe COVID-19 infection, and those on immunosuppressive drugs or those with conditions which alter the way their immune systems work are currently included on the UK Government's list of Extremely Clinically Vulnerable people and are advised to shield at home. However, it is unclear within this group what specific factors could lead to severe COVID-19 infection.

The aim of this study is to allow families of immunosuppressed children and young people to self-record their experiences of COVID-19 and other viral respiratory illnesses during the COVID-19 epidemic. Participants are provided with online information and asked to fill in online questionnaires at baseline and weekly thereafter. Information collected includes medications which affect the immune system, symptoms, contact with health care providers, test results and impact on daily activities. Data will be collected and analysed weekly to monitor any potential risk factors for severe disease.

This study is complementary to, and not overlapping with, the global ISARIC World Health Organisation protocol that will be studying COVID-19 cases admitted to all NHS Trusts, including all children.

FALCON COVID-19

- **Non-commercial observational study led by the University of Manchester NHS Foundation Trust**
- **Led by Dr Tara Smith at Denmark Hill**

About
Accurate diagnosis of infection, identification of immunity and monitoring the clinical progression of Sars-CoV-2 infection are of paramount importance to the UK's response to the pandemic. Widespread population testing was difficult as it was limited by test availability, human resources and long test turnaround times. This limited the ability to control the spread of infection and to develop effective clinical pathways to enable early social isolation of infected patients and early treatment for those most at risk.

The life sciences industry responded by developing multiple new in vitro diagnostic tests (IVDs) that provide diagnosis of active infection, analysis of the immune response to Sars-CoV-2 infection and prediction of prognosis of those with suspected or confirmed infection. To be used confidently, these tests require efficient yet robust clinical evaluation and so the FALCON COVID-19 study was designed to evaluate the multiple assays.

Medicago Coronavirus-Like Particle COVID-19 Vaccine

- **Commercial Phase 3 interventional clinical trial sponsored by Medicago R&D Inc.**
- **Led by Dr James Galloway at the King's Clinical Research Facility**

About
Vaccination is a highly effective in reducing transmission of Sars-CoV-2 and protecting people from the most serious effects of COVID-19. Canadian biopharmaceutical company Medicago's CoVLP vaccine consists of a plant-derived viral-like particle made up of lab-formulated replicas of the Sars-CoV-2 spike protein - the part of the virus which the immune system naturally mounts a response against - alongside an immune response-boosting adjuvant.

Global Phase 3 trials of the vaccine aimed to test the safety and efficacy of two doses of the vaccine, given three weeks apart, in preventing symptomatic COVID-19, serious disease and death. At the Trust, the trial was held at the King's Clinical Research Facility at Denmark Hill and led by Dr James Galloway. The 'crossover' design of the trial ensured that all participants received the full experimental dose at some point in the study, as those who received the experimental vaccine for the first two dosings would then go on to receive a placebo for the last two dosings, whereas those receiving a placebo for the first dosing would then receive the experimental vaccine for the last dosing.

DIAMONDS Search

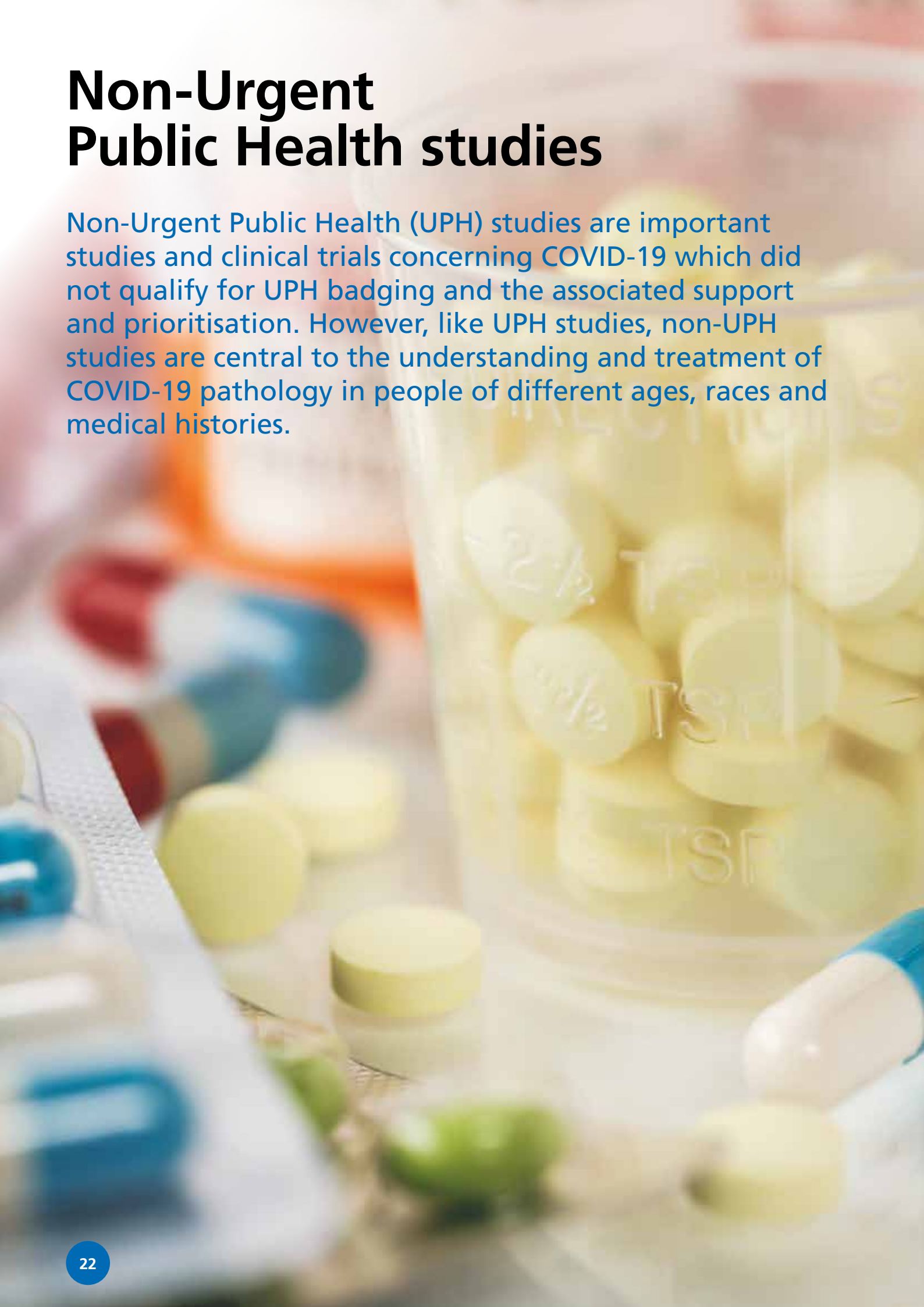
- **Non-commercial observational study led by Imperial College London**
- **Led by Dr Akash Deep at Denmark Hill**

About
The DIAMONDS (Diagnosis and Management of Febrile Illness using RNA Personalised Molecular Signature Diagnosis) project is a five-year EU-funded Horizon 2020 research initiative that was initially launched at the beginning of 2020 to develop a molecular test based on personalised gene signatures which could quickly diagnoses serious infections and inflammatory diseases. However, at the start of the COVID-19 pandemic, this study was altered to focus on the development of RNA-based diagnostics to help guide the clinical management of patients with confirmed or suspected Sars-CoV-2 infection.

Researchers working on the DIAMONDS Search study aim to recruit people of all ages with mild to severe COVID-19 and take blood samples which will allow for the measurement of and determination of host gene expression that can differentiate between the different manifestations of COVID-19. Going forward, this will enable healthcare workers to quickly diagnose Sars-CoV-2 infection, but also to personalise treatment depending on the underlying pathology of the disease in each person.

Non-Urgent Public Health studies

Non-Urgent Public Health (UPH) studies are important studies and clinical trials concerning COVID-19 which did not qualify for UPH badging and the associated support and prioritisation. However, like UPH studies, non-UPH studies are central to the understanding and treatment of COVID-19 pathology in people of different ages, races and medical histories.



COVID Dialysis Case series - Risk Factors, Characteristics and Outcomes of CoVID-19 Positive Dialysis Patients

This observational study, led by Dr Eirini Lioudaki at Denmark Hill, aimed to describe demographic, clinical, laboratory, and radiological characteristics, risk-factors and outcomes of dialysis patients with COVID-19 in order to improve their clinical management.

SPARC-1 - SARS-nCoV Pediatric AKI Registry and Collaborative

This is an observational study, led by Dr Akash Deep at Denmark Hill, that aims to determine the prevalence, rate and severity of Acute Kidney Injury in children with suspected or confirmed children with COVID-19 that have been admitted into paediatric intensive care.

AKI biomarkers in COVID-19

Acute Kidney Failure (AKI) is common in people that are critically ill with COVID-19 and those affected have an increased mortality risk. Two biomarkers, TIMP-2 and IGFBP7 can predict AKI, yet it is unknown whether these can be used to predict AKI in patients severely ill with COVID-19 and so this observational study, led by Professor Gudrun Kunst, aims find out whether these biomarkers can be of use or whether other biomarkers must be used in these patients.

COVID SALES: Radiological assessment of the lung apices for abnormalities consistent with Sars-CoV-2 infection in acute stroke CT studies

COVID Sales, led at the PRUH and Denmark Hill by Dr Tom Booth, is an observational study that aims to see whether Computed Tomography (CT) scans performed on people with suspected stroke can also help to diagnose Sars-CoV-2 infection via detection of pulmonary changes in lung apices. If effective, this may lead to increased detection of active Sars-CoV-2 infection, allowing for earlier treatment and better protection for associated hospital staff.

COVIDTrach: a UK national cohort study of mechanically ventilated COVID-19 patients undergoing tracheostomy

COVIDTrach, led by Dr Kathleen Fan at the PRUH and Denmark Hill, is a collaborative observational study that analyses the outcomes of ventilated COVID-19 patients that undergo a tracheotomy, as it is currently unclear whether and to what extent these patients benefit from this procedure. Furthermore, as health care professionals may be put at increased infection risk from performing the procedure, COVIDTrach will also examine the rates of Sars-CoV-2 infection in these staff.

CovPall: improving palliative care for COVID-19 patients

The CovPall study, led by Professor Irene Higginson at the PRUH and Denmark Hill, set out to survey healthcare professionals in palliative care services and hospices to find out how they were responding to the COVID-19 pandemic as well as the problems they were facing.

MK-4482 Study in Non-Hospitalised Adults with COVID-19

This Phase 2/3 commercial interventional clinical trial aimed to test the safety and efficacy of biopharmaceutical company Merck's novel antiviral MK-4482 (Molnupiravir) for the treatment of COVID-19. Having a broad-spectrum of efficacy against many viruses and other coronaviruses, researchers, led by Dr Kosh Agarwal at Denmark Hill, aimed to find out if Molnupiravir reduced COVID-19 symptoms as well as determining its optimum dosage in non-hospitalised participants.

MK-4482 Study in Hospitalised Adults with COVID-19

In this Phase 2/3 commercial interventional clinical trial led by Dr Kosh Agarwal at Denmark Hill, hospitalised participants with COVID-19 were given either MK-4482 (Molnupiravir) or a placebo to see if Molnupiravir reduced COVID-19 symptoms as well as determining its optimum dosage in hospitalised participants.

TACTIC E: mulTi-Arm Therapeutic study in pre-ICu patients admitted with Covid-19 – Experimental drugs and mechanisms

TACTIC E is a non-commercial interventional platform trial, led by Dr James Galloway at Denmark Hill, which aims to see if experimental immunomodulatory therapies can prevent the progression of patients hospitalised with severe COVID-19 to organ failure or death.

ATOMIC2

The ATOMIC2 trial, led at Denmark Hill and the PRUH by Dr Fleur Cantle, is a Phase 2/3 clinical trial investigating whether the common antibiotic Azithromycin can prevent patients with confirmed COVID-19 from progressing to severe disease. Azithromycin is safe and inexpensive and has already been proven to have a range of antibacterial, anti-inflammatory and antiviral properties and so, if found to be effective, it may be delivered to patients quickly.

Symprove as an add-on to COVID-19 management

Many COVID-19 patients suffer gastrointestinal problems and experience major changes to their gut microflora. A probiotic called Sivomix was previously found to improve gastrointestinal symptoms in hospitalised patients with COVID-19 and reduce the requirement for mechanical ventilation. In this clinical trial, researchers led by Dr Bu Hayee aim to compare the potential benefits of another commercially available probiotic Symprove to Sivomix or a placebo in patients hospitalised with COVID-19.

SOAP study

This observational study, led by Dr Piers Patten, aims to determine how people with blood cancer or solid tumours respond immunologically to either Sars-CoV-2 infection and/or vaccination against the virus with a view to predicting how severe disease may be in this group and how protective vaccination may be. The trial is still open, yet researchers have already found that while those with solid tumours could fight COVID-19 in a similar way to those without cancer, people with blood cancer had a varied response to the infection and took many people longer to clear the infection.

COVID-19 infection in patients with haematological disorders

This observational study, led by Dr Pramila Krishnamurthy, aims to determine how COVID-19 affects people with haematological disorders. The immune systems of people in this group can be either be suppressed by the condition they are affected by or the drugs used to treat the condition, leaving them particularly vulnerable to infection.

PACE

The PACE study is an observational study led at Denmark Hill by Dr Pramila Krishnamurthy which aims to determine how patients receiving chemotherapy for Acute Myeloid Leukaemia (AML) respond to COVID-19 infection. Both AML and chemotherapy can impact the immune system, making patients more likely to pick up infections and so it is important to understand the risk that COVID-19 poses to this group.

IMET 1.0: Immunometabolism in sepsis, inflammation and liver failure syndromes

This study, led by Dr Mark McPhail at Denmark Hill and the PRUH, aims to better predict and diagnose infection complications in a number of conditions, including COVID-19. Sepsis occurs when the body's immune system has an abnormal response to infection causing one or more organs to fail. The immune and metabolic responses can be measured in blood and in breath and used to help clinicians to decide if a patient is at risk of or has sepsis. This study will seek to find why these changes occur and if simpler diagnostic tests can be produced.

BME Covid: Biological Mechanisms underlying susceptibility of BAME people to severe COVID-19 (BME-COVID)

People in Black and Minority Ethnic groups are disproportionately affected by severe COVID-19. BME Covid, led at Denmark Hill by Professor Ajay Shah, is an observational study which will examine potential biological pathways underlying this increased risk using data from existing cohorts and by genotyping patients hospitalised with COVID-19.

CoV-AFRICA: Long COVID in people with African Ancestry

This observational study, led by Professor Frank Post, consists of a mainly participant-focused questionnaire about possible long-term physical/mental health consequences of COVID-19, taking into account social-economic status, physical health, COVID-19 antibody status in those not yet vaccinated. More general measurements, such as levels of C-reactive protein (an marker of inflammation) as well biobanking of blood and urine will be carried out. Enrollment is currently taking place across the 14 Gen-Africa participating sites.

PIM-COV: The psychological impact of surviving an intensive care admission due to COVID-19 on patients in the UK

At the peak of the COVID-19 pandemic, patients reported significantly higher stress levels than healthy controls, and similar symptoms were reported a year later, with women being more likely to experience psychiatric problems than men. The PIM-COV study, led at Denmark Hill and the PRUH by Research Nurse Sian Saha, aims to assess the short- and long-term psychological impact on patients who have survived an admission to intensive care due to COVID-19, and identify possible predictors of anxiety, depression and trauma symptoms in this patient group.

GCS - NeuroCOVID paediatric substudy

Since the start of the COVID-19 pandemic, a range of mild to severe neurological complications have been reported by those infected with Sars-CoV-2, such as headache, loss of taste or smell, seizures, come and encephalitis. The Global Consortium Study (GCS) of Neurological Dysfunction in COVID-19, led by Dr Akash Deep, aims to determine the prevalence of neurological complications in people hospitalised with COVID-19, identify predictors of neurological complications and use a range of biomarkers to elucidate any potential mechanisms behind these complications. The GCS will also determine the impact of neurological complications on functional and cognitive ability following infection.

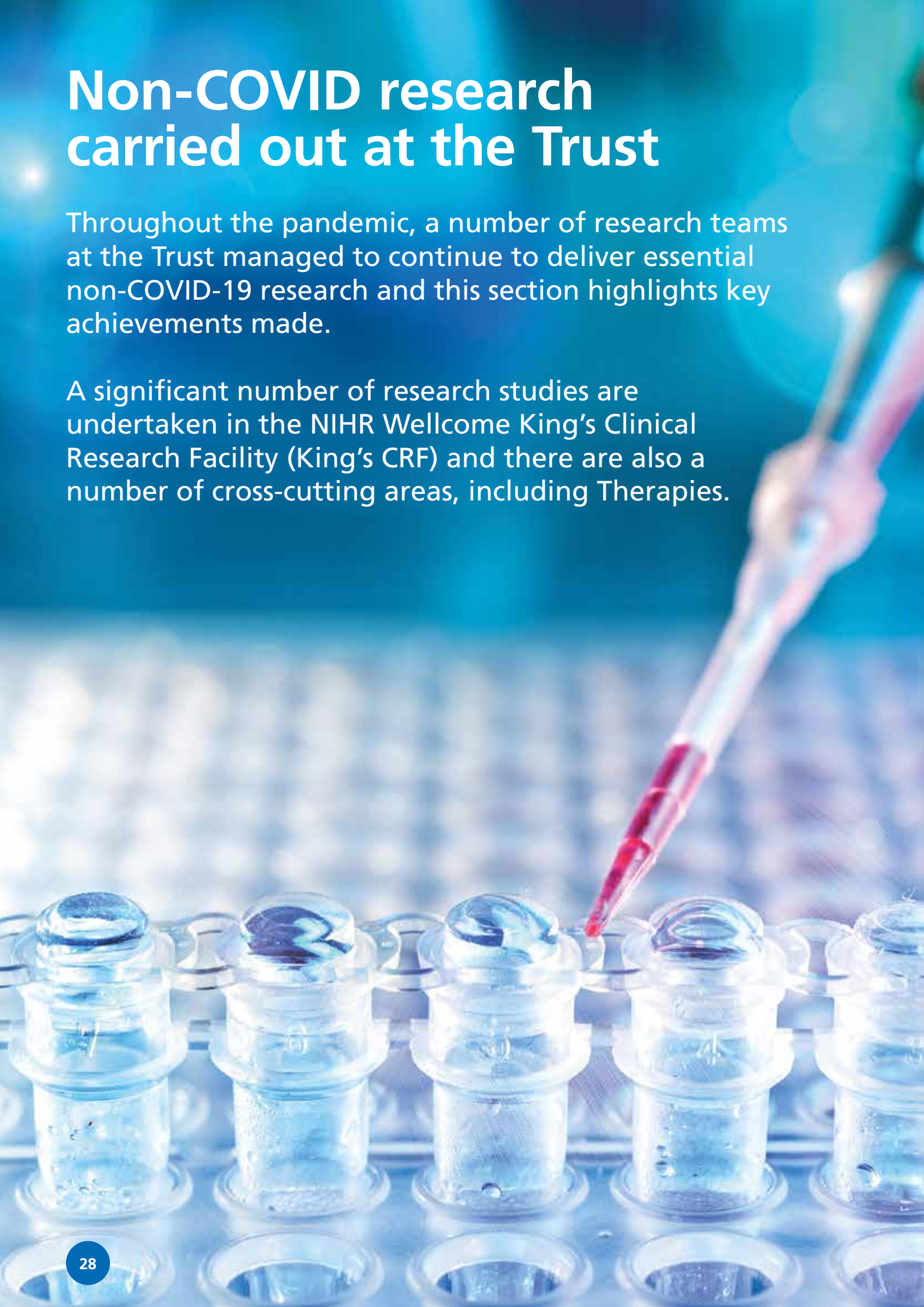
COVID-PD

COVID-19-related social isolation may have negative effects on vulnerable people living with long-term conditions such as Parkinson's disease, however social support and promoting activities of daily living lead to improvements in medication adherence, symptoms and environmental management. The COVID-PD study, led at Denmark Hill by Professor K Ray Chaudhuri, is collecting data from patient questionnaires to determine the quality of life of Parkinson's disease patients and how this impacts on their symptoms during the COVID-19 pandemic. Data will be compared to "Before Isolation' data already obtained in a study called NILS (Non-motor International Longitudinal Study).

Non-COVID research carried out at the Trust

Throughout the pandemic, a number of research teams at the Trust managed to continue to deliver essential non-COVID-19 research and this section highlights key achievements made.

A significant number of research studies are undertaken in the NIHR Wellcome King's Clinical Research Facility (King's CRF) and there are also a number of cross-cutting areas, including Therapies.



New RDU Structure

RDU 1 – Neurosciences, Stroke, Neuroradiology, Age and Aging

RDU Lead: Professor Ray Chaudhuri
Neurosciences Speciality Lead: Professor Ray Chaudhuri
Stroke Speciality Lead: Dr Laszlo Sztriha
Neuroradiology Speciality Lead: Dr Thomas Booth

RDU 2 – Cardiovascular and Breast Cancer

RDU Lead: Professor Theresa McDonagh
Cardiovascular Speciality Lead: Professor Theresa McDonagh

RDU 3 – Women's Health and Fetal Medicine

RDU Lead: Professor Kypros Nicolaides
Fetal Medicine Speciality Lead: Professor Kypros Nicolaides
Women's Health Speciality Lead: Dr Dudley Robinson

RDU 4 – Haematology, Precision Science and Palliative Care

RDU Lead: Dr Piers Patten
Heamatology Speciality Lead: Dr Piers Patten
Precision Science Speciality Lead: Dr Piers Patten
Palliative Care Speciality Lead: Dr Sabrina Bajwah

RDU 5 – Liver, Gastroenterology and Rheumatology

RDU Lead: Dr Mark McPhail
Liver Speciality Lead: Dr Mark McPhail
Gastroenterology Speciality Lead: Dr Alexandra Kent
Rheumatology Speciality Lead: Dr James Galloway

RDU 6 – Renal, Urology, Diabetes and Endocrinology

RDU Lead: Dr Sapna Shah
Renal Speciality Lead: Dr Sapna Shah
Urology Speciality Lead: Dr Gordon Muir
Diabetes Specialtiy Lead: Dr Prash Vas
Endocrine and Obesity Lead: Dr Georgios Dimitriadis

RDU 7 – HIV & Sexual Health, Ophthalmology, Dermatology and Dental

RDU Lead: Professor Frank Post
HIV & Sexual Health Speciality Lead: Professor Frank Post
Ophthalmology Speciality Lead: Professor Tim Jackson
Dental Speciality Lead: Professor Tara Renton

RDU 8 – Anaesthetics, Critical Care, Emergency Department and Trauma (ACET), Pain, Respiratory and Orthopaedics

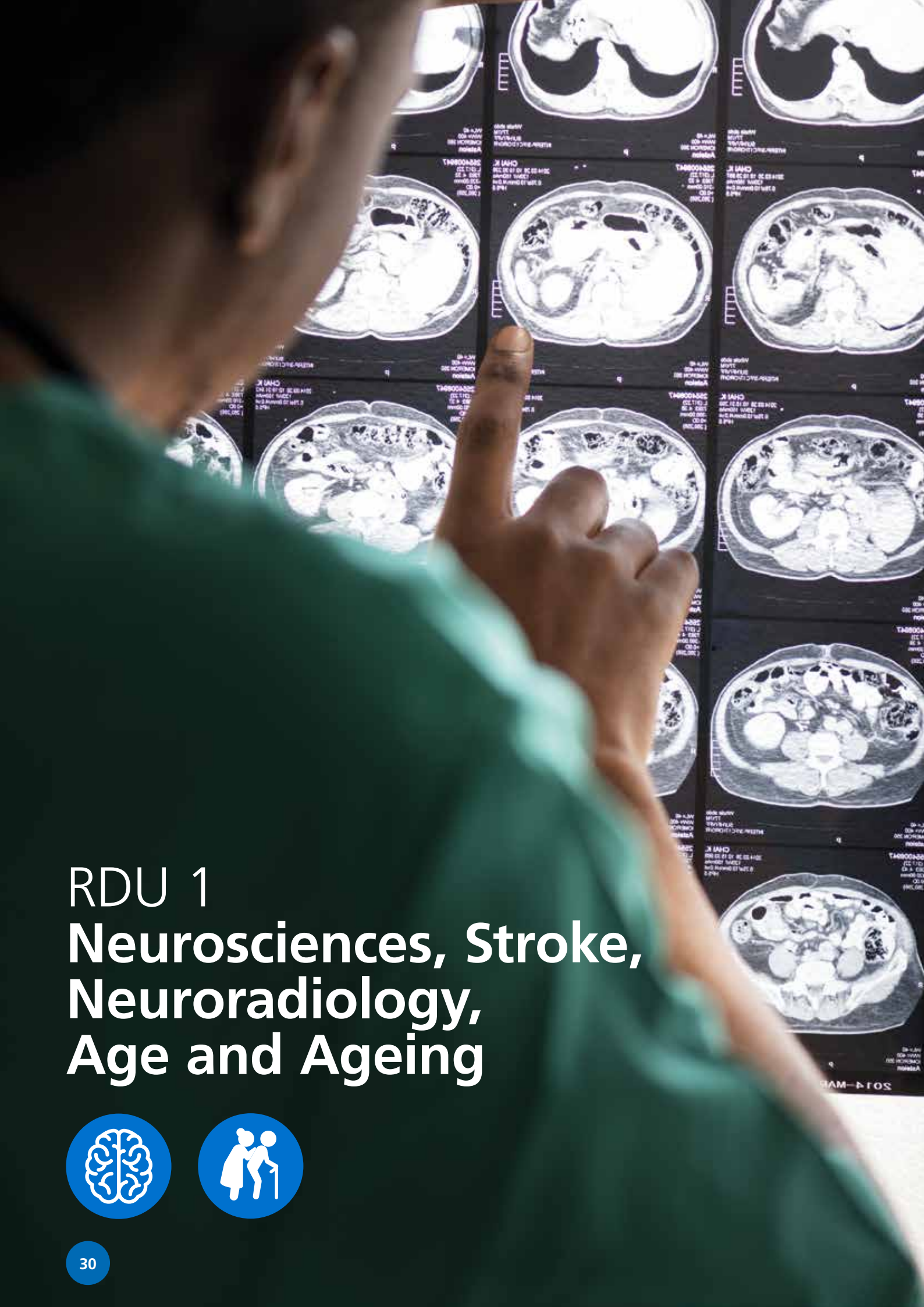
RDU Lead: Dr Phil Hopkins
Anaesthetics Speciality Lead: Professor Gudrun Kunst
Critical Care Speciality Lead: Dr Phil Hopkins
Emergency Department Speciality Lead: Dr Fleur Cantle
Orthopaedic Surgery Speciality Lead: Dr Ines Reichert

RDU 9 – Children

RDU Lead: Dr Atul Gupta
Speciality Lead: Dr Atul Gupta

Cross-cutting areas of Research

Therapies: Dr Sharlene Greenwood
Pharmacy Esther Makanju
Radiology: Professor Paul Sidhu
Pathology: Dr Mohammad Ibrahim



RDU 1
Neurosciences, Stroke, Neuroradiology, Age and Ageing

Neuroscience

The Neuroscience team at KCH is part of the most research-active RDUs at the Trust: currently there are 103 open clinical trials and studies within the Neuroscience team alone. In spite of the devastating impact of COVID-19 on research in general, the last year saw some significant advances within the Neuroscience team as well as delivery of important, informative COVID-19 studies described earlier in this booklet.

Patient-focused clinical outcomes are key to value-based healthcare and the KCH Parkinson's research team have continued to receive grants from the Movement Disorders Society to develop a patient-completed version of the now-global non-motor symptoms scale for Parkinson's disease. It is expected that this scale will become a quality standard for licensing authorities for drugs across the world.

Pain is a major unmet need in Parkinson's and there is a requirement for further research into this issue. Together with Dr Kirsty Bannister at King's College London, RDU1 and Neuroscience sub-speciality lead Professor K Ray Chaudhuri secured a £350,000 grant from Parkinson's UK and Scion Pharma to explore pain pathways in Parkinson's using a novel, sophisticated somatosensory technology. The study is due to start later in 2021.

Led by KCH Professor of Epilepsy Mark Richardson and in partnership with Danish company UNEEG Medical, the Subcutaneous EEG study aims to develop a method for forecasting epileptic seizures through investigation of long-term dynamics of seizure occurrences, stress, sleep and other factors. Subcutaneous electroencephalography (EEG) devices are implanted under the skin on the scalp. And the devices will record continuous brain activity for up to 12 months and patients have been trained in downloading their data from the device. People with epilepsy regard the development of a seizure forecasting method as extremely important, as it represents a step towards reducing the frequent injuries and potential fatality caused by seizures.

Neuroscience research team are also carrying out a number of commercial clinical trials. For example, the BouNDless trial, which launched at the Trust in September 2020, is aiming to test the standard Parkinson's disease drugs levodopa and carbidopa for the reduction of motor symptoms of Parkinson's disease.

While oral administration of these two drugs has been the standard treatment for 40 years, long-term use can result in the benefits of the drug progressively shortening and fluctuations in motor function between doses. Researchers on this global Phase 3 trial, led by Professor Chaudhuri, hope that – if safe - a continuous infusion of the two drugs can reduce fluctuations in motor function in comparison to oral administration, resulting in better quality of life for people with Parkinson's disease.

Other key studies that are ongoing include SPRING, a randomised controlled trial led by Professor Keyoumars Ashkan that is assessing the potential benefits of prophylactic anti-seizure drugs in brain tumour patients prior to surgery and MIROCALS, led by Professor Ammar Al-Chalabi, which is investigating the use of immunotherapy to reduce neuro-inflammation in people with Amyotrophic Lateral Sclerosis (ALS).

Another important study, led at KCH by Consultant Occupational Therapist Mr Bill Tahtis, is a feasibility study which aims to determine how best to carry out large-scale prospective study for the treatment of benign paroxysmal positional vertigo (BPPV) following traumatic brain injury (TBI). Affecting half of acute cases of TBI, it's currently unknown which treatment and at what time most effective. Plans for the feasibility study were published last year in the journal Pilot and Feasibilty Studies and should pave the way for better treatment of BPPV.

An example of a Subcutaneous EEG device

Neuroradiology

The Neuroradiology research team is made up of clinical neuroradiologists and neurologists from KCH, the PRUH and Guy's and St Thomas' NHS Foundation Trust along with academic scientists from King's College London and University College London. As well as academics and clinicians, supporting organisers and facilitators from within the team are crucial to research delivery.

Deep learning using artificial intelligence (AI) typically requires tens of thousands of labelled images to achieve the best possible performance in image recognition tasks. This represents a bottleneck to the development of deep learning systems for complex image datasets, particularly MRI which is fundamental to neurological abnormality detection.

To tackle this, in 2018 the Neuroradiology team set up the ALARM (Automated Labelling using an Attention model for Radiology reports of MRI scans) project. In this study, brain MRI image labelling was automated by deriving important labels from radiology reports and accurately assigning them to the corresponding MRI examinations. Using this method, this year the team were able to label more than 100,000 MRI examinations at scale in under 30 minutes. This has never been achieved before and, if performed manually, would previously have taken years. This novel data has now been published in the journal European Radiology.

Furthermore, the teams' validation method was uniquely robust. Rather than solely evaluating our model performance on unseen radiology reports, the team also evaluated their model performance on unseen images. Whilst this might seem obvious, this has been challenging to do in medical imaging because it requires an enormous team of expert radiologists. Fortunately, the Neuroradiology team is a perfect synthesis of clinicians and scientists.

By overcoming this bottleneck, the team have massively facilitated future deep learning image recognition tasks and this will almost certainly accelerate the arrival of automated brain MRI readers into the clinic. The downstream impact on clinicians is yet to be determined but the potential is huge. Image recognition tasks of neurological abnormalities, if proven to be generalizable (i.e. still perform accurately) in multiple hospitals, will almost certainly help radiologists with tasks such as report prioritisation and even diagnosis. The potential for patient benefit through timely diagnosis is enormous.

Further challenges will be to perform the deep learning image recognition tasks which have multiple technical challenges, and once this is achieved, to ensure the developed models are generalizable. The team are working on these challenges and obtaining clean data from multiple hospitals across the UK is one important step, and to do this, the team are running a NIHR portfolio adopted study – the MR Imaging Abnormality Deep Learning Identification (MIDI) study - across the UK to prospectively collect brain MRI data.

Tom Booth, Neuroradiology research team

Stroke

King's Stroke research consists of one operational lead, two research nurses and three research coordinators. Working across Denmark Hill and the PRUH, the team offer a portfolio of interventional trials and observational studies. This ranges from hyper-acute treatment in A&E to secondary prevention and observational studies designed to address fundamental knowledge gaps in stroke.

For the past year, the King's Stroke research team have divided their time between delivering the Stroke research portfolio and assisting with COVID-19 research. Despite running a smaller portfolio at reduced capacity, the team have increased commercial research and academic research activity in two notable studies.

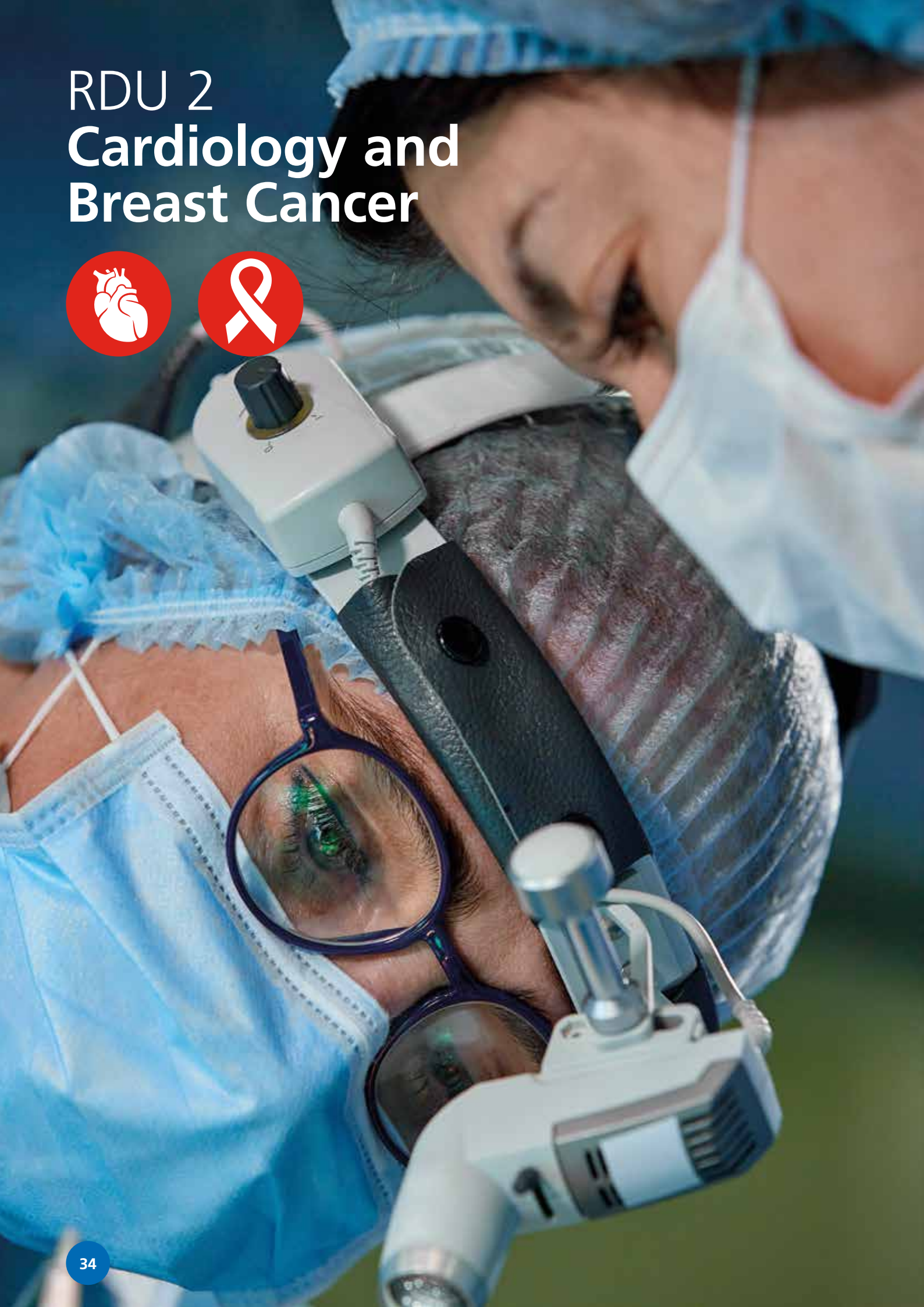
The first recruitment success was for a Phase 2a randomised controlled trial titled BIAL. The primary objective of BIAL is to assess if the approved drug Eslicarbazepine acetate (ESL) can prevent epilepsy in stroke patients at high risk of developing unprovoked seizures. Seizures can affect stroke outcomes – increased mortality, longer hospitalisation and more disability – thus it is important to prevent the development of seizures after stroke.

With six patients recruited in the past year alone, KCH is the second highest recruiting centre of the 21 sites taking part around the world. This is a testament to the hard work of the research team and the Principal Investigator, Dr Yee Mah. The second notable recruitment success came from an academic observational study titled Rates Risks and Routes to Reduce Vascular Dementia (R4VaD). Patients with stroke or Transient Ischaemic Attacks (TIAs) are at increased risk of post-stroke cognitive impairment and vascular dementia but risk prediction for the individual is difficult. R4VAD aims to improve knowledge about risks factors by determining the rate of cognitive impairment and dementia in stroke survivor up to two years post-onset. Results from the trial will lead to improved risk prediction that understands the influence of neuroimaging, vascular, inflammatory and genetic markers – on the likelihood of cognitive impairment or vascular dementia?

With a total of 49 patients recruited across KCH and this past year, the Trust is now the third highest recruiting centre of 53 sites taking part nationally.

King's Stroke research aims to continue this momentum in the next financial year with plans to reopen the rest of the portfolio imminently.

The Stroke research team



RDU 2
Cardiology and Breast Cancer

Cardiology

The Cardiac research team is made up of eight Research Nurses and a Research Facilitator and is led by Cardiac Lead Research Nurse Jon Breeze. The team supports studies across all subspecialties within Cardiology, with a portfolio of 60-70 active studies running at any one time.

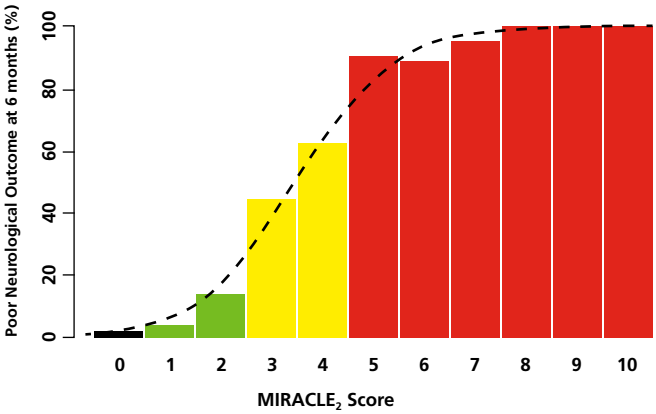
As with all research departments at KCH, 2020/21 was memorable for a variety of reasons. Every research nurse in the team was redeployed to help the clinical service and, upon return, support Urgent Public Health research. Against this backdrop, it has been heartening to see that the department continues to contribute to ground-breaking, innovative research that is at the cutting-edge of Cardiology. Much of this is home-grown, as illustrated by the excellent work in the field of Out Of Hospital Cardiac Arrest (OOHCA).

OOHCA is a major public health burden which can lead to considerable morbidity and mortality and it has been highlighted as a priority condition by NHS England and the British Heart Foundation (BHF). Patients have an extremely high risk of long-term brain damage after cardiac arrest, but this can be challenging to predict early on after admission.

Consultant Cardiologist Dr. Nilesh Pareek and his colleagues at the BHF Centre of Excellence, King's College London and King's College Hospital developed a novel risk score for use by clinicians at heart attack centres to predict brain damage in these patients.

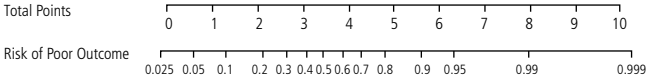
The risk score, known as MIRACLE2, was developed to help clinical decisions, improve the selection of appropriate treatments and inform family discussion early after admission. Results from a recent observational study found that MIRACLE2 predicted brain injury with high accuracy and, when validating the performance of the score in nearly 900 patients from three heart attack centres in Europe, the score performed well, with risk groups being defined as low risk (MIRACLE2 ≤2 = 5.6% risk of poor outcome); intermediate risk (MIRACLE2 of 3-4 = 55.4% of poor outcome); and high risk (MIRACLE2 ≥5 = 92.3% risk of poor outcome).

The risk score has already been incorporated into national pathways of care through the British Cardiovascular Interventional Society guidelines and has the potential to lead to important improvements in care for this patient group. Once the performance of the score has been further evaluated in other healthcare settings, future international clinical trials using the score are planned.



The MIRACLE2 score chart. N. Pareek et al. European Heart Journal, 41;47,14 December 2020, https://doi.org/10.1093/eurheartj/ehaa570

	Variable	Definition	Points
M	Missed	Unwitnessed Arrest	1
I	Initial Rhythm	Non-shockable Rhythm	1
R	Reactivity of Pupils	No Pupil Reactivity on ROSC	1
A	Age	0 - 60 years 60 - 80 years >80 years	0 1 3
C	Changing Rhythms	Any 2 of VF/PEA/Asystole	1
L	Low pH	pH <7.20	1
E_2	Epinephrine	Any Epinephrine Dose	2
		$MIRACLE_2$ Score	10



Positive correlation of the MIRACLE2 score with neurological outcome. N. Pareek et al. European Heart Journal, 41;47,14 December 2020, https://doi.org/10.1093/eurheartj/ehaa570

RDU 3
Women's Health and Fetal Medicine

Women's Health

Early Pregnancy Unit
The Early Pregnancy Unit have continued to be a key part of the UK-wide research network in Early Pregnancy problems, seeing the August 2020 publication of the MIFEMISO study in the Lancet which showed that mifepristone pre-treatment was more effective than misoprostol alone for the management of missed miscarriage. Led by Miss Jemma Johns and Miss Jackie Ross, the team also published papers on diverse topics such as the outcome of pregnancies with low progesterone levels and ultrasound features of early molar pregnancy and immature ovarian teratomas.

Midwifery
Midwifery research has seen substantial growth over the last year both at Denmark Hill and at the PRUH. Midwife Hayley Martin has been awarded an NIHR pre-doctoral clinical fellowship award and midwife Ana Lagarto Sintra Dos Santos is completing the same fellowship after moving to join KCH due to its growing reputation as a midwifery research centre. Research midwife Sophie Webster has been appointed as regional lead midwife for the GBS3 Trial, which aims to prevent Strep B infections in newborns by testing pregnant women for the infection prior to giving birth.

The midwifery research team has demonstrated substantial growth through focused leadership from NIHR 70@70 Senior Midwife Research Leader, Katherine Clark. There are now 13 Intrapartum Research Champions across sites enabling research to be undertaken during labour care for the first time in many years.

Maternity
Maternal-Foetal Medicine and Obstetrics consultant Mr Nick Kametas continues to lead his team to publish work on hypertensive disorders of pregnancy as well as being highly collaborative with the Fetal Medicine, Liver and Renal teams. He was appointed as CRN South London Research Specialty Lead for Reproductive Health and Childbirth.

The renal pregnancy team, led by Dr Kate Bramham, continue to be successful in grant applications including collaborating with the UK Obstetric Surveillance study to gain funding from Alexion Pharmaceuticals to lead a national cohort study of severe pregnancy associated Acute Kidney Injury. The ORCHARD (Observational cohort with embedded Randomised Controlled trials to study pregnancy-Associated progression of Renal Disease) trial, run by Dr Kate Bramham and Dr Priscilla Smith, has been recruiting successfully despite obvious challenges.

The Women's Health research team

Urogynaecology
Despite marked interruption over the last year, the urogynaecology team, led by Professor Linda Cardozo and Mr Dudley Robinson, have continued to publish prolifically with 37 peer reviewed articles being published in international journals including Clinical Obesity, International Urogynaecology Journal and Neurology and Urodynamics.

Fetal Medicine

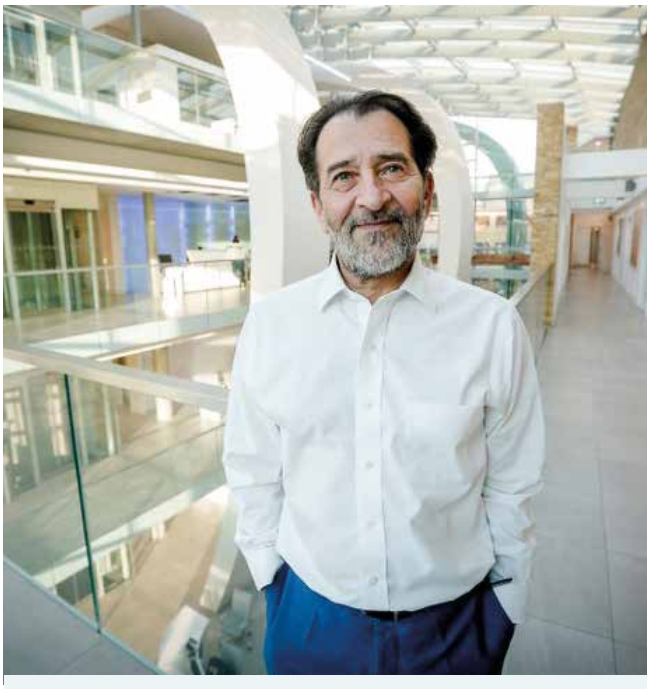
The Harris Birthright Research Centre for Fetal Medicine, located within the Fetal Medicine Research Institute, has been provided a high-quality service to thousands of pregnant women throughout the COVID-19 pandemic. The Institute allows for the combined delivery of KCH NHS services with world-class research, teaching and practice in foetal medicine, and provides a range of services such as; ultrasound scanning, consulting and treatment rooms as well as diagnostic and research laboratories.

Besides routine clinical practise, the unit has one of the highest rates of recruitment by KCH for CRN portfolio studies, ensuring that cutting-edge research is continually being delivered. Research at the Centre is spearheaded by RDU and Fetal Medicine research Lead Professor Kypros Nicolaides, who has published more than 1,500 scientific papers in peer-reviewed international journals throughout his career. This year, Professor Nicolaides was internationally acknowledged with his election to the National Academy of Medicine in the USA, one of the highest honours in medicine.

Despite the pandemic, the Centre continued to play a major role in education and research. Last year, the team at the Centre organised educational biweekly webinars that were completely free of charge and attended by more than 15,000 participants from 150 countries around the world, providing the most updated data from renowned experts in the field.

In the last year alone, the team have published nearly 60 research papers on a wide range of topics spanning foetal medicine, with a cutting edge research project concerning the role of vaginal progesterone in the prevention of pre-term delivery of twins being published in the high-impact American Journal of Obstetrics and Gynecology in January this year.

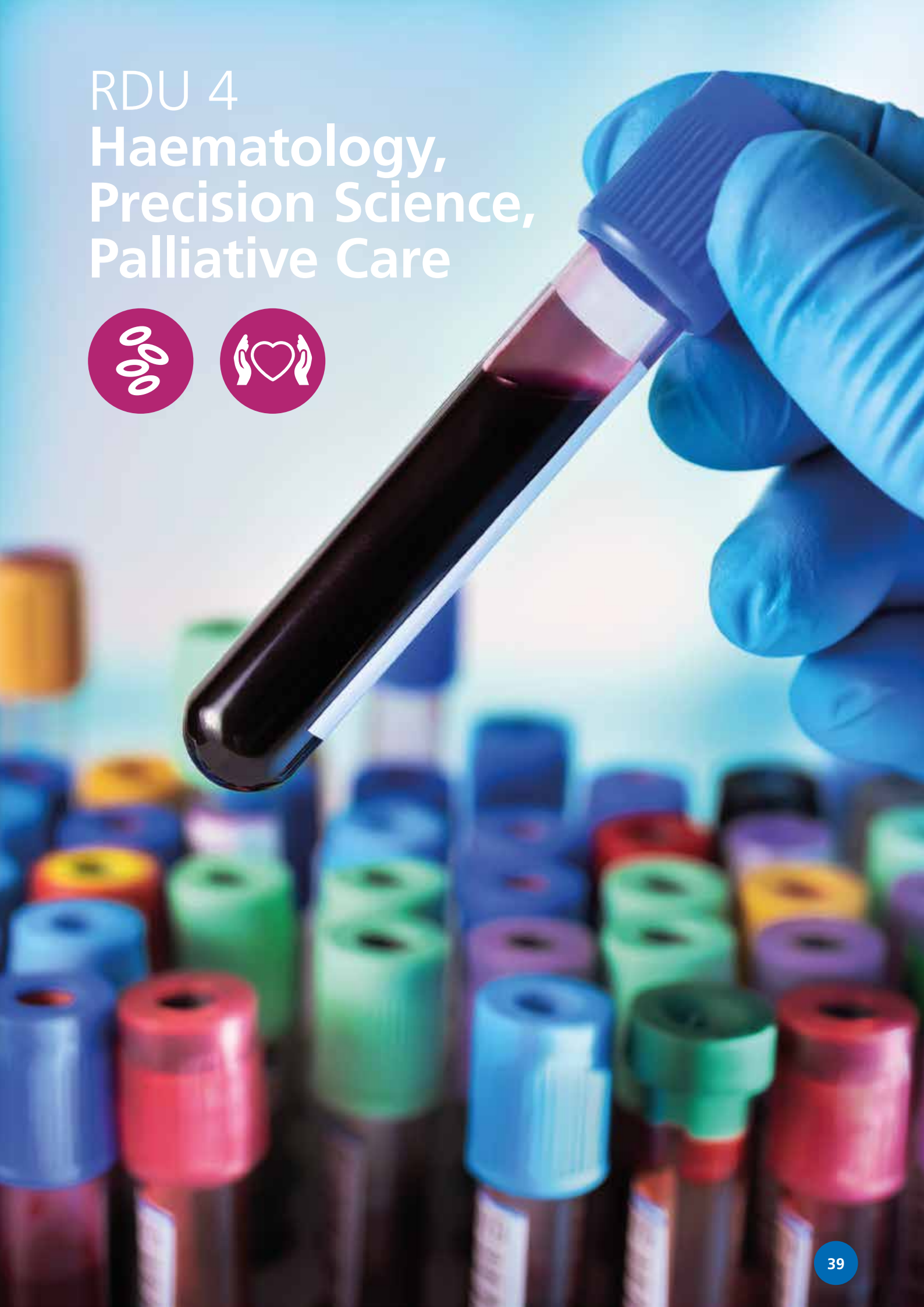
Progesterone is widely used in single-baby pregnancies as it prevents pre-term delivery in those at risk, As all twin pregnancies carry a higher risk of pre-term delivery than single-baby pregnancies, progesterone is also given to these women, yet there is no evidence to suggest this is actually preventative.



Professor Kypros Nicolaides

In the largest study of its kind, led by KCH research fellow Mr. Anoop Rehal and Professor Nicolaides, almost 1200 women in 22 hospitals across Europe that were pregnant with twins were enrolled and given either progesterone or a placebo. The results showed that for most women pregnant with twins, even high doses of progesterone did not reduce the incidence of pre-term birth and was in fact associated with increased incidence. Considering the widespread use of progesterone in twin pregnancies, this work will likely impact on standard practices when managing twin pregnancies.

RDU 4
Haematology, Precision Science, Palliative Care



Haematology

The Haematology research team is led by Consultant Haematologist Dr Piers Patten alongside 25 staff members made up of data managers, trial coordinators, research nurses, regulatory coordinator and a research fellow.

The Clinical Trial and Clinical Research portfolio for the Haematology team was dramatically affected by COVID-19, with all non-COVID-19 trial recruitment paused at the beginning of the pandemic. However, continuation of treatment for existing trial patients was allowed and the team showed great adaptability in being able to continue to deliver trials by making use of some increased flexibility of previously rigid regulations and coordinating remote visits with monitoring.

The Haematology team is an important Haemato-oncology centre, and is both Trials Acceleration Programme (TAP) centre and an IMPACT centre. IMPACT is the UK's first ever clinical trials partnership dedicated to improving the outcomes of stem cell transplants in patients and this year, the team's Transplant Director Dr Victoria Potter was appointed as a Deputy Clinical Director to this programme. In March 2021, IMPACT facilitated the completion of the one-year follow up of the PRO-DLI trial. This KCH-led study, led by Dr Potter, is the first randomised study of un-manipulated donor lymphocyte infusions (DLI) for the prevention of relapse post-transplant in patients with Acute Myeloid Leukaemia (AML) or myelodysplastic syndromes (MDS) to be delivered worldwide.

Furthermore, despite the pandemic, the team were able to continue delivering clinical trials of Chimeric Antigen Receptor (CAR) -T cell therapy, whereby immune cells are genetically modified to target and destroy specific cancer cells, for both relapsed refractory lymphoma (e.g. the Phase 2 ELARA study) and myeloma (e.g. the Phase 2 and 3 KARMMA2 and KARMMA3 studies). These trials are part of their cellular therapy research programme of using Advanced Therapeutic Investigational Medicinal Products (ATIMPs) for blood cancers.

Future projects include building upon previous successful delivery of their first in-human B cell-targeted CAR-T cells for adult B cell Acute Lymphoblastic Leukaemia (the CALM study, published in the Lancet last year) and producing a portfolio of investigator-initiated trials underpinned by translational research from the KHP academic health sciences centre. This includes investigating mechanisms of resistance, developing inducible and dual-antigen targeted CAR-T cells as well as designing novel allogeneic CAR-T cell strategies.

Haematology research team members

Palliative Care

In what has been a challenging year for patients with breathlessness, the Palliative Care research team, led by Dr Sabrina Bajwah, has continued to drive forward breathlessness research and have been innovative in adapting their practices to ensure its continuation during the pandemic. Despite 50% of research staff being redeployed to ITU during the pandemic, KCH was the highest recruiting NHS Trust for palliative care patients nationally in 2020/21.

In November 2020, KCH successfully opened the KCL-led BETTER-B trial. This EU-funded project for which Professor Irene Higginson is Chief Investigator (led at KCH by Dr Sabrina Bajwah) is testing whether established antidepressant mirtazapine could be used to treat chronic breathlessness – a very common and distressing symptom of advanced chronic respiratory diseases. The trial will recruit 324 patients as well as their informal caregivers across the UK, Ireland, Germany, Italy and Poland. Remote consenting and data collection ensured vulnerable patients can still be safely offered the opportunity to participate in this trial.

In addition, the BETTER-B work programme also includes the production of European-wide guidance on the management of breathlessness in palliative and end of life care, the delivery and analysis of an online survey of physicians which aims to understand current clinical management

Dr Sabrina Bajwah and Professor Irene Higginson, leaders of the BETTER-B trial.

of breathlessness, and qualitative interviews with trial participants to further understand their experiences. The programme brings together clinical and academic experts in the field of breathlessness and is a great example of the team's continued international collaborations. For more information, please visit the project website https://betterbreathe.eu/.

Support services for patients living with chronic breathlessness improve patients ' self-management and reduce their distress due to breathlessness. However, the provision and access to such services within the UK's National Health Service is limited. Delivering online breathlessness support may be one way of improving access to non-pharmacological self-management interventions for people living with chronic breathlessness. Over the last year, Dr Charles Reilly has developed the SELF-BREATHE app (https://app.self-breathe.co.uk) with input from digital health experts, clinicians, and patients as part of his NIHR Clinical Lectureship. The aim is to help patients improve their breathlessness self-management at home, providing patients with simple self-guided non-pharmacological treatments such as breathing control exercises, home exercise programmes and daily symptom monitoring. Despite some challenges related to redeployment and respiratory clinic shutting down, KCH recruitment is going well and the study has just opened at the PRUH.

Dr Charles Reilly, leader of the SELF-BREATHE study

RDU 5
Liver, Gastroenterology and Rheumatology

Liver

The Liver research team was at the heart of the COVID-19 research delivery at KCH, coordinating the RDU-wide team of clinicians and research personnel who worked to deliver the many important trials supported by the Trust. Although recruitment into non-COVID-19 studies was suspended, the Liver team continued to look after and monitor patients already enrolled in research projects while continuing to publish cutting-edge research high impact journals.

In March 2021, team member Dr Saima Ajaz published the paper *"Mitochondrial dysfunction as a mechanistic biomarker in patients with non-alcoholic fatty liver disease (NAFLD)"* in the journal Mitochondrion, which detailed the team's development of biomarkers for fibrosis progression in Non-Alcoholic Fatty Liver Disease (NAFLD).

The following April, Clinical Fellow Dr Oliver Tavabie collaborated with the United States Acute Liver Failure Study Group to publish results of a state-of-the-art DNA-based biomarker study in acute liver failure caused by paracetamol toxicity. Titled *"A novel microRNA-based prognostic model outperforms standard prognostic models in patients with acetaminophen-induced acute liver failure"* and published in the Journal of Hepatology, the researchers describe certain proteins found in the blood that can inform doctors which patients are likely to require a liver transplant and which are most likely to recover from paracetamol toxicity without one, potentially reducing the need for liver transplants and freeing up donated livers for those more in need.

Now that research projects are restarting, there is much more in the pipeline for the Liver research team. For example, senior fellow Dr Thomas Tranah, was awarded a prestigious 3-year Medical Research Council Research Training Fellowship to investigate the faecal microbiome as a therapeutic target for restoring the function of a specific type of immune cell in liver cirrhosis, as a potential way to reduce high rates of infection in patients with the disease.

Professor of Hepatology at the KCH Institute of Liver Studies, Debbie Shawcross, has been awarded £2.5 million by the NIHR Efficacy and Evaluation of Mechanisms (EME) funding stream to lead the **PROMISE Trial**: A **PRO**spective double-blind placebo-controlled multicentre trial of faecal **MI**crobiota tran**S**plantation to improve outcom**E**s in patients with cirrhosis. This trial will evaluate whether faecal transplants from healthy donors to cirrhosis patients will reduce the levels of harmful bacteria in their intestines, which is associated with the development of infection - the leading cause of mortality in this group. Reducing infection for these could reduce complications and hospital admissions that could improve transplant-free survival.

Overall, the Liver team has responded admirably to the requirements of COVID-19 and is now emerging stronger and expanding its core research areas. They are looking ahead to the challenges and opportunities offered by the newly reconfigured RDUs and feel confident that working together will improve the research prospects they can offer patients.

Gastroenterology

The Gastroenterology research team is led by Consultant Gastroenterologist Dr Alexandra Kent and consists of 11 consultants from Gastroenterology and Colorectal Surgery, three research fellows and three research nurses who support the delivery of multiple research projects across Gastroenterology, Endoscopy and Colorectal Surgery. Over the last year, the team has recruited-to-target for 14 commercial trials and 11 non-commercial studies including local, national, and international trials.

The interests of the Gastroenterology team include a range of clinical studies in Inflammatory Bowel Disease (IBD), Coeliac disease, Irritable Bowel Syndrome (IBS), Diverticular Disease (DD) and Advanced Therapeutic Endoscopy.

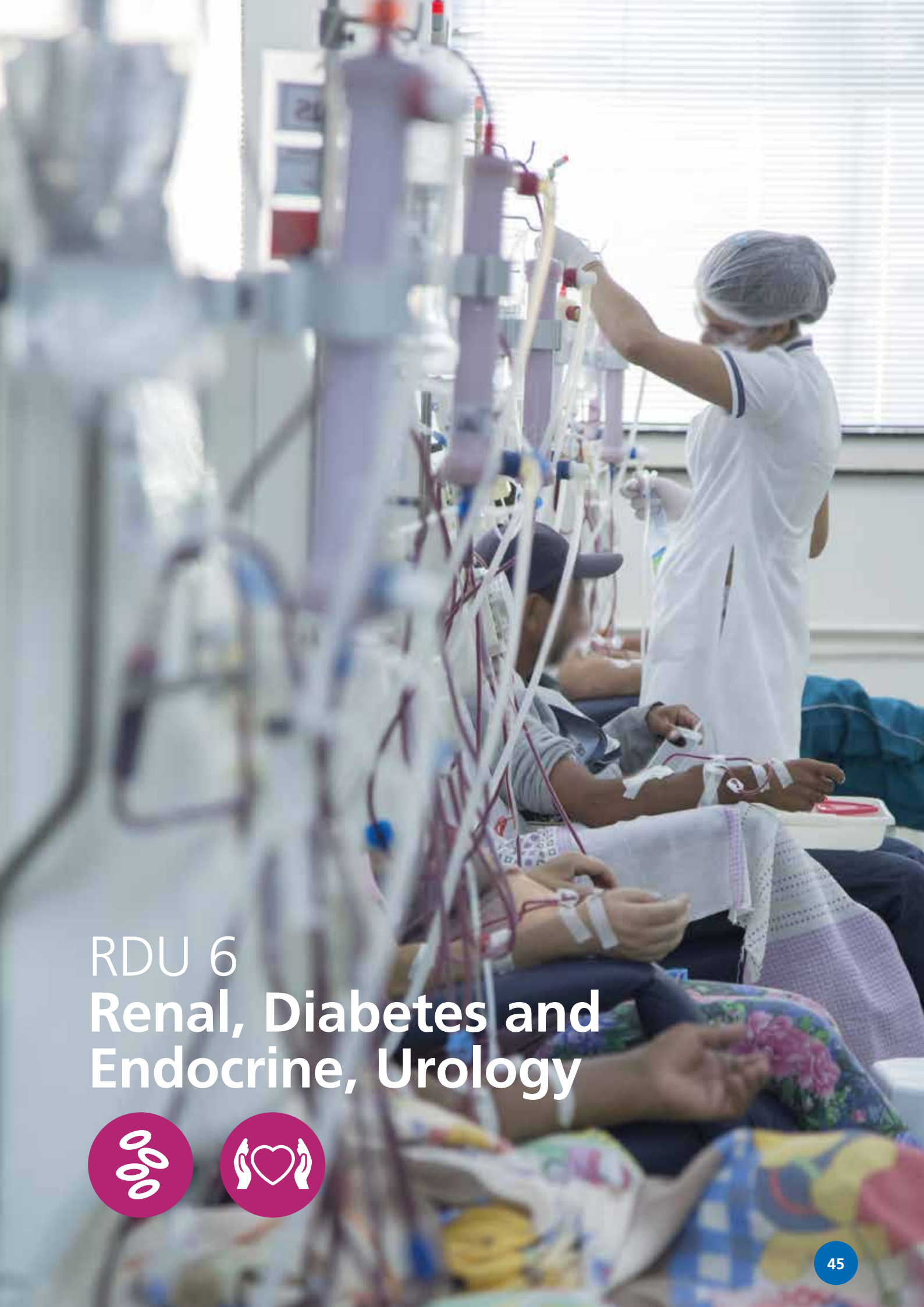
Endoscopy research
KCH is a leading UK site for Therapeutic Endoscopy with a particular focus on teaching and research in Endoscopic Submucosal Dissection (ESD), recruiting to a multicentre ESD outcomes study and the POPS study. The team is proud to be leading the first randomised, placebo-controlled PECoD trial on the potential benefits of- prophylactic endoscopic clipping for DD.

The team is one of the UK's leading recruiters to studies relating to state-of-the-art endoscopic imaging technology, artificial intelligence (AI) and computer-aided diagnosis systems. A key success from the team in FY20/21 was the recruitment of over 300 patients for studies with a focus on AI in Endoscopy, including EndoBRAIN International, GI Genius, I-scan and BLAST. Excitingly, the team is currently pursuing novel areas including robotic endoscopy and remote systems.

IBD research
There has been an expansion in the number of IBD commercial studies, in particular IL-23 and JAK inhibitor studies which aim to modulate pathogenic inflammatory immune responses in IBD. This has increased access for KCH IBD patients to new and novel therapies. In the last year, the team have also recruited to PROFILE, a biomarker study aiming to optimise IBD management and are developing research to investigate e-health and apps to support self-directed management in IBD and Patient Initiated Follow-Up.

Going forward, the Gastroenterology team aim to complete recruitment to their major studies and intend to present details of their work at local and international seminars and conferences.

Members of the Gastroenterology research team



RDU 6

Renal, Diabetes and Endocrine, Urology

Renal, Diabetes and Endocrine, Urology

RDU 6 is led by Dr Sapna Shah together with Dr Kate Bramham and Dr Sharlene Greenwood, Clinical Leads for Renal Exercise and Rehabilitation, Mr Gordon Muir, Clinical Lead for Urology and Dr Prash Vas, Clinical Lead for Diabetes. The team of Primary Investigators (PIs), supported by 21 research delivery staff, have a portfolio of approximately 50 studies.

Most face-to-face clinical trial work was paused during COVID-19, yet the team from RDU 6 continued to recruit and follow-up patients utilising remote monitoring whenever possible. In addition, the team were proud to be actively diverted to support the UPH COVID studies and clinical services during the pandemic.

Renal Sub-speciality and RDU 6 Team Lead, Dr Sapna Shah

Throughout the COVID-19 pandemic, **the Renal research team**, led by Dr Sapna Shah, continued to recruit to and increase their diverse portfolio of commercial and non-commercial studies in 2020-2021 despite the challenges of the COVID-19 pandemic. These include clinical trials in advanced chronic kidney disease, renal bone disease and calciphylaxis (accumulation of calcium in small blood vessels in the fat and skin), renal anaemia, chronic kidney disease (CKD), glomerulonephritis, kidney transplantation and dialysis.

In September 2020, the team opened recruitment for a Phase 3 clinical trial of biopharmaceutical company Sanifit's potential new drug for calciphylaxis - SNF472. Occurring frequently in patients with CKD, calciphylaxis results in painful and debilitating skin lesions caused by the accumulation of calcium in skin and fat tissue. While it is rare, affecting 1-4% of dialysis patients, it kills over half of those affected within a year of diagnosis.

The EMPA-KIDNEY trial, a clinical trial assessing cardio-renal outcomes in CKD with the SGLT2 inhibitor Empagliflozin which opened in 2019, was kept on track throughout the pandemic with study lead Consultant Nephrologist Dr Phin Kon recruiting 35 patients in the last year. Previous studies have found that SGLT2 inhibitors can block some of the pathogenic mechanisms behind CKD and have shown significant reductions in morbidity and mortality for patients with diabetic and non-diabetic CKD. Researchers hope that Empagliflozin may slow kidney disease progression and reduce cardiovascular events in those with CKD.

Additionally, Renal Clinical Lead and Consultant Nephrologist Dr Martin Ford continued to recruit to the NIHR-funded SIMPLIFIED study, which is evaluating the effect of Vitamin D supplementation on outcomes in patients with kidney failure receiving dialysis. RDU 6 Lead Dr Sapna Shah also utilised remote and home visits to continue to deliver the commercial study ASCEND-ND, which is evaluating the effects of HIF stabilisers on anaemia related to renal disease.

Finally, the team continued throughout the pandemic to recruit to studies evaluating novel therapies for rare renal conditions that can lead to kidney failure, such as IgA nephropathy and Focal Segmental Glomerulosclerosis.

Throughout the pandemic, the **Renal Exercise and Rehabilitation team**, led by Dr Sharlene Greenwood, has been supporting studies that have remained open during the COVID-19 pandemic, as well as supporting a novel mobile community phlebotomy service for clinical follow-up of blood testing for people living with kidney disease who were shielding during the pandemic.
Several interventional

Renal excercise and Rehabilitation Sub-speciality Lead Dr Sharlene Greenwood

studies were adapted during the pandemic to allow for home-based exercise and also virtual follow-up. In June 2020, the team launched a novel digital health technology intervention - Kidney Beam. Developed by KCH and Beam, and funded by Kidney Research UK. Kidney Beam www.beamfeelgood.com is a web-based self-management programme designed to allow people with kidney disease to learn about their condition and provide support to them, both physically and emotionally, during the COVID-19 pandemic and beyond. The website offers live and on-demand movement classes, and behaviour change support tools to increase physical activity, as well as tools to improve mood and manage negative emotions associated with having kidney disease.

Urology Sub-speciality Lead, Dr Gordon Muir

A 12-month multi-centre definitive study to evaluate the clinical value and cost-effectiveness of the digital health technology was funded by Kidney Research UK in December 2020. This trial will provide the data required for commissioning of the digital health technology, and has the potential to transform delivery of physical and emotional wellbeing for people living with kidney disease in the UK. During 2019/20, the team has published 27 peer-reviewed manuscripts and has attracted £854,049 in grant funding for investigator-led studies.

In 2020, **Urology** consultants were lead authors in world-first publications in prostate cancer diagnostics, male body image and genital problems, and in bladder neurophysiology. The team have also recently established the pathophysiology behind the 'Postural Tachycardia syndrome (PoTS)' bladder.

Current projects involve clinical trials in focal prostate cancer therapy, male body dysmorphia, novel techniques in managing benign prostate disease and prevention of UTI's.

KCH has long been a leading UK site in a number of clinical trials, including prostate focal therapy and benign prostate disease, and are world leaders in minimally invasive prostate techniques, treatment and teaching. At the end of 2020, Dr Jonathan Makanjuola was awarded an NIHR grant in collaboration with Guy's and St Thomas' and King's College London for the PROState AI Cancer–Decision Support (PROSAIC-DS) study. This study provides an opportunity to augment cancer Multidisciplinary Team Meetings with the power of AI to substantially increase their efficiency and effectiveness and is due to start in the next few months.

Diabetes Sub-speciality Lead, Dr Prashanth Vas

The **Diabetes, Endocrinology and Obesity team**, led by Drs Prash Vas and Georgios Dimitriadis, have a wide portfolio of clinical research spanning experimental medicine, clinical trials and commercial research across type 1 and type 2 diabetes, obesity and diabetes foot complications.

During COVID-19 lockdown, they kept a number of studies on track by collecting data online, developing a system for home blood sample collection for HbA1c (a measure of diabetes control) and using patient-recorded outcomes. These studies include a large multi-centre randomised controlled trial HARPdoc, led by Professor Stephanie Amiel and funded by leading type 1 diabetes research charity JDRF, investigating novel behavioural intervention for people with recurrent hypoglycaemia and Dr Pratik Choudhary's large EU-funded project, HypoMETRICS, which recruited the UK contribution to 600 people with diabetes to a global study which is investigating the impact of hypoglycaemia on the lives of people with diabetes.

In October 2020, KCH Consultant Diabetes Physician and Director of the King's Health Partners (KHP) Institute for Diabetes, Endocrinology and Obesity Dr David Hopkins was able to launch the H2O – Health Outcomes Observatories, an EU funded project to develop national data observatories for long-term conditions across Europe. Dr James Crane and Dr Hopkins are currently collaborating with diabetes and endocrinology specialist Professor Barbara McGowan to perform AI-based analysis of chest CTs to correlate the amount of visceral fat with molecular inflammation.

RDU 6's plans for the next year include consolidating the new RDU and working collaboratively to undertake research studies relevant for the local population. The Unit's experience during the pandemic has informed their strategy with the aim of developing their clinical trial programme to facilitate more remote management of patients in the post-COVID environment.

RDU 7

HIV & Sexual Health, Ophthalmology, Dermatology and Dental

HIV, Sexual Health and The Havens

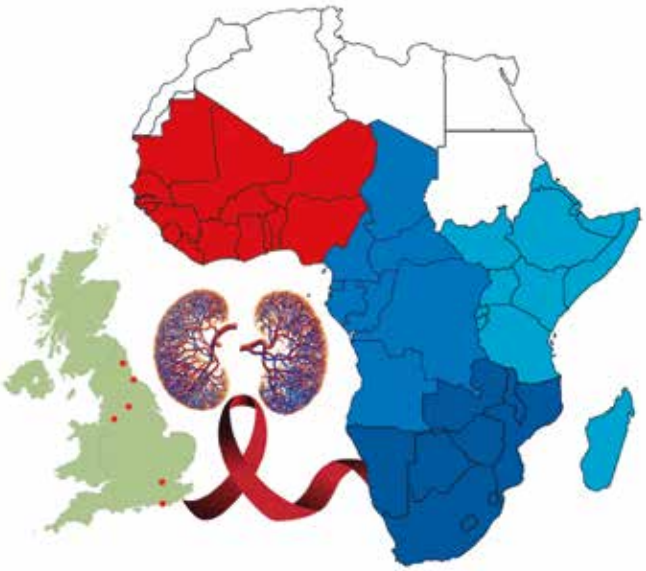
The HIV, Sexual Health and The Havens research team is headed by Professor Frank Post, leading Clinical Research Fellows, PhD students, Research Delivery staff and a Research manager. They come from a diverse background including clinical trials, nursing, quantitative and qualitative experience and allow the team to deliver on a varied range of studies.

The team manages one of the largest cohorts of people of African ancestry with HIV in the UK. This population is disproportionally affected by hypertension, diabetes and kidney disease. Supported by 15 sites across the UK, in 2018-2020 the team enrolled over 3,000 people into the GEN-AFRICA study to explore the genetic basis of severe kidney disease in black people with HIV.

The study results, recently published in EClinical Medicine, described aspects of the clinical epidemiology of kidney disease in people of African ancestry with HIV and confirmed major roles of the genes APOL1 and sickle cell gene. These results will lead to improvements in the diagnosis and management of people living with HIV and kidney disease worldwide. GEN-AFRICA has led to two further studies investigating health issues in people of African ancestry: the role of social determinants in the development of diabetes, cardiovascular and kidney disease (CKD-AFRICA), and the incidence of and health beliefs surrounding COVID-19 (CoV-AFRICA). The team work closely with the Africa Advocacy Foundation to ensure the findings are shared appropriately with the affected communities.

The team is also exploring the sexual and reproductive health needs of Trans and Non-Binary people. The Trans & Non-binary Reference Intervals While on Hormone Therapy Study (TransRIHTS) aims to identify a new reference range for blood tests which are affected by sex, as it is unclear what intervals should be used for transgender people who are on hormone therapy. Answering this question will allow doctors to identify disease in Trans people faster and with greater accuracy.

Additionally, The Havens, established in 2000 by a consultant from the HIV & Sexual Health Team, work closely with the Team, sharing staff and expertise. The Havens is an international leader in the care for victims of sexual assault in London. They have a research programme focused on the experience of service users, ways of maximising the chances of prosecution of the perpetrators and improving and understanding how to ensure staff are trained to deliver the best care available.



Ophthalmology

The Ophthalmology research team at King's College Hospital is led by Professor Timothy Jackson, Mr Haralabos Eleftheriadis and Mr Gerassimos Lascaratos. In addition to supporting the wider NHS in responding to the pandemic, the team has continued to run clinics and carry out research activities throughout the COVID-19 period, and is committed to building on the successful delivery of clinical trials leading to novel therapies and sustainable, impactful improvements in patient care.

The Ophthalmology team runs an ever growing number of both investigator-initiated and industry-sponsored clinical trials with primary research areas in three leading causes of sight loss: age-related macular degeneration (AMD), glaucoma and diabetic retinopathy (DR). Additionally, the team has experience with leading large, multicentre, national and international clinical trials, including pioneering technologies such as retinal implants and robotically-controlled precision radiotherapy.

One of the studies currently being led by the team is the TIGER study, a pan-European, multicentre, randomised-controlled surgical trial led by Professor Tim Jackson. The study seeks to determine the optimal management of submacular haemorrhage,a rare but devastating complication of wet AMD, and is the recipient of a €2m grant awarded in 2020 from the European Society of Retina Specialists (Euretina) and leading UK sight loss charity Fight for Sight.

The team are also setting up and recruiting to a number of industry-sponsored studies for AMD, glaucoma and diabetic retinopathy. NEON NPDR is an early phase study investigating the efficacy and safety of a novel once-daily oral tablet called Runcaciguat to reduce the risk of sight-threatening disease in patients with non-proliferative diabetic retinopathy, whereas Triton is a Phase 3 study evaluating the efficacy and safety of an eye implant to facilitate the slow-release of bimatoprost in patients with early glaucoma or ocular hypertension. The team are also opening recruitment to ALTIMETER, a phase 2b study investigating visual and blood/eye biomarker outcomes in patients with diabetic macular oedema (DMO) following treatment with Faricimab, a novel drug for the disease.

The Ophthalmology research team

Dental

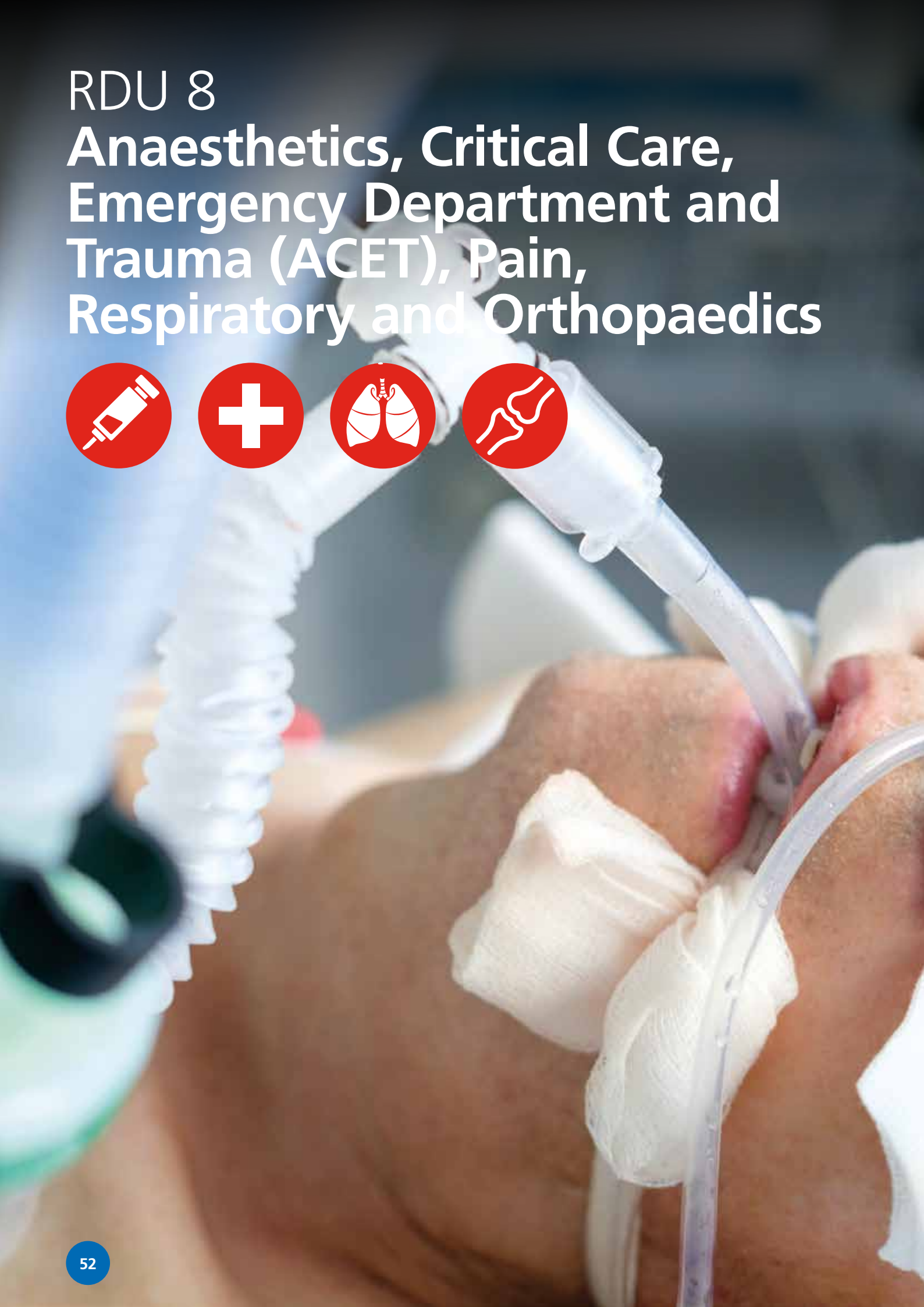
The Orofacial Pain (OFP) service was set up ten years ago at KCH by Professor Tara Renton and is now an international leading service with clinical and research collaborations which focus on optimising the diagnosis and management of patients with OFP. The interdisciplinary Dental team includes; clinical psychologists, liaison psychiatrists, different dental specialties, neurosurgery, headache neurologists and ear nose and throat specialists. Over the last few years the team has recruited over a thousand patients attending the OFP service to research projects and published over 150 peer-reviewed papers.

With MRC funding, the team collaborates with the Centre for Neuroscience Imaging, evaluating post-surgical neural pain circuits and activity related to post third molar surgical pain.

Wisdom tooth surgery is the most commonly used analgesic study model in man due to the intermittent nature of the presurgical pain and the need for surgery. This model has allowed the team to identify acute and unique pain circuits, evaluate ongoing pain and predict pain in patients.

In the last year the team have opened up three new studies and published 28 papers including in the Journal of Pain.

RDU 8
Anaesthetics, Critical Care, Emergency Department and Trauma (ACET), Pain, Respiratory and Orthopaedics



ACET

The Anaesthetics, Critical Care, Emergency Medicine and Trauma (ACET) team at KCH is led by RDU 8 Lead Dr Phil Hopkins (Critical Care), Dr Fleur Cantle (Emergency Medicine) and Professor Gudrun Kunst (Anaesthetics). A team of research nurses focused on the various areas within research are led by ACET Lead Research Nurse John Smith.

In October 2020, Hannah Cotton, Research Nurse within the ACET research team set up a Patient and Public Involvement and Engagement (PPIE) group for 'in-house' Emergency Medicine and Trauma research. The group is made up of people who have previously visited the Emergency Department as either a patient or a carer and its key aim is to ensure that the research the ACET research team conducts is relevant, of interest and acceptable to patients.

By working with the PPIE group, the team can tailor their study design to ensure all these factors are met. The primary meeting introduced how the team conducts research in emergency situations. Two further meetings discussed group priorities for Emergency research and the presentation of a new research study, focusing on the consent procedures for the group's feedback.

Eleanor Corcoran, Senior Research Nurse within the ACET Research team has recently secured funding to start off the INSIGHT research project. The INSIGHT project is investigating the impact of training nurses, Advanced Critical Care Practitioners, doctors, and physiotherapists to perform novel whole-body point-of-care ultrasound (PoCUS) 'INSIGHT' scans on patient outcome and healthcare costs, as well as the feasibility and acceptability of performing and using the INSIGHT scan within the ICU.

Currently PoCUS training is predominantly undertaken by doctors with as little as 6% reaching competency. Training up different staff groups to perform the INSIGHT scan will increase the workforce of PoCUS-trained staff and therefore increase the number of patients that may benefit from routine PoCUS scanning. This may help identify abnormal pathology earlier in a patient's ICU admission, reducing the need for imaging involving harmful radiation, and minimise the risk of prolonged ICU stay.

During the COVID-19 pandemic, recruitment for clinical studies within Anaesthetic research, part of ACET, was reduced. However, academic and research activities continued at different levels resulting in the publication of two textbooks with KCH anaesthetic consultants as principal editors as well as the set-up of a number of clinical studies.

In March 2020, at the start of the COVID-19 pandemic, Dr Benjamin Milne and Dr Thomas Gilbey, were in their first year of being South East London's first-ever NIHR-funded Clinical Academic Fellows (ACFs) ACF year and have now set up research projects within anaesthesia that started in May 2021.

Members of the ACET research team

Trauma & Orthopaedic Surgery

The last year has seen the Trauma & Orthopaedic Surgery research team and the Orthopaedic researchers make substantial strides in research output, collaborations, publications and research delivery. Over fifteen Orthopaedic PIs, supported by junior PIs, across the Trust have taken part in multiple successful collaborations, leading to the delivery of high quality evidence-based research and related publications.

The KCH Orthopaedic Research Unit has made its mark nationally and internationally by taking part in most of the available national trials, particularly in Orthopaedic Trauma, and has received multiple awards for data quality, excellence of research execution and high recruitment, under the lead of Ines Reichert, Consultant Orthopaedic Surgeon / R&I sub-speciality Lead and Kerim Gokturk, Clinical Research Manager.

The research unit has developed a vigorous systematic approach to screening and recruitment. Various strategies are employed to successfully increase research participation from the Trust's young and diverse patient community. The team actively engages and involves clinicians of all grades in clinical research, by supporting and promoting an open and inclusive research culture. Reflecting a marked increase in research, in the last financial year the Orthopaedic and Trauma research team has expanded its capacity by appointing four Research Nurses and two Clinical Research Fellows.

Strong collaborations resulted in securing an NIHR Health Technology Assessment Grant in partnership with Imperial College for the DM PAD Study, which is co-led by Orthopaedic Consultant Mr Raju Ahluwalia and focuses on determining the best test for poor circulation in peripheral arterial disease – a key cause of leg amputation in people with diabetes.

The team have also begun to recruit participants to the CHIP study, which is initiated and led by Haematology Professor Ghulam Mufti and co-led by Ms Ines Reichert in Orthopaedics. With 100 of its target 5000+ participants already recruited, the study aims to understand clonal haemopoiesis and immune modulation in the healthy-ageing population and in people with myeloid neoplasms and bone marrow failure.

The Hindfoot Ankle Reconstruction Nail Trial (HARnT), mapping surgical treatment of complex ankle fractures in the UK has been born out of a collaboration between KCH Orthopaedics, the British Orthopaedic Trainees Association (BOTA) and the Orthopaedic Trauma Society (OTS).

The success stories of the last year are reflected by a noteworthy rise in the number of peer-reviewed publications by the KCH Trauma & Orthopaedic Surgery researchers. These publications cover numerous topic-based research including Complex Fractures and Infection, Diabetic Foot, Upper Limb as well as the implementation of KHP initiative IMPARTS (Integrating Mental and Physical healthcare: Research Training and Services) into limb reconstruction.

The Orthopaedic Research team takes great pride in its inclusive and supportive approach and continuously puts effort towards delivering high-quality research, which contributes to the evidence base and is increasingly underpinning Orthopaedic and Trauma Surgery.

Members of the Trauma & Orthopaedic Surgery research team

RDU 9
Children

Children

In the past year, the Paediatric research team have faced many challenges including redeployment and staff changes. Nevertheless, the team has worked hard to maintain and build upon their involvement in paediatric clinical trials and studies for the benefit of patients at KCH and around the world.

The paediatric research team ran the PEDFIC1 study (A Double-Blind, Randomized, Placebo-Controlled, Phase 3 Study to Demonstrate Efficacy and Safety of A4250 in Children with Progressive Familial Intrahepatic Cholestasis (PFIC) Types 1 and 2) which investigated the effects of the drug A420, also known as odevixibat, for children who have a rare genetic condition –PFIC - that causes debilitating itch, affecting all aspects of their lives. Recent results have shown that the medication has a significant effect in reducing itch, being well tolerated with very low incidence of diarrhoea, suggesting that trial medication may become the first drug for PFIC patients. Screening and study visits continue to be carried out for a cohort of patients taking part in the follow-on clinical trial PEDFIC2, which will determine the long-term safety and efficacy profile of odevixibat for PFIC.

The Paediatric research team are also involved in the DIAMONDS study (Diagnosis and Management of Febrile Illness using RNA Personalised Molecular Signature Diagnosis), which launched in June 2020. This interesting study aims to create a new diagnostic test that can accurately determine what illness a patient has when they come to hospital with common symptoms like fever. This could assist diagnosis and selection of the correct treatment for a broad cohort of patients. The diagnostic device, called 'personalised medicine signature device', uses each individual patient's gene expression to identify genetic signatures which are associated with specific infectious or inflammatory diseases.

The Paediatric research team has and continues to adapt and fine-tune its practices in order to maintain excellent patient care and standards in research during what has been an extremely challenging year. They look forward to seeing more paediatric patients working in collaboration with staff across the Variety Children's hospital. They continue to take on new clinical trials and studies to work towards a shared goal of providing new treatments and improving paediatric patient care.

King's Clinical Research Facility (CRF)

King's Clinical Research Facility (CRF)

The NIHR Wellcome King's Clinical Research Facility (CRF) is one of 23 Clinical Research Facilities for Experimental Medicine supported nationally by the NIHR and academically by King's Health Partners, an Academic Health Sciences Centre collaboration between King's College London and the South London and Maudsley, Guy's and St Thomas' and King's College Hospital NHS Foundation Trusts.

Located at Denmark Hill, the site houses high-quality experimental medicine facilities where specialist clinical research and support staff work together on patient-orientated commercial and non-commercial studies.

During the COVID-19 pandemic, the King's CRF and its staff supported 13 interventional COVID-19 clinical trials – namely Phase 3 trials of Novavax's COVID-19 vaccine and Gilead's antiviral remdesivir and also the national PHE-sponsored SIREN study. However, the King's CRF also supported the launch of many non-COVID-19 studies, ranging in topic from liver failure to depression. In November 2020, Professor Anil Dhawan was awarded a grant from the Medical Research Council (MRC) to investigate the safety, efficacy and tolerability of transplanting liver cells encased in mesenchymal stromal

King's CRF staff

cells inside alginate microbeads for the treatment of acute liver failure in paediatric patients. All work will be carried out at the King's CRF's Cell Therapy Unit and, if successful, the trial – called the HELP study – could pave the way for liver cell transplantation to replace the need for whole donor livers in some cases of acute liver failure, thus reducing mortality of those who would otherwise be on the liver transplant waiting list.

Earlier this year, the King's CRF, alongside King's College London, was selected by Small-Medium Enterprise (SME) Neurocentrx to deliver Phase 1 and Phase 2 clinical trials in to the treatment of major depressive disorder with oral ketamine – a drug which have previously only been licensed as an injectable or nasal spray treatment. Led by Professor Allan Young from King's College London, the trials are scheduled to commence later this year.

Throughout the pandemic, the Amyotrophic Lateral Sclerosis team, led by Professor Chris Shaw, remained active and provided continued treatment for patients taking part in three trials using Antisense Oligonucleotide (ASO) therapy. Recently, ASO therapy has emerged as an exciting and novel promising strategy for the treatment of various neurodegenerative and neuromuscular disorders.

Finally, while Patient and Public Engagement and Involvement (PPIE) has been a challenge due to national lockdown guidance, the PPIE team at the King's CRF managed to continue events mainly through social media and online webinars to promote knowledge, understanding and participation in research. In March this year, research staff from the King's CRF worked with Haberdasher Aske's Knights Academy in Lewisham to deliver a virtual session with 25 students from years 10-13 at the school. The session featured an introduction to the Facility and clinical trials by CRF Manager Elka Giemza followed by short talks from a research assistant, research co-ordinator and a doctor about their various roles and how, academically, they got to the positions where they are now. The students' feedback was generally positive, with many learning something new about the way clinical trials are carried out at the King's CRF.

The Cell Therapy Unit at the King's CRF

Supporting Services

Pharmacy

The Pharmacy Clinical Trials team continues to play a vital role in the delivery of clinical research across the Trust. They work with all RDUs to support the development of innovative therapies for patients and remain involved throughout the lifecycle of clinical trials, ensuring Investigational Medicinal Products (IMPs) are procured, handled, stored, dispensed and used safely; also maintaining all necessary paperwork.

Over the course of the last year, despite challenges experienced during the COVID pandemic, the team were able to help open 65 new studies, including many of the COVID-19 trials such as RECOVERY and Gilead's Phase 3 trial of remdesevir.

Going forward, the focus will be on developing the PRUH as a site to ensure that pharmacy staff are skilled to conduct research in order to support Trust strategy of increasing research activity at the site.

During 2020/21, the Pharmacy Academic Research Unit (ARU) was set up and established. The aim of the ARU is to partner excellence in pharmacy practice with academic output to ensure patients are given the very best in pharmaceutical care. During their first year, the Unit launched their strategy, held academic meetings, succeeded in funding, published findings, established new collaborations, supervised PhD to completion and began a new PhD Fellowships Education Award.

The ARU has had a range of achievements in the last year, with 23 peer-reviewed publications and conference presentations as well as three successful grants applications.

Future plans include increasing pharmacists as principal investigators and new roles for pharmacy technicians in research.

To contact the Pharmacy Clinical Trials team, email Esther Makanju at esther.makanju1@nhs.net.

To contact the ARU, email Dr Cathrine McKenzie at cathrine.mckenzie @nhs.net.

Members of the Pharmacy Academic Research Unit at the Trust

Radiology

The Radiology Department includes the sections of Breast Radiology, Neuroimaging and Nuclear Medicine, as well as all other imaging sub specialties. The Radiology Department is 'cross-site', encompassing all the south site hospitals. The department has an active research program in collaboration with all research teams at KCH that require imaging input into research projects.

All studies that the Radiology department collaborate with undergo a rigorous internal radiology assessment, with particular emphasis on legal requirements for imaging which requires radiation, particularly additional imaging that is above standard of care. A dedicated team, including a radiation protection officer, review all projects that have an imaging component.

While supporting a large number of NIHR portfolio and commercial studies within the Trust, the team's in-house research team has produced a significant number of self-funded research projects with over 200 publications in the last five years.

Current studies include the PROSPECTS trial which will compare the cost-effectiveness of traditional 2D mammograms to new 3D breast imagining technology, or the CEUS-LIRADS trial which will assess the diagnostic performance of different ultrasound contrasting agents.

Pathology

Viapath analytics supports research across King's Health Partners (KHP). This encompasses the pathology disciplines of Blood Sciences, Clinical Biochemistry, Reference Chemistry, Reference Haematology, Clinical Transplantation, Diagnostic Immunology and Allergy, Genetics, Tissue Sciences, Haemostasis and Thrombosis, Nutristasis, Infection Sciences and Contract Research. Laboratories are accredited to the UKAS ISO15189 standards for medical laboratory quality and competence.

Viapath analytics supports both NIHR portfolio and commercial studies, as well as providing a specialist service to staff within KHP, but also to wider NHS organisations, national academic faculties, international collaborators and commercial institutions. This is achieved through the development of new tests and supporting Trust speciality trainees in FRCPath and higher research degrees (MSc, PhD) by providing the technical expertise in delivering in-house research projects.

Viapath analytics supports many studies with the investigation of routine pathology endpoints and also in bespoke biomarker pathology exploratory endpoints where services are specially designed specific to the study and delivered using multiple analytical platforms as well as manual set-up and pre-analytical processing requirements.

Recent studies include the Genetic markers of kidney disease progression in people of African heritage in the UK CHIC cohort, which required the analysis of over 3000 stored samples for albumin-creatinine ratio, and the LIPOSAX study, which is investigating the metabolic effects of Liraglutide (GLP-1 receptor agonist) in patients with overweight or in patients who are overweight or obese.

Please direct all pathology related research enquiries to the Contract Research Contracts team at kch-tr.Viapath-ClinicalTrialEnquiries@nhs.net

Research & Innovation

Research & Innovation Office

The Research and Innovation (R&I) Office is part of the Corporate Division of King's College Hospital NHS Foundation Trust, reporting via the directors of Research and Innovation to the Trust Medical Director. The R&I team undertakes six key functions - Research Governance, Contracts, Finance, Data, Quality Assurance and Communications - to support researchers from KCH and King's College London in the planning, set-up completion and delivery of non-commercial clinical trials and studies at the Trust.

Research Governance

Rahman Ahmed

Adriana Fanigliulo

Kirsty Hedditch

Lizzie Bingle

The Research Governance team is made up of a R&I Governance Administrator Conor Murtagh who supports two Assistant Research Facilitators; Lizzie Bingle and one to be confirmed, three Research Facilitators – Kirsty Hedditch, Adriana Fanigliulo and Danielle Lyon. They are overseen by Research Governance Specialist Jasmine Palmer and the team report to Research & Innovation Governance Manager Rahman Ahmed.

The team plays a key role in coordinating and facilitating research, acting to ensure that new and on-going research across King's Health Partners is supported and developed to the highest ethical, legal and scientific standards. This varies from early contact and engagement with researchers regarding their research idea, to the feasibility, funding of the trial and how the study can be conducted at NHS sites with patients' rights, safety and wellbeing upheld.

Conor Murtagh

Contracts

Rania Mikhail

Michelle Laver

The majority of research studies rely to some extent on involvement from external organisations, whether in the preliminary phase (securing funding, arranging collaborations, database set-up), or at a later stage (sample analysis, statistical support, site engagement). Every interaction with an external organisation requires a contract, which accurately reflects what the parties have agreed, and to protect the interests of patients, staff and the Trust when conducting research.

The R&I Contracts team consists of Rania Mikhail (Contracts Manager), Michelle Laver (Senior Contracts Associate) and a Contracts Administrator (appointment pending) and sits within the wider R&I team. The team supports Trust investigators and study teams by providing advice and processing contracts to facilitate KCH-sponsored / co-sponsored and non-commercial collaborative or site-only research. Regular engagement with the Governance, Costings and R&I Finance teams, in addition to liaising with numerous other teams across the Trust and externally, ensure that contracts effectively support research from a legal, regulatory and ethical standpoint and limit the risk to patients, staff and the Trust.

Finance

Dancyl Ionut

Deqa Mohamed

Carolina Tamayo

The R&I Finance Team is led by R&I Finance Facilitator Dancyl Ionut, alongside Research Costing Officer Deqa Mohamed and Finance Administrator Carolina Tamayo. The team's key focuses are on cost attributions and income facilitation of site payments for non-commercial studies, as well as liaising regularly with RDUs and sponsors for finance-related support. The team also deal with requisition and purchase order queries, reconcile fiscal year activities and supporting finance management as necessary.

Data

Nayab Chaudhury

Laura Freer

A key aim for the government's Life Science Industrial Strategy is for providers of NHS services to have a dramatic and sustained improvement in the initiation and delivery of clinical research. The Data team, led by Data Officer Nayab Chaudhury and supported by Business Support Assistant Laura Freer, uses data from research conducted at KCH to evidence the Trust's portfolio of research and how it is benchmarked against other organisations in order to track the Trust's progress on this aim.

The main roles of the Data team include national and local metric management and reporting for KCH R&I. The team also monitor at the performance of studies, research teams and R&I in order to identify areas of improvement. Clinical trial and study management is done by the team through the online database Edge as well as the clinical trials database ClinicalTrials.gov.

Quality Assurance

Rahman Ahmed

The Research Governance Manager Rahman Ahmed and Quality Assurance (QA) Facilitator Niamh Finnegan play a key role in the co-ordination of working practices and policy implementation to ensure that the Trust is at all times compliant with both internal policies and external regulatory frameworks. They have an expert knowledge of regulatory frameworks and will be able to liaise at a high level with all stakeholders within KHP.

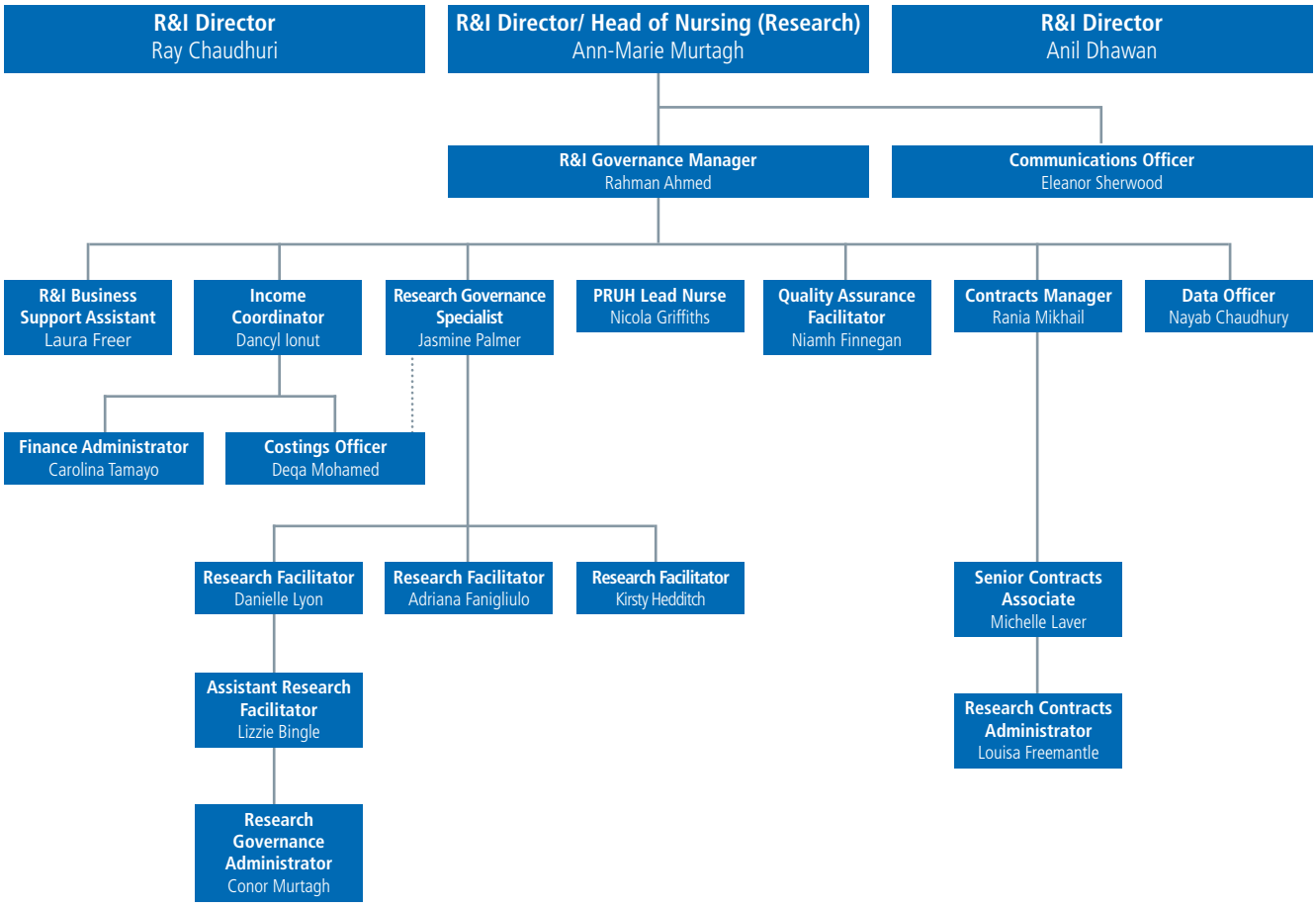
The support provided varies from safety reporting, adverse incident reporting, information governance and human tissue samples arrangements for studies, Each RDU has designated QA links to help support the research on the ground to identify and mitigate any shortfalls when conducting research at KCH.

Research Communications

Eleanor Sherwood

The R&I Communications Officer, Eleanor Sherwood, is involved with both the internal and external communication of research-related information in order to boost the visibility of and celebrate the research being delivered at the Trust, as well as facilitating recruitment into clinical trials and studies. For example, Eleanor works closely with the Trust Corporate Communications team to disseminate research achievements to local and national news outlets as well as the Trust website and social media outlets. She is also instrumental in promoting research-related news and Trust and NIHR-led research opportunities to staff at the Trust - for example through a regular Research Newsletter - and helps to organise multiple internal and external research outreach events such as the regular Research Grand Rounds and the R&I Research Meeting.

R&I Organisational Chart



Congratulations Corner

Congratulations Corner

In the last year there have been numerous important achievements made by KCH staff. Below is a snapshot of the highlights!

In December 2020, Netflix UK aired the first episode of a documentary series featuring four ground-breaking surgeons from around the world, including Professor Kypros Nicolaides from the Fetal Medicine research team. A pioneer of foetal surgery, Professor Nicolaides' discoveries have revolutionised the field and the documentary features his innovative work in endoscopic laser surgery for the treatment of twin-to-twin transfusion syndrome, a life-threatening pre-natal condition. In summer 2021, the series was awarded a BAFTA.

In March 2021, the NIHR/Wellcome King's Clinical Research Facility Director Peter Goadsby, along with Professors Lars Edvinsson, Michael Moskowitz and Jes Oleson, was awarded the 2021 Brain Prize by the Lundbeck Foundation. The prize, worth 10 million Danish Kroner (around £1.15 million) was awarded due to their ground-breaking work on the causes and treatment of migraine.

Professor Peter Goadsby

Also in March 2021, Consultant Neurologist and Professor of Neurology and Complex Disease Genetics Ammar Al-Chalabi was appointed to the NIHR College of Senior Investigators for 2021. Researchers are awarded this position based on their internationally excellent research and its value and significance to patients and the public.

Professor Tim Jackson

Earlier this year, Professor Tim Jackson, Ophthalmology Research Lead, was ranked a leading expert in wet age-related macular degeneration, the leading cause of sight loss in the UK. The independent ranking, by Expertscape, was based on publications over the last decade.

Argyro Syngelaki

In March 2021, Dr Argyro Syngelaki, a Specialist Consultant Midwife working at the Fetal Medicine institute, has been appointed as an Honorary Senior Lecturer at the Faculty of Life Science and Medicine, King's College London. During her time at the Fetal Medicine Research Institute, Dr Syngelaki acquired two PhD degrees, the first in diabetes and obesity in pregnancy and the second in screening for pregnancy complications at 11-13 weeks and has published over 160 scientific publications in international peer-reviewed journals. In her new role as Honorary Senior Lecturer, Argyro is keen to use her experience and academic excellence to benefit undergraduate and postgraduate teaching and higher degree supervision.

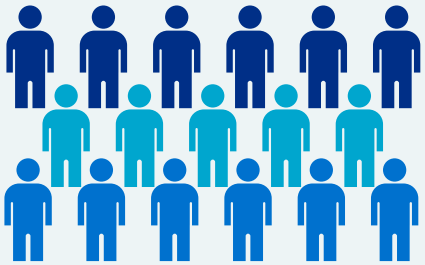
Finally, this year the neuro-oncology service at KCH, led by Professor Keyoumars Askhan, was designated a Centre of Excellence for the care and treatment of brain tumours by the Tessa Jowell Brain Cancer Mission. The service at King's was measured on a range of criteria including excellent clinical practice and training opportunities; emphasis on patient quality of life; providing clinical trials; and offering a high standard of research opportunities.

Useful Information

The year in numbers....

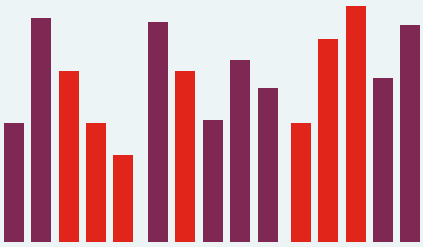
Here we look back at 2020's research output in numbers, from the number of participants in research studies to value of commercial contracts.

NUMBER OF PARTICIPANTS IN RESEARCH STUDIES 2020



19,675

NUMBER OF RESEARCH STUDIES OPEN IN 2020



835

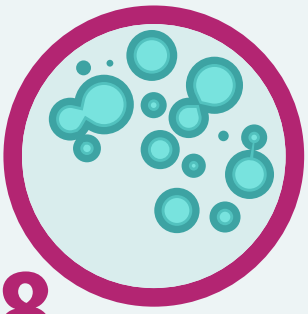
NUMBER OF NEW NON - COMMERCIAL PORTFOLIO STUDIES APPROVED

92

NUMBER OF NEW COMMERCIAL STUDIES OPENED IN 2020

71

NUMBER OF NON-COMMERCIAL RESEARCH CONTRACTS FULLY EXECUTED IN 2020



228

NUMBER OF SUBSTANTIAL AMENDMENTS PROCESSED IN 2020

223

NUMBER OF NON SUBSTANTIAL AMENDMENTS PROCESSED IN 2020

240

NUMBER OF FULL TIME RESEARCH STAFF

191

COMMERCIAL CONTRACT VALUE OF RESEARCH STUDIES IN 2020

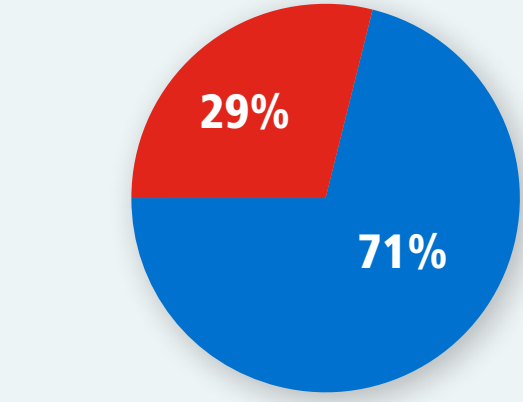
£12 million

Diversity & inclusion in Research

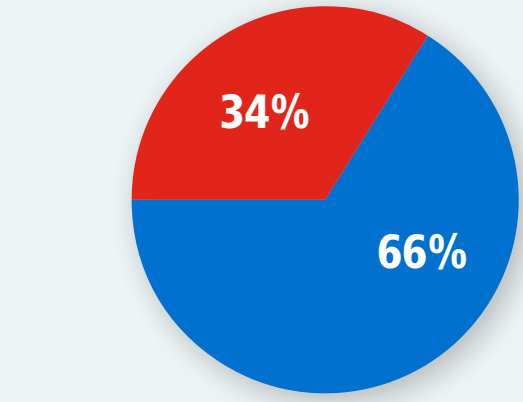
Diversity in research is a key aspect of the KCH R&I Strategy and a major focus is on addressing disparities of care related to ethnic origin of patients - especially those from black and minority ethnic and "hard to reach" groups. The work, led by Professor K Ray Chaudhuri from KCH helped and advised the KCH Vaccine Hesitancy Advisory group and included community-facing webinars such as "COVID-19 vaccine BAME conversation: facts and education" held on 11 February 2021 and attended by a wide audience with an extensive question and answer session.

In conjunction with the Applied Research Collaboration (ARC) and the NIHR CRN South London, Professor Ray Chaudhuri has championed the issue of low participation black and minority ethnic communities in commercial and non-commercial research studies across the Trust, in particular Denmark Hill. Many barriers have been identified, such as poor trust in secondary care researchers and studies, the pattern of communication as well as unconscious bias of researchers towards inclusion of these groups.

Efforts to address these issues have begun, and some data now available indicates that the KCH model of engaging communities, implementing diversity in workforce, building trust and improving communication seems to be effective in improving black and minority ethnic inclusion in NIHR Urgent Public Health Studies such as Covid CNS and SIREN. Furthermore, KCH and the PRUH participated in one of the COVID-19 vaccine studies and registered the highest number of non-white participants compared with global data that was published in the New England Journal of Medicine. This data and that from the KCH model was discussed by Professor Chaudhuri at a nationwide 'Inclusion in Research" webinar, run by media company UKRD, where the need for inclusion into research of diverse communities was cited as a matter of utmost priority.



Recruitment of ethnic minority (EM) and white subjects to the COVID CNS study



Recruitment of ethnic minority (EM) and white subjects to the SIREN study

KCH Research Delivery Unit (RDU) Leads

Dr Julie Whitney
Speciality Lead:
Age and Ageing
julie.whitney@nhs.net

Dr Gudrun Kunst
Speciality Lead:
Anaesthetics
gudrun.kunst@nhs.net

Prof Theresa McDonagh
RDU 2 Lead
Speciality Lead:
Cardiovascular
t.mcdonagh@nhs.net

Dr Atul Gupta
RDU 9 Lead
Speciality Lead:
Children
atulgupta1@nhs.net

Dr Phil Hopkins
RDU 8 Lead
Speciality Lead:
Critical Care
p.hopkins@nhs.net

Prof Tara Renton
Speciality Lead:
Dental
t.renton@nhs.net

Dr Prashanth Vas
Speciality Lead: Diabetes
prashanth.vas@nhs.net

Dr Fleur Cantle
Speciality Lead:
Emergency Department
fleur.cantle@nhs.net

Prof Kypros Nicolaides
RDU 3 Lead
Speciality Lead:
Fetal Medicine
k.nicolaides@nhs.net
kypros@fetalmedicine.com

Dr Mohammad Ibrahim
General Pathology
mohammad.ibrahim@nhs.net

Prof Paul Sidhu
General Radiology
paulsidhu@nhs.net

Dr Alexandra Kent
Speciality Lead:
Gastroenterology
alexandra.kent@nhs.net

Dr Piers Patten
RDU 4 Lead
Speciality Lead:
Haematology and
Precision Science
piers.patten1@nhs.net

Prof Frank Post
RDU 7 Lead
Speciality Lead:
HIV and Sexual Health
frank.post@kcl.ac.uk

Dr Mark McPhail
RDU 5 Lead
Speciality Lead:
Liver
mmcphail@nhs.net

Dr Thomas Booth
Speciality Lead:
Neuroradiology
thomasbooth@nhs.net

Prof K Ray Chaudhuri
RDU 1 Lead
Speciality Lead:
Neurosciences
ray.chaudhuri@nhs.net

Prof Timothy Jackson
Speciality Lead:
Ophthalmology
t.jackson1@nhs.net

Dr Ines Reichert
Speciality Lead:
Orthopaedic Surgery
i.reichert@nhs.net

Dr Sabrina Bajwah
Speciality Lead:
Palliative Care
sbajwah@nhs.net

Esther Makanju
Pharmacy Lead
esther.makanju1@nhs.net

Dr Deepak Rao
PRUH R&I Lead
deepak.rao@nhs.net

Dr Georgios Dimitriadis
Speciality Lead: Endocrine
& Obesity
PRUH R&I Co-Lead
g.dimitriadis@nhs.net

Dr Mohammad Albarjas
PRUH R&I Co-Lead
mohammadalbarjas@nhs.net

Dr Sapna Shah
RDU 6 Lead
Speciality Lead: Renal
sapna.shah@nhs.net

Dr James Galloway
Speciality Lead:
Rheumatology
james.galloway@nhs.net

Dr Laszlo Sztriha
Speciality Lead:
Stroke
laszlo.sztriha@nhs.net

Dr Sharlene Greenwood
Therapies Lead
sharlene.greenwood@nhs.net

Dr Gordon Muir
Speciality Lead: Urology
gordon.muir@nhs.net

Dr Dudley Robinson
Speciality Lead: Women's Health
dudley.robinson@nhs.net

Research Delivery Managers and Matrons (RDMs)

RDU 1
Alex Rizos
Neuroscience
a.rizos@nhs.net

RDU 1
Jonnie Aeron-Thomas
Stroke
j.aeron-thomas@nhs.net

RDU 2
Jonathan Breeze
Cardiology
jonathan.breeze@nhs.net

RDU 3
Argyro Syngelaki
Fetal Medicine
argyro.syngelaki@nhs.net

RDU 3
Katherine Clark
Women's Health
katherineclark1@nhs.net

RDU 4
Lorraine Catt
Haematology
lorraine.catt@nhs.net

RDU 4
Maria Liskova
Haematology
maria.liskova@nhs.net

RDU 5
Vernie Ramalingam
Liver
vernie.ramalingam@nhs.net

RDU 5
Lee Meng Choong
Gastro
leemeng.choong@nhs.net

RDU 6
Leela Goldstein
Renal
leela.goldstein@nhs.net

RDU 6
Andrew Pernet
Diabetes
andrewpernet@nhs.net

RDU 7
Riti Desai
Ophthalmology
ritidesai@nhs.net

RDU 7
Lucy Campbell
HIV/ Sexual Health
lucy.campbell1@nhs.net

RDU 8
John Smith
ACET
john.smith27@nhs.net

RDU 8
Kerim Gokturk
Orthopaedics
agokturk@nhs.net

RDU 9
Katie Tupper
Paediatrics (Maternity)
katietupper@nhs.net

RDU 9
Ivan Caro
Paediatrics (Maternity cover)
ivancaro@nhs.net

King's Health Partners Clinical Trials Office

The King's Health Partners Clinical Trials Office (KHP CTO) was set up to formalise the pre-existing collaborations between partner organisations, to develop their clinical trials potential and to increase the quality and delivery of clinical trials.

KHP-CTO partner Organisations

NHS King's College Hospital NHS Foundation Trust

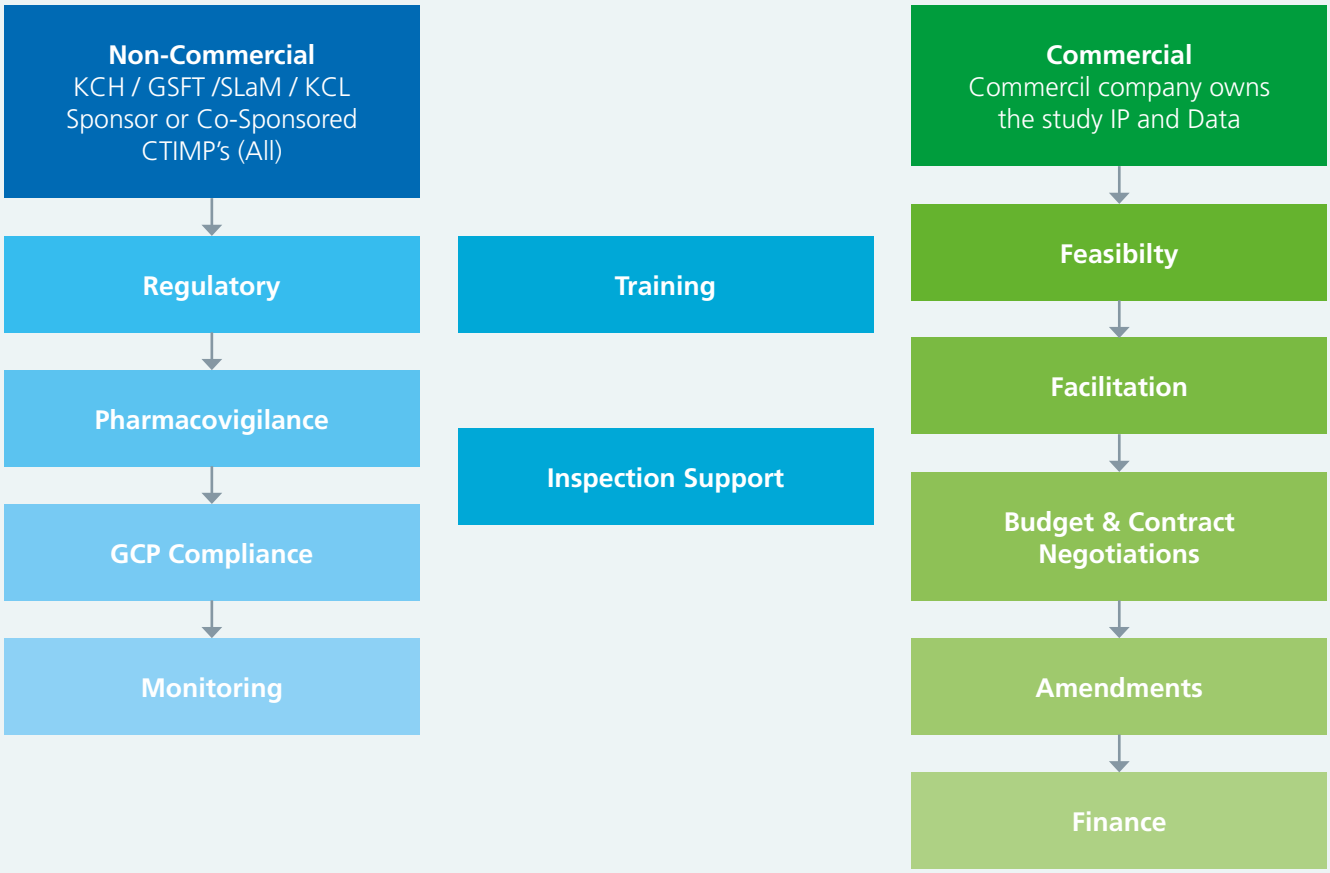
NHS South London and Maudsley NHS Foundation Trust

NHS Guy's and St Thomas' NHS Foundation Trust

King's College London

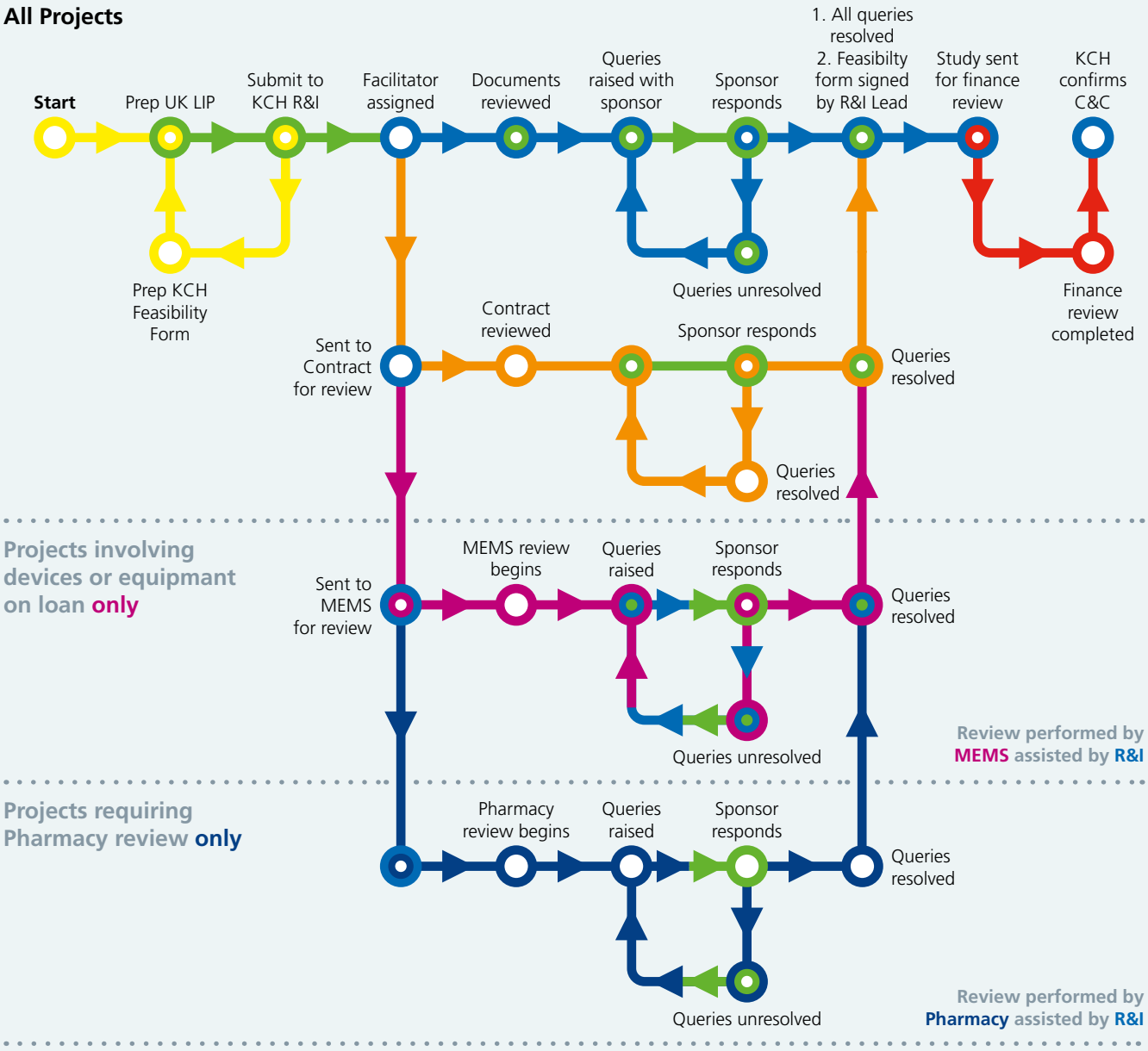
The KHP CTO has two sections: the Commercial Team which provides a single interface for those wishing to conduct trials sponsored by the pharmaceutical and allied healthcare industries and the Quality Team that supports investigators at KHP's institutions who undertake clinical trials where KHP are the sponsor or co-sponsor, to ensure delivery of the statutory obligations contingent on sponsorship of drug trials.

The functional set up of the KHP CTO



Project Approval 'Tube Map'

This map details the complete approval pathway for site only studies at KCH. If you are unsure if your study is a 'site only study' and eligible to use this pathway, please refer to the decision tool at http://www.hra-decisiontools.org.uk/research/.



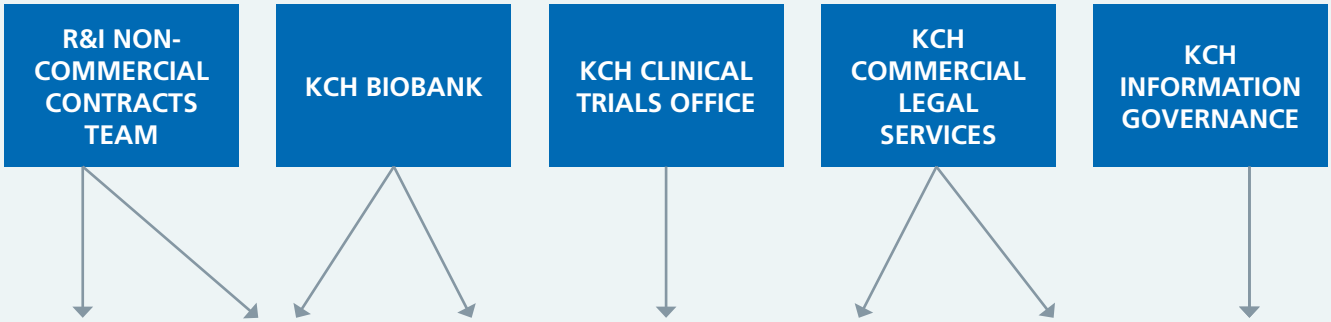
Key

Lines = *pathway information flow*
Circles = *an event without which the application cannot progress*
Colour = *party responsible for information flow/event*

Where two or mor parties are involved this will be represented by concentric circles:

= Sponsor
= KCH PI
= KCH R&I
= KCH Contracts
= MEMS
= Pharmacy

Examples of R&I Contracts



NON-COMMERCIAL RESEARCH CONTRACTS

Participating Site
mNCA/site agreement

Sponsor (investigator -initiated)
CDA
Funding agreement
Collaboration agreement
Sub-funding agreement
SLA
Technical agreement
Device loan agreement (with MIA indemnity)
mNCA
MTA
Amendment
Novation

EXTERNAL REQUEST (MTA)

Received by Biobank for assessment of samples provision, *Biobank fees and shipping preparation and costs
Passed to R&I NC Contracts to provide and finalise MTA (non-negotiable terms)
Returned to Biobank for approval and first signature
Passed to R&I NC Contracts for second signature (KCH) and final signature from requestor

INTERNAL REQUEST (KCH TRUST)

Received by Biobank
Assessment of sample provision and issue of Internal Recipient MTA by Biobank
Review, finalisation and processing for signature by Biobank

*BIOBANK FEES

Set structure subject to material type and requestor (industry or non-commercial entity)

COMMERCIAL RESEARCH CONTRACTS

Participating site agreements
CDA/NDA
provider/ supplier contracts for commercial research only

COMMERCIAL/ BUSINESS CONTRACTS

Innovate UK
HDR UK
CLAHRC (KCH host) – review only
CRN Sub-contracts
Fee for service contracts
Service evaluation
SLA for commercial activity at KCH
MTAs with commercial companies (non-commercial sponsored research) – review only
Financial assessment of KCH data

INELLECTUAL PROPERTY (IP) MANAGEMENT

IP terms for KCH collaboration with commercial partners (in KCH sponsored studies)
Revenue sharing agreements
IP advice – wording/process/ responsibilities

DATA SHARING/ TRANSFER

KCH (KHP) DSA/OTA templates
Review of non-KCH/KHP DSAs

Key
CDA = *Confidential Disclosure Agreement*
CLAHRC = *Collaboration for Leadership in Applied Health and Research Care*
CRN = *Clinical Research Network*
DSA = *Data Sharing Agreement*
DTA = *Data Transfer Agreement*
HDR UK = *Health Data Research UK*
MIA = *Master Indemnity Agreement*
mNCA = *Model Non-Commercial Agreement*
MTA = Materials Transfer Agreement
NC = *Non-Commercial*
NDA = Non-Disclosure Agreement

Abbreviations and Acronyms

AHSN	Academic Health Science Network
ALBs	Arms Length Bodies
AMRC	Association of Medical Research Charities
ARC	Applied Research Collaboration
BMJ	British Medical Journal
BRC	Biomedical Research Centre
CLAHRC	Collaborations for Leadership in Applied Health Research and Care
CRF	Clinical Research Facility
CRN	Clinical Research Network
CRUK	Cancer Research United Kingdom
CTA	Clinical Trials Assistant
CTU	Cell Therapy Unit
GCP	Good Clinical Practice
HSMR	Hospital Standardised Mortality Ratio
HTA	Human Tissue Authority
IfLS	Institute of Life Sciences
IoPPN	Institute of Psychiatry, Psychology& Neuroscience
KCH	King's College Hospital
KCL	King's College London
KHP	King's Health Partners
KHP CTO	King's Health Partners Clinical Trials Office
KPI	Key Performance Indicators
LHS	Learning Health System
MRC	Medical Research Council
NHS	National Health Service
NIHR	National Institute for Health Research
PIN	Patient Involvement Network
PPIE	Patient and Public Involvement and Engagement
PRUH	Princess Royal University Hospital
R&I	Research & Innovation
RCF	Research Capability Funding
RDM	Research Delivery Manager
RDU	Research Delivery Unit
SLaM	South London and Maudsley Hospital
SOP	Standard Operating Procedure
SRL	Speciality Research Lead

Notes

Notes

Contacts list

Research & Innovation Office
The R&I Office
King's College Hospital NHS Foundation Trust
First Floor Coldharbour Works
245A Coldharbour Lane
Brixton SW9 8RR
kch-tr.research@nhs.net
020 3299 1980

R&I Contracts
kch-tr.researchcontracts@nhs.net

R&I Quality Assurance
kch-tr.researchqualityassurance@nhs.net

R&I Data
kch-tr.data@nhs.net

R&I Finance
kch-tr.finrl@nhs.net

R&I Invoices
kch-tr.ncsiteincome@nhs.net

R&I Costing
kch-tr.rd-researchcosting@nhs.net

R&I Purchase Orders
kch-tr.researchpurchaseorders@nhs.net

Clinical Trials Pharmacy
kch-tr.ClinicalTrialsPharmacy@nhs.net

ACET Team
kch-tr.acetresearch@nhs.net

Haematology
kch-tr.hrutrialsetup@nhs.net

Liver
kch-tr.liverresearchgov@nhs.net

Ophthalmology
kch-tr.ophthalmologyresearch@nhs.net

KHP CTO Feasibility
khpctofeasibility@kcl.ac.uk

KHP CTO Study Approvals
khpctofacilitator@kcl.ac.uk

KHP CTO Protocol Amendments
khpctoamendments@kcl.ac.uk

KHP CTO Commercial Finances and Invoicing
finance-khpcto@kcl.ac.uk

KHP CTO Data
khpcto.commercialdata@kcl.ac.uk

Clinical Research Associate Team
khpcto.crateam@kcl.ac.uk

KHP CTO Training Team
khp-ctotrainingteam@kcl.ac.uk

Clinical Research Facility
kingscrf@kcl.ac.uk

Clinical Trials Pharmacy
kch-tr.clinicaltrialspharmacy@nhs.net

Rheumatology
rheumatology-ctg@kcl.ac.uk

Stroke
kch-tr.kingsresearch@nhs.net

Paediatrics
kch-tr.paediatricresearch@nhs.net