Responding to a pandemic
UK universities' research into COVID-19
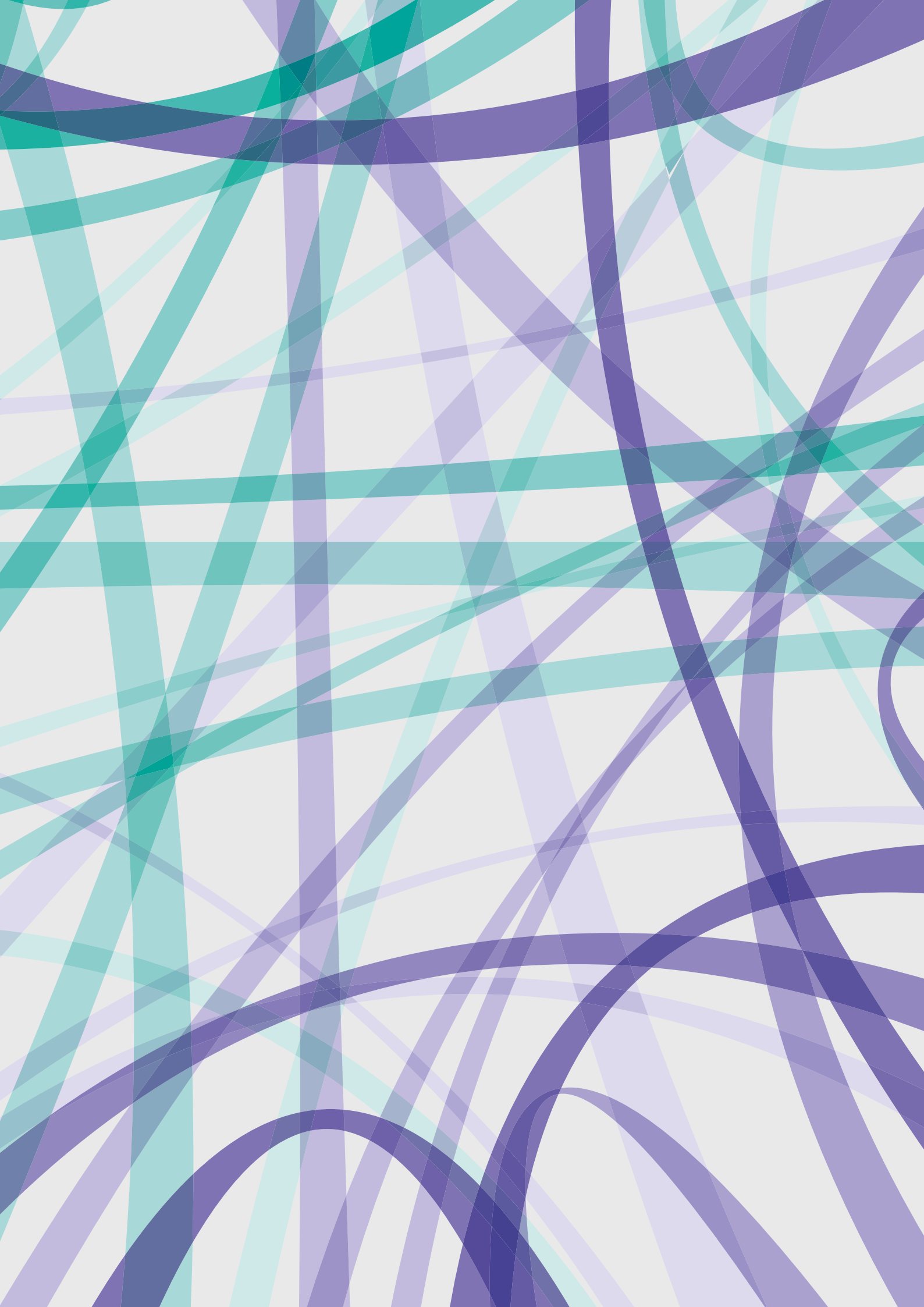
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Foreword

Despite only representing 0.9% of the global population, the UK is known for punching above its weight in research. In 2018 the UK's field-weighted citation impact (FWCI), a measure of research impact, was highest among all G7 countries[1]. This commitment to research and development has meant that UK researchers are helping to lead the global scientific response to the coronavirus pandemic. Universities and their medical schools are often at the forefront of this work, producing cutting edge research that is influencing how we treat and prevent COVID-19.

Universities have always maintained a strong relationship with the NHS. As well as providing its future workforce, universities work with the health service to develop new treatments and technologies that drive improvements in patient care. This research is often led by clinical academics: health professionals who work in universities and engage in clinical work in NHS Trusts, GP practices and public health settings. It is then no surprise that when the nation faced a major health crisis, universities stepped up to help guide the UK's response.

In this publication we have highlighted several studies undertaken at UK universities which have made a difference to our understanding and management of COVID-19.

The publication is organised into five themes:

- Characterising a novel virus
- Driving improvements in treatment and patient care
- Informing the evolving policy response
- Supporting education and training
- Understanding the wider impact of COVID-19

It should be noted that this represents only a small percentage of COVID-19 research being performed in universities, but it does provide a glimpse into the variety of research that is taking place.

The success of the UK's scientific response to COVID-19 has been facilitated by substantial investment through various funding bodies and important collaboration with industry. Many of the case studies in this publication have received funding though organisations such as the Medical Research Council, National Institute of Health Research, Wellcome Trust and other research charities. Long term flexible investment into research is central to the Government's R&D Roadmap and the pandemic has clearly shown that, even in the short-term, strategic and focused funding can yield meaningful results.

We are already seeing the benefits of UK university research in the global fight against COVID-19. The biggest breakthrough has been the development of safe and effective vaccines, a remarkable scientific feat that has helped save countless lives. In addition to the vaccine effort, UK universities have led the way in advancing therapeutics through ground-breaking clinical trials and new technologies which have both saved lives and vastly improved the outcomes of patients that become ill with the virus.

"In a time of difficulty and loss for so many people and communities, research into COVID-19 has provided a beacon of hope."

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1. International comparison of the UK research base (2019), https://www.gov.uk/government/publications/international-comparison-of-the-uk-research-base-2019

Our ability to conduct this essential work is strengthened by employing clinical academics who work at the boundary of healthcare delivery and research. Their contribution is invaluable not only in addressing the impact of the pandemic but also in improving our management and treatment of health outside of COVID-19. When the pandemic arrived in the UK, thousands of clinical academic consultants and trainees took the initiative to return to clinical practice and support the NHS's response to the virus.[2] A key concern for the sector is that these trainees are now given the time and resource to progress their research and education careers. It is vital that we adequately support clinical academics returning from the COVID-19 frontline to ensure we continue to champion research-focused healthcare and maintain the UK's position as a world leader in science and research.

The UK has always fostered a research-rich environment but the coronavirus pandemic has reminded us just how important this is. As the case studies in this publication clearly illustrate, clinical research improves lives and makes a tangible difference to public health, society and the economy. Maintaining a healthy research culture in all aspects of healthcare will help us prepare against any future threat to public health. While coronavirus research has been invaluable, the pressures of the pandemic have disrupted and stalled important research into other health conditions. It will be important that as we restart non-covid related research we ensure that appropriate funding and support is available.

The Department of Health and Social Care has recently released its strategy on how UK clinical research delivery can move forward and learn from the lessons of the pandemic.[3] To meet these actions it is crucial that, just as we have done during the pandemic, the spirit of collaboration between universities, the NHS, industry, research charities and all those who have contributed to the pandemic response is maintained and embedded into our research infrastructure. What we have achieved through collective effort in crisis is significant and if we can support these partnerships we have the opportunity to rebuild a more resilient and diverse research ecosystem that can transform the future of healthcare.

In a time of difficulty and loss for so many people and communities, research into COVID-19 has provided a beacon of hope. It is our belief that in recovering from the pandemic the UK's expertise in research can be harnessed for the benefit of all.

Professor Malcolm Reed and Professor John Atherton
Co-Chairs of the Medical Schools Council

2. Clinical Academic Training Forum, Addressing the challenges of the COVID-19 second wave or another pandemic (2020), https://acmedsci.ac.uk/file-download/30131605
3. UK Government, Saving and Improving Lives: The Future of UK Clinical Research Delivery (2021), https://www.gov.uk/government/publications/the-future-of-uk-clinical-research-delivery

Characterising a novel virus

Coronaviruses, a group of viruses that can cause mild to severe respiratory illness, have been studied by scientists for decades. However, many of the early challenges faced by researchers trying to understand COVID-19 resulted from it being a "novel" strain of coronavirus that had not been previously identified in humans.

Its novel nature meant that we did not have existing evidence on how to identify COVID-19, its transmission rates and the impact of contracting the disease. Characterising the virus has required enormous global scientific effort and collaboration which has led to huge advancements in our understanding of COVID-19.

The case studies in this section demonstrate some of the ways in which universities and researchers are building our understanding of the characteristics of COVID-19. With work ranging from improvements in testing to exploring the genomics of the virus, it highlights that building an evidence-based response requires continued development and learning.

COVID-19 Genomics UK (COG-UK) consortium
University of Cambridge

Together with the Wellcome Sanger Institute, the University of Cambridge is leading the national COVID-19 Genomics UK (COG-UK) consortium, a pioneer in the use of large-scale sequencing of SARS-CoV-2, to understand viral transmission and evolution and to inform public health responses and vaccine development.

Funded by a £20 million investment from the Department of Health and Social Care (DHSC), UK Research and Innovation (UKRI) and the Wellcome Sanger Institute, COG-UK provides sequencing, methodologies and analysis tools for use throughout the UK. The consortium is an innovative partnership between four Public Health Agencies of the UK, sixteen academic institutional partners across the four nations, the Wellcome Sanger Institute, and diagnostic laboratory partners including multiple NHS laboratories and the Lighthouse Labs.

SARS-CoV-2, the coronavirus that causes COVID-19, is an RNA virus and as such its genetic code is prone to errors each time it replicates. Sequencing the genetic code of the virus can provide valuable information on its biology and transmission.

COG-UK has now sequenced and analysed more than half a million SARS-CoV-2 genomes and is making a substantial impact on national and global efforts to understand and tackle the pandemic. The consortium enabled the combination of genomic data with patients' medical records to provide real time information to help hospitals review their infection control on a weekly basis and highlighted less well-documented

Credit: Laura Olivares Boldu, Genome Research Limited
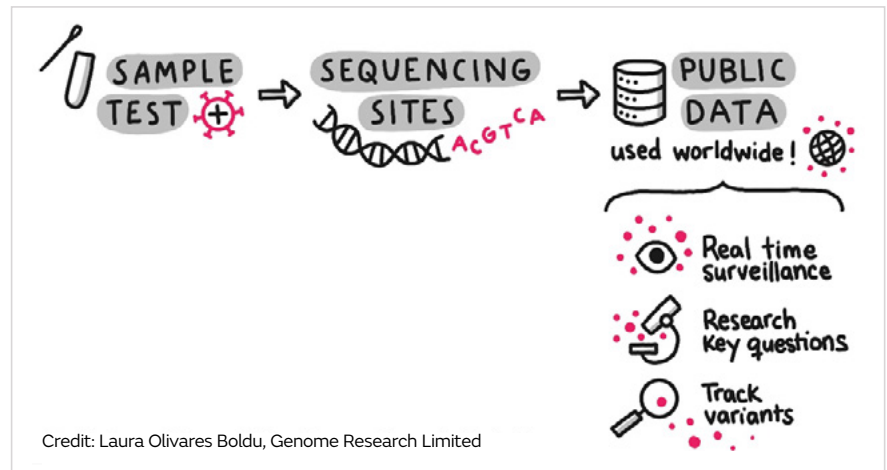
transmission networks, such as care homes, outpatient units and ambulance services.

"COG-UK has now sequenced and analysed more than half a million SARS-CoV-2 genomes and is making a substantial impact on national and global efforts"

The achievements to date, both in the volumes of data produced and the impact on human health, have far outpaced anything thought possible when setting up the consortium in April 2020. The consortium has developed freely available bioinformatics and data sharing tools and has provided data on viral transmission in care homes, universities, hospitals and through international travel, has enabled the tracking and analysis of viral variants.

The consortium has facilitated the development of a sustainable sequencing network across the UK. Having provided the knowledge, expertise, and facilities to set up UK-wide SARS-CoV-2 genome sequencing and analysis, they are now in the process of passing on this know-how to the UK Health Security Agency to facilitate the creation of a national pathogen genomics service.

COG-UK continues to create novel tools and analyse the unprecedented viral genomic dataset generated to date, advancing the understanding of the evolution and transmission of SARS-CoV-2 during the current pandemic and informing global responses to future viral threats. The consortium shares the knowledge and experiences gained to support the establishment or expansion of SARS-CoV-2 programmes in other countries worldwide.

Lead researcher: Sharon Peacock

Answering urgent questions about COVID-19 through the ISARIC4C study

University of Edinburgh, University of Liverpool, Imperial College London

The novel nature of SARS-CoV-2 has meant that there is still a lot we do not know about the virus. The ISARIC4C study, co-led by the Universities of Edinburgh, Liverpool, and Imperial College London is answering some of the most urgent questions about COVID-19.

"This includes detailed analysis of over 200,000 individuals in hospital with the virus which resulted in the first comprehensive description of COVID-19"

The ISARIC4C study and the leadership of the global pandemic preparedness effort for research in outbreaks of SARI (severe acute respiratory infections) meant researchers were able to study the very first patients presenting with COVID-19 in the UK. Within weeks, ISARIC4C provided the World Health Organisation with material to define a global reference standard for SARS-CoV2 serology (antibody response) which is still in use. The ISARIC4C group of doctors and scientists have continued answering urgent questions about COVID-19 to improve our understanding of the disease. This includes detailed analysis of over 200,000 individuals in hospital with the virus which resulted in the
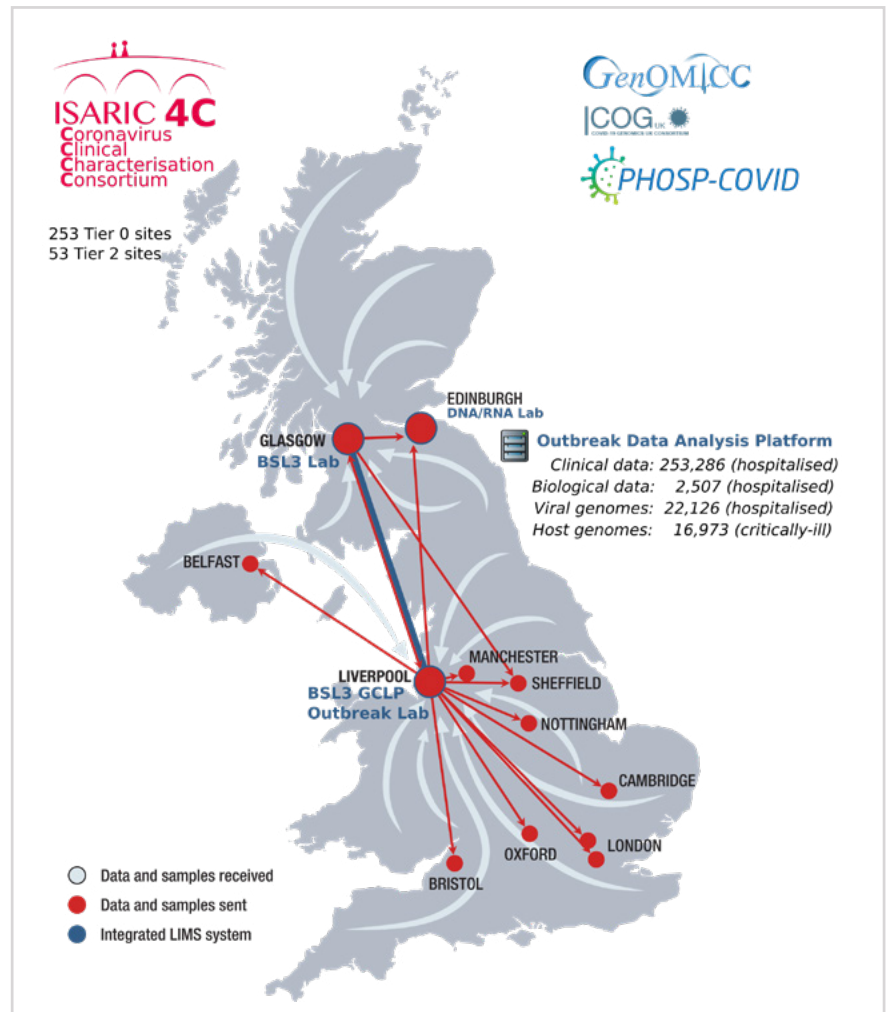
first comprehensive description of COVID-19 in UK hospitalised patients, new understanding of genetic mechanisms of disease and predicted risk outcomes to patients that has helped prioritise in-hospital patient care.

The study has led to multiple publications identifying groups at high risk from COVID-19 and importantly, researchers developed the ISARIC-4C mortality score which is widely used to help clinicians treat patients with COVID-19 worldwide, as well as being used by policy makers to guide anti-viral treatments.

Lead researchers: Kenneth Baillie, Calum Semple, Peter Openshaw, Annemarie Docherty, Ewen Harrison

Understanding the genetic factors that cause COVID-19 illness

University of Edinburgh

The University of Edinburgh-led GenOMICC study (Genetics of Mortality in Critical Care) is an open, collaborative, global community of doctors and scientists trying to understand and treat critical illness. The study started in 2015 to explore the genetic factors underlying critical illness caused by emerging infections, sepsis and other conditions. It is the largest study of its kind anywhere in the world.

"These genetic discoveries significantly advanced global understanding of the causal processes underlying life-threatening disease in COVID-19"

To help understand and treat COVID-19 GenOMICC has recruited patients in almost every intensive care unit in the UK and with over 13,000 patient volunteers it is the largest consented research study in critical care history. By focusing on a carefully defined group of patients, the study was able to make genetic discoveries incredibly quickly. Crucially, within five months of the first case of COVID-19 in a UK intensive care unit, researchers discovered four human genes underlying critical vulnerability to COVID-19. Following this, the team discovered causal evidence

in support of four potential host-directed therapeutic targets in the virus.

These genetic discoveries significantly advanced global understanding of the causal processes underlying life-threatening disease in COVID-19 and directly suggested targeted drug treatments for the virus. One of these treatments, Baricitinib, was added to the RECOVERY trial, an international clinical trial that aims to identify treatments for people hospitalised with COVID-19, almost immediately. A second treatment supported by GenOMICC, Dimethyl fumarate, targets a process that was highlighted by the study finding that a specific gene, DPP9, plays a key role in life-threatening COVID-19. This treatment is now also included in the RECOVERY trial.

Lead researcher: Kenneth Baillie

Fast-tracking a national COVID-19 test centre

University of Cambridge

In April 2020, the University of Cambridge partnered with AstraZeneca and GSK to create The Cambridge COVID-19 Test Centre. Located at the University of Cambridge's Anne McLaren Building, it was one of the Lighthouse Laboratories set up across the country to meet the demand for PCR tests at the beginning of the pandemic and boost the UK's COVID-19 testing capabilities.

Innovative cutting-edge technology in robotics and automation were installed to ensure the testing facility was both resilient and highly effective. An entire supply chain was sourced in five weeks, an operation which would usually take six months.

"The centre processed more than three million tests over a year. In addition to making a major contribution to the NHS Test and Trace programme"

Soon after its launch the centre was brought into the Government's national diagnostic lab network. This collaboration combined the expertise of two pharmaceutical partners with the University's leading interdisciplinary research capabilities and led to the creation of a highly efficient and effective laboratory, combining molecular biology expertise with state-of-the-art automation. In the second phase Charles River joined the collaboration.

University of Cambridge's Ann McLaren Building

An innovative new COVID-19 test was designed and created for the centre with a team from Primerdesign, part of the international diagnostics company Novacyt. The technique could be used across a number of different testing platforms to determine the presence of COVID-19, creating a more rapid testing process and making the Lighthouse network less dependent on specific consumables. The testing innovation and improvements developed at the test centre helped form a strong foundation for a robust and sustainable testing network across the UK. Specific innovations included reducing reaction volumes, and introduction of heat inactivation and direct-to-PCR protocols.

The centre processed more than three million tests over a year. In addition to making a major contribution to the NHS Test and Trace programme, the centre provided tests for successful programmes demonstrating the value of asymptomatic testing of healthcare workers and pooled asymptomatic screening of students.

Lead researchers: Chris Abell, Andy Neely and Patrick Maxwell, and partners from GSK, Charles River and AstraZeneca

New COVID-19 test gives accurate results in under five minutes

University of Birmingham

Researchers at the University of Birmingham have developed a new COVID-19 test that reduces testing time from 30 minutes to less than five and delivers accurate results.

"The Birmingham team's technique can use very short, single strands of DNA for the replication process which can be completed in a matter of minutes and reduce the overall time needed to produce results"

The team set out to design a new method for testing that combined the ease of use and speed of lateral flow testing with the sensitivity of an RNA test. The most accurate COVID-19 tests currently in use are based on detecting viral RNA – and the most common of these use a technique called RT-PCR (polymerase chain reaction). The RT-PCR test is a two-step process, which involves first converting the RNA to DNA followed by a step that 'amplifies' the material many times over.
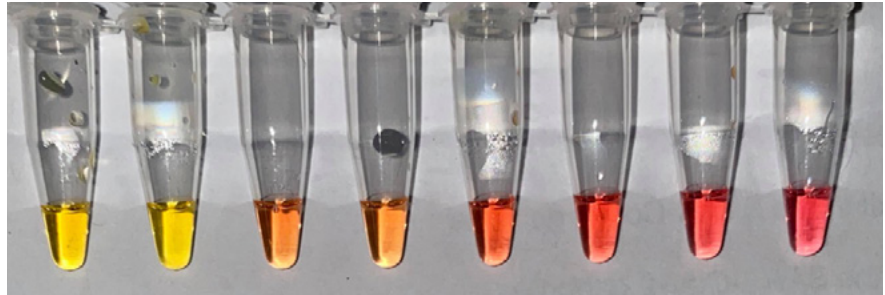
By utilising an alternative amplification method called RTF-EXPAR (Reverse Transcriptase Free Exponential Amplification Reaction), the Birmingham team's technique can use very short, single strands of DNA for the replication process which can be completed in a matter of minutes and reduce the overall time needed to produce results. The test does not require samples to be treated at high temperatures and can be performed using standard laboratory equipment, making it readily deployable.

The researchers anticipate that further development work could lead to a simple handheld test which could give 'on the spot' results and thus rapid diagnosis. While the method was developed specifically to reduce COVID-19 testing time and increase testing throughput, in the long-term the use of the RTF EXPAR technology is expected to extend to other RNA-based viruses and infectious agents such as bacteria as well as other diseases including cancer.

Lead researchers: Tim Dafforn, James Tucker, Andrew Beggs, Jake Carter

Understanding the pathology of COVID-19
Hull York Medical School, Newcastle University

The World Health Organisation has reported several million deaths worldwide attributable to the COVID-19 pandemic, yet the precise reasons why some people die following SARS-CoV-2 infection and others do not is yet to be fully established. The study of pathology is fundamental to understanding cause of death.

Initial studies of autopsy tissues from patients who died from COVID-19 identified the nature of the inflammatory response and provided evidence for changes in blood vessels indicative of thrombotic events. A molecular understanding of these pathological changes was, however, lacking. To fill this knowledge gap, researchers at Hull York Medical School, Newcastle University and the Wellcome Sanger Institute joined forces as part of the UK Coronavirus Immunology Consortium to study tissue from COVID-19 patients using cutting-edge imaging-based molecular pathology techniques.

The researchers assembled one of the largest autopsy cohorts in the world, obtaining samples from tissue banks in London, Newcastle and Edinburgh, that cover a spectrum of ages, community acquired and hospital deaths and first and second wave cases. NHS pathologists are working alongside academics, technologists and data scientists to document the diverse pathology seen in individual patients and across patient groups. Uniquely, this collaboration has allowed the use of a range of technologies rarely available in any single institution, including protein and transcriptomic digital spatial profiling and imaging mass cytometry.

> **"The researchers assembled one of the largest autopsy cohorts in the world, obtaining samples from tissue banks in London, Newcastle and Edinburgh"**

This research will enable deep phenotyping (assessing traits) of distinct inflammatory cell subsets, with a focus on T lymphocytes and myeloid cells, to characterise their relationship to the heterogeneous patterns of pathology observed in these patients.

Additionally, the phenotyping panels include the targets of drugs that are already in use to treat other diseases, paving the way for the research to identify new therapeutic options to treat patients with COVID-19. The team-working approach developed during this study provides the basis for a longer-term sustainable network able to rapidly deliver insights into the pathology associated with emerging diseases.

Lead researchers: Paul Kaye and Andy Fisher

Exploring how the immune system responds to COVID-19

King's College London

King's College London is pioneering research to better understand how the immune system responds to the SARS-CoV-2 virus, to determine what an adequate immune response looks like and how this information can be harnessed to create novel tests and treatments. It will also help inform why some patients fare far worse than others, and why some people do not seem to be affected at all.

"The King's College London work on defining sepsis has informed a World Health Organisation resolution highlighting sepsis as a global health priority. "

Severe COVID-19 is an example of viral sepsis, a severe response of the human immune system to infections. Previous work conducted by researchers at King's College London identified diagnostic biomarkers for early detection of the immune response associated with sepsis among patients requiring emergency care with an infection, but the relevance or otherwise of those to COVID-19 required experimental investigation. Happily, the practical foundations for this had been built by capacity-building in high-throughput immune-profiling and data analysis, which began in response to the swine flu pandemic.

When COVID-19 arrived in the UK, King's researchers worked closely with emergency care and infection disease clinicians at Guy's & St Thomas' NHS Foundation Trust (GSTT), responding rapidly to assess the immune system changes associated with COVID-19 infection. This study – COVID-IP, a collaboration between King's, GSTT and The Francis Crick Institute – was at the time the largest comprehensive assessment of immune biomarkers of severe COVID-19 (based on 63 adult patients admitted to GSTT), identifying those biomarkers associated with poor prognosis, those that are similar to sepsis, and those that help predict the risk of severe COVID-19 illness.

Researchers also identified immunological changes observed in children with the rare COVID-related illness, Multisystem Inflammatory Syndrome in Children (MIS-C), revealing it was a serious immunopathological condition, quite distinct from Kawasaki's disease despite its superficial resemblance.

As a result of their COVID-IP and MIS-C studies, the lead researchers were invited to give evidence to the House of Lords Science & Technology Select Committee and to the All-Party Parliamentary Group on the immunology of COVID-19. The King's College London work on defining sepsis has informed a World Health Organisation resolution highlighting sepsis as a global health priority. Additionally, the application of COVID-IP to cancer patients infected with and/or vaccinated against SARS-CoV-2 provoked the UK Government to prioritise "ring vaccination" of those who care for cancer patients.

Lead researchers: Adrian Hayday and Manu Shankar-Hari

New diagnostic tool uses cell surface sugars to rapidly detect COVID-19

University of Warwick

Researchers at the University of Warwick have developed a new approach to detect coronavirus using glycans (sugars) found on cell surfaces. This approach offers significant benefits including a rapid result, requires no specialist lab equipment or training and is based on unique detection technology.

> **"This approach offers significant benefits including a rapid result, requires no specialist lab equipment or training and is based on unique detection technology"**

When the pandemic hit, there was an urgent, global need to increase diagnostic testing capacity for COVID-19 infections. The GibsonGroup at the University of Warwick, working with their partners Iceni Diagnostics Ltd, set out to explore how SARS-COV-2 recognised glycans found on cell surfaces and used this knowledge to create a new method of rapid testing. Iceni have since taken a global license to this technology and are co-developing this with the Warwick team as part of a growing industry and academic collaboration.

It is well established that pathogens (viruses, bacteria and toxins) gain entry to their host by binding to specialised glycans on the surface of our cells – a classic example being influenza. Using a nanoparticle-based detection platform, the research team discovered that the SARS-COV-2 spike protein could bind to a certain class of glycans (sialic acids).

The teams at the University of Warwick and Iceni set out to use this new knowledge to develop an alternative approach to lateral flow diagnostics (LFDs). Current LFDs (such pregnancy tests or rapid COVID tests) are based on the principle of using antibodies on the surface of a nitrocellulose (paper) strip and on gold nanoparticles (which give the 'red line'). The team wanted to replace these with glycans, which had not been widely explored but can bring benefits in terms of ease of production, stability, and potentially, cost. The researchers developed prototypes which were capable of detecting the spike protein in a rapid paper-based format and collaborated with Coventry Hospital to evaluate the primary samples.

This work is important as it shows that LFDs can be adapted 'beyond antibodies' with the glycan recognition potentially able to provide additional information and be rolled out rapidly for new and emerging diseases as they can be quickly assembled without the need to identify and scale antibodies.

Lead researchers: Matthew Gibson, Alexander Baker and Sarah-Jane Richards

Iceni Diagnostics: Robert Field and Simone Dedola

Driving improvements in treatments and patient care

In all aspects of healthcare it is important that we continue to seek innovation in science that will drive improvements in patient outcomes. However within the context of a global pandemic caused by a novel virus which is being understood in real time, the responsibility is even greater.

The largest global achievement so far is of course the development of safe and effective vaccines, but while vaccines help to reduce the risk of being infected and substantially reduce the chance of becoming hospitalised with the virus, they are just one part of our arsenal against COVID-19. It is also important that we have effective treatments to support those who become ill with the disease.

Since the first wave of the pandemic, huge improvements have been made in COVID-19 therapeutics and the UK is leading this response. The world's largest clinical trial, involving more than 12,000 patients, is being led by a UK university and is identifying treatments that may be beneficial for adults hospitalised with COVID-19. The trial has found that for every 100 patients on a ventilator for 28 days, 60 patients were already likely to recover, and 12 patients were likely to survive due to a new drug.[4]

As well as showcasing a small number of the numerous clinical trials being investigated across the UK, this section also explores some of the advancements in medical technologies that have helped improve outcomes for COVID-19 patients.

4. Source: The Recovery Trial

The Oxford-AstraZeneca Covid vaccine

University of Oxford

The University of Oxford's Jenner Institute and the Oxford Vaccine Group have been at the forefront of scientific endeavour to develop vaccines for diseases of major global importance for more than 30 years. When a novel respiratory virus began circulating in China at the end of 2019, the team quickly started work to develop a vaccine, without yet knowing whether it would be needed.

> **"To date the partnership has manufactured 1.3 billion doses of the vaccine"**

It soon emerged that the pathogen responsible for COVID-19 was a novel coronavirus, SARS-CoV-2, and that there was a high risk that a localised outbreak in Wuhan could develop into a global pandemic. When Shanghai virologist Professor Zhang Yongzhen first decoded the virus's genetic structure and published his results on the internet, Professors Sarah Gilbert and Andrew Pollard gathered a team who immediately began working on developing a vaccine for SARS-CoV-2 using Zhang's data.

The Oxford team had already used ChAdOx1 vaccine technology to produce candidate vaccines against a number of pathogens including flu, Zika and Middle East Respiratory Syndrome (MERS), another coronavirus. The ChAdOx1 vaccine is a chimpanzee adenovirus vaccine vector. This is a harmless, weakened adenovirus that usually causes the common cold in chimpanzees. Armed with evidence that ChAdOx1 had been shown to develop a strong immune response from one dose in other vaccines, the team set to work to genetically change it so that it would not trigger infection in people. They then further modified it so that it carried the genetic code for SARS-CoV-2. When the vaccine enters cells inside the body, it uses this genetic code to produce the surface spike protein of the coronavirus. This induces an immune response, priming the immune system to attack the coronavirus if it later infects the body.

However it was not just the immunology of the new disease that the team had to attend to; in order to be successful it was important that the vaccine should be safe, effective, and possible to manufacture, transport and store. The team at the University of Oxford signed an agreement with the pharmaceutical company AstraZeneca to produce and scale up distribution of the vaccine should it be successful in clinical trials.

Manufacturing a vaccine in sufficient quantities to tackle a global pandemic was no easy task. The solution to this problem came when Dr Carina Joe found a way of creating up to 10 times more vaccine from a modified manufacturing process. Work which would have normally taken years could be compressed into a few months, and with a distributed manufacturing model involving manufacturers in multiple countries, production could be scaled up to deliver a vaccine for the world.

From April 2020 the Oxford-AstraZeneca team began clinical trials for the ChAdOx1 nCoV-19 vaccine. Based on the available evidence from clinical trials, the team found that two doses of the Oxford AstraZeneca vaccine were effective at reducing COVID-19 infections.

The Oxford-AstraZeneca vaccine has prevented thousands of hospitalisations and deaths. It has been shown to be stable, easily manufactured and can be transported and stored at domestic fridge temperature which allows the vaccine to be rapidly administered in existing healthcare settings. A key element of Oxford's partnership with AstraZeneca is a joint commitment to provide the vaccine on a not-for-profit basis for the duration of the pandemic across the world, and in perpetuity to low- and middle-income countries. The vaccine was approved for emergency use in the UK in December 2020, and has now been approved in a number of countries, marking an important milestone in the fight against COVID-19. To date the partnership has manufactured 1.3 billion doses of the vaccine that have been released to more than 170 countries worldwide.

Lead researchers: Sarah Gilbert, Andrew Pollard, Teresa Lambe, Sandy Douglas, Catherine Green, Adrian Hill

The RECOVERY trial finds multiple treatments for people hospitalised with COVID-19

University of Oxford

The world's largest randomised clinical trial of COVID-19 treatments, known as RECOVERY, was up and running in just nine days. It found the first major defence against COVID-19, dexamethasone, which reduces deaths among the sickest patients by one third, and went on to show that tocilizumab could be used to shorten the time COVID-19 patients spend in hospital.

"A later study calculated that the drug would have saved roughly 12,000 lives in the UK between July and December 2020, or around 650,000 lives globally over the same period"

The RECOVERY trial was established as a randomised clinical trial to test a range of potential treatments for patients hospitalised with COVID-19. Initially set up to test four possible treatment options in a few thousand hospitalised COVID-19 patients, the trial has in one year enrolled over 40,000 patients and investigated 10 treatments. Its results have demonstrated the benefits of the steroid dexamethasone and the IL-6-targeting antibody tocilizumab, while showing the lack of efficacy of some high-profile ideas for treatment such as hydroxychloroquine and aspirin.

The first major breakthrough came in June 2020 when the research team found that the steroid dexamethasone reduced deaths by one-third in ventilated patients, though did not give any added benefit to patients who did not require respiratory support. Based on these results, one death would be prevented by treatment of around eight ventilated patients or around 25 patients requiring oxygen alone. A later study calculated that the drug would have saved roughly 12,000 lives in the UK between July and December 2020, or around 650,000 lives globally over the same period.

RECOVERY has continued to produce ground-breaking research, showing that tocilizumab, an anti-inflammatory drug often used to treat rheumatoid arthritis, reduces the need for a mechanical ventilator and shortens the time COVID-19 patients spend in hospital. It has also shown that several widely shared ideas for treatments simply do not work.

Hydroxychloroquine had received a lot of media attention in early 2020 and was used widely to treat COVID patients, despite the absence of any good evidence. In June 2020, the RECOVERY trial concluded that hydroxychloroquine had no beneficial effect in patients hospitalized with COVID-19 and stopped enrolling patients to that arm of the trial immediately. The trial continues to investigate a range of treatments, and in 2021 launched RECOVERY International, to evaluate COVID-19 therapies that may be suitable for low-resource countries.

Thanks to the ground-breaking work of RECOVERY, clinicians treating patients hospitalised with severe COVID-19 now have two treatments that are known to improve survival. From having no known effective drugs when the pandemic first started, patients are now offered treatments that have been robustly proven to reduce death and improve other outcomes, such as the length of hospital stay and the need for mechanical ventilation. Above all, it is a prime example of how large-scale randomised trials can operate at the heart of high-quality healthcare to improve health outcomes and save lives.

Lead researchers: Peter Horby and Martin Landray

Identifying repurposed therapies for COVID-19 treatment

Queen's University Belfast

Novel therapies and vaccines can take years to be developed and approved, so in an effort to fast-track the search for a treatment for COVID-19, researchers at Queen's University Belfast examined how existing drugs might be repurposed to treat patients with COVID-19.

When the COVID-19 pandemic hit in early 2020, Professor Ken Mills and Dr Ahlam Ali of the Patrick G Johnston Centre for Cancer Research were in the process of trying to identify repurposed therapeutic agents for the treatment of blood cancers by using an algorithm driven combination drug screen. Realising the potential of drug repurposing for finding a treatment for COVID-19, the team joined forces with Professor Ultan Power, a virologist from the Wellcome Wolfson Institute for Experimental Medicine, to jump-start the search for a treatment.

"The project entailed screening over 2,500 drugs that had been approved by the US Food and Drug Administration to see whether any of them, individually or in combination, were capable of stopping the virus"

The project entailed screening over 2,500 drugs that had been approved by the US Food and Drug Administration to see whether any of them, individually or in combination, were capable of stopping the virus. Research groups around the globe were at that time focused on vaccines or single-agent anti-virals, but this technique could be used to identify combinations of therapies which showed anti-viral activities but were potentially not known as such. Using technology known as "multiple screening for interacting compounds" (MuSIC), the team were able to screen a library of anti-viral and anti-inflammatory drugs to find drugs with potential activity against SARS-CoV-2.

Testing drugs individually is a time consuming and expensive process; by gathering agents into pools of 10 that covered all pair-wise combinations, the team were able to reduce the screen from around 74,000 wells to just 3900. The effect of viral infection and growth was measured to identify wells with potential activities. These wells were then deconvoluted into 45 wells to cover all possible pairwise combinations from each "positive" well. Screening across different models and validation steps then identified several possible single-agents and pairwise combinations with very few of these having any previously known anti-viral activity.

These agents are being further screened for efficacy for halting viral infection, replication and anti-inflammatory actions. The potential impact of these repurposed agents is that they are already used in the clinic (albeit not as anti-viral agents) so they are safe, usually easy to administer, and often off patent, so low in cost.

Lead researchers: Ahlam Ali, Ken Mills, Ultan Power

Clinical trial to investigate whether vitamin D protects against COVID-19

Queen Mary, University of London

Throughout the COVID-19 pandemic there have been debates as to whether vitamin D – the 'sunshine vitamin' – could play a key role in protecting people from COVID-19; however, definite evidence on this is lacking. Researchers from Queen Mary University of London, funded by Barts Charity and the Fischer Family Trust, have launched a clinical trial, CORONAVIT, to definitively answer the question.

"The CORONAVIT trial will answer the question of whether vitamin D offers protection against COVID-19"

A total of 6200 people are participating in the clinical trial to find out whether a 'test-and-treat' approach to correct people's vitamin D deficiency during winter will reduce the risk and/or severity of COVID-19 and other acute respiratory infections.

UK sunshine is too weak to make vitamin D in the skin between October and April, and dietary sources of vitamin D are limited; consequently, around 2 in 5 of the UK adult population have inadequate levels of vitamin D over winter and spring. The UK government recommends that the general population considers taking vitamin D supplements at a dose of 400 International Units (IU) or 10 micrograms per day during winter and spring. This has been extended to a recommendation of year-round supplementation in view of potentially decreased sun exposure during lockdowns.

However, data from the Queen Mary team shows that 2 in 3 people were not following Government advice to take vitamin D during winter and spring. The intervention to be evaluated involves carrying out a postal finger prick vitamin D test, which is processed in an NHS lab. Participants who are found to have low levels of vitamin D in their blood will then be given six months' supply of either 800 or 3,200 IU of vitamin D a day. The research team will then track the incidence of doctor-diagnosed or laboratory-confirmed acute respiratory infection in the participants, including COVID-19, to see whether vitamin D supplementation has had an effect on their risk and severity of infection.

The CORONAVIT trial will answer the question of whether vitamin D offers protection against COVID-19. Vitamin D supplements are low in cost, low in risk and widely accessible; if proven effective, they could significantly aid in our global fight against the virus. A sub-study, separately funded by the Exilarch's Foundation and DSM Nutritional Products, is also being carried out to investigate whether vitamin D can boost immune responses to coronavirus following COVID-19 vaccination.

Lead researchers: Adrian Martineau and David Jolliffe

Developing a COVID-19 vaccine nasal spray

Lancaster University

The invasive nature of delivering vaccines into a host through needles can be a difficult experience for some patients. Researchers at Lancaster University have successfully engineered a COVID-19 vaccine which can be administered through the nose, potentially helping to address these issues and present a low-cost vaccine candidate suitable for low- and middle-income countries.

The researchers administered two doses of the vaccine via a nasal spray in animal trials which are the first stage in vaccine development. This elicited robust antibodies and T cell responses which were enough to be able to neutralize SARS-CoV-2. There was also a significant reduction in lung pathology, inflammation and clinical disease in the rodents who received the vaccine.

"They found that administering this vaccine through a nasal spray completely protected the animals from shedding the virus which causes viral transmission"

The vaccine is based on a common poultry virus called the Newcastle Disease Virus (NDV), which can replicate in humans but is harmless. The scientists engineered NDV to produce the spike proteins of the SARS-CoV-2 virus which causes COVID-19, tricking the body into mounting an immune response against SARS-CoV-2. Researchers at Lancaster University, led by Dr Muhammad Munir, investigated how effective their NDV-based vaccine was against SARS-CoV-2. They found that administering this vaccine through a nasal spray completely protected the animals from shedding the virus which causes viral transmission. This means the immunization of the upper respiratory tract through a nasal spray can prevent individuals from spreading the virus and developing infections elsewhere in the body. Though the vaccine showed promising safety and efficacy in this animal model, human trials are still required to determine its applicability and to obtain regulatory approvals.

A vaccine nasal spray offers several advantages over conventional approaches including non-invasive administration, the induction of local immunity as well as being an alternative for people afraid of needles or with blood clotting co-morbidities. The vaccine could also provide a low-cost alternative for the developing world, as it can be scaled up using the existing global infrastructure currently in use for influenza virus vaccines.

**Lead researchers: John Worthington, Lucy Jackson-Jones, Muhammad Munir**

Manufacturing a lifesaving breathing aid for COVID-19 patients

University College London

University College London (UCL) engineers worked with clinicians at University College London Hospitals NHS Foundation Trust (UCLH) and staff at Mercedes Formula One to engineer a breathing aid that can help COVID-19 patients with serious lung infections to breathe more easily without the need to use invasive ventilators.

A non-invasive breathing support device, known as Continuous Positive Airway Pressure (CPAP), has proved critical in helping COVID-19 patients with serious lung disease to improve their low blood oxygen levels and breathe more easily. While CPAP devices were used extensively in hospitals in Italy and China in early 2020, they were initially in short supply in UK hospitals. In response, engineers at UCL and Mercedes-AMG HPP worked tirelessly to reverse-engineer an old device that was purely mechanical and which could be mass-manufactured rapidly. The device, named the UCL-Ventura, took fewer than 100 hours to produce and test in volunteers. It then underwent patient evaluations at UCLH and sister hospitals in the London area before approval for use in COVID-19 patients by the UK medicines regulator, MHRA. Further refinement of the device and circuitry reduced oxygen use by up to 70%. This was an important modification as there were concerns over limited oxygen supplies in some hospitals.

Deployed to over 130 hospitals across the NHS network, the UCL-Ventura has helped to save lives by ensuring that ventilators, a precious resource both in terms of machine numbers and the trained staff to
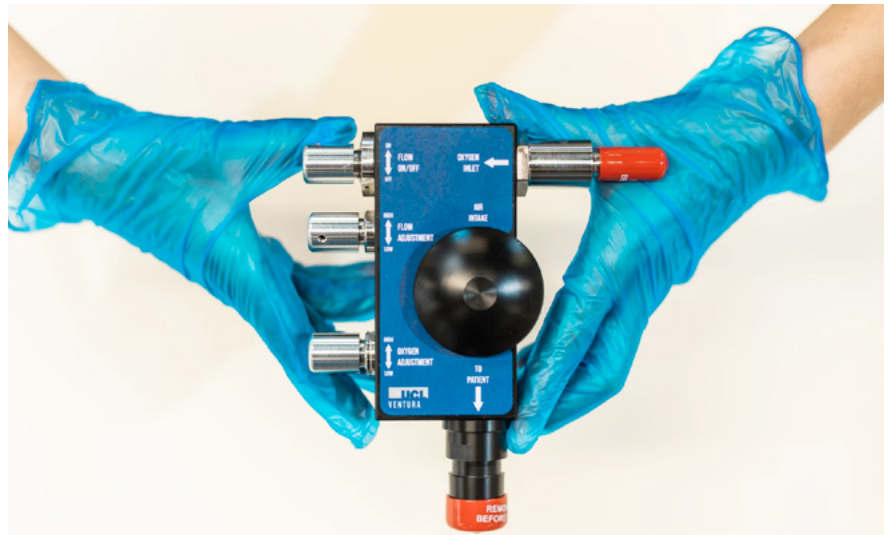
operate them, are reserved for the most severely ill patients. Clinicians have found that many patients treated with CPAP can avoid mechanical ventilation and recover more quickly as a result.

"Clinicians have found that many patients treated with CPAP can avoid mechanical ventilation and recover more quickly as a result"

After a UK Government order, the UCL-Ventura device was produced at a rate exceeding 1,000 a day at the HPP technology centre in Brixworth, Northamptonshire. 40 machines that would normally produce Formula 1 car engine pistons and turbochargers were used to tool the CPAP devices; indeed, the entire Brixworth facility was

repurposed to meet this demand. From idea conception, 10,000 devices were made and delivered in just one month.

As well as saving lives in the UK, there has been a huge effort to support demand from other countries in need. UCL and Mercedes HPP released the full design and manufacturing instructions at no cost to local bona fide organisations, leading to over 25,000 devices being manufactured to date in hubs across the world. This combined with UK government donations and charitable purchases mean that patients in over 25 countries are being treated using UCL-Ventura CPAPs in countries as diverse as Peru, Mexico, Paraguay, Cuba, South Africa, Uganda, Palestine, Ukraine, Iran, India, Pakistan, Tajikistan, Nepal, Maldives, Sri Lanka, Bangladesh and the Philippines.

Lead researchers: Rebecca Shipley, Mervyn Singer, Tim Baker, David Brealey, David Lomas

Rollout of personal respirators protecting NHS frontline staff during the pandemic

University of Southampton

An innovative protective respirator, developed in Southampton, is helping to protect NHS frontline staff to remain safe and work in comfort while treating patients with COVID-19.

At the beginning of the pandemic, hospital staff treating COVID-19 patients were concerned about the high risk of infection due to the supply chain issues with personal protective equipment (PPE). One week before the UK lockdown was announced, engineers and clinicians at the University of Southampton and University Hospital Southampton came together to design a personal respirator that could deliver a higher level of protection than surgical masks while being comfortable to wear for a full 12-hour shift.

> **"It has improved communication with patients, as the entire face is visible through the mask, and is greatly reducing the environmental impact of disposable mask use."**

The respirator, known as PeRSo (the Personal Respirator Southampton), covers the wearer's head and has a plastic visor to protect their face. It delivers clean air through a High Efficiency Particulate Air (HEPA) filter with a belt-mounted fan pack, which can be worn throughout a long shift and reused after appropriate cleaning. This provides multiple benefits; the device can filter 99.95% air particles, providing much greater protection than standard PPE, and is reusable, merely needing recharging between shifts. It has improved communication with patients, as the entire face is visible through the mask, and is greatly reducing the environmental impact of disposable mask use.

Over 1,600 PeRSo devices were deployed at University Hospital Southampton during wave 1, and over 3,600 during wave 2, all requested by staff members. In addition over 10,000 units were purchased by NHS Trusts, with supply to over 20 different trusts. Quantitative analysis of the Southampton deployment showed the respirators were preferred by staff and patients and associated with low staff absence during wave 2. Economic analysis demonstrates that respirators are cost-saving after approximately 8 weeks. The prototype design has been published as an open specification so it is available to other manufacturers around the world. The partnership has launched the PeRSo-DW (Developing World) and is providing open-source modifications for components available to low resource countries.

The Southampton team behind PeRSo have been recognised in a number of fora for developing solutions to save lives during the pandemic. The Royal Academy of Engineering awarded the team with a President's Special Award for Pandemic Service and the project leads, Professors Paul Elkington and Hywel Morgan, were awarded MBEs in the Queen's Birthday Honours for services to medicine and services to biomedical engineering respectively.

Lead researchers: Paul Elkington and Hywel Morgan

Beyond borders: opening an oxygen plant in Malawi in response to COVID-19

University of Liverpool

Adults admitted to hospital with critical illnesses are vulnerable and at high risk of morbidity and mortality, especially in low-income countries where resources are severely limited. When the COVID-19 pandemic reached Malawi it was clear that limited supplies of oxygen and PPE would present a serious challenge to saving lives. In response, the Malawi-Liverpool-Wellcome Programme (MLW) opened an oxygen concentration plant to supply life-saving oxygen to the Queen Elizabeth Central Hospital and surrounding district hospitals amid the coronavirus outbreak.

The Malawi-Liverpool-Wellcome Programme is a partnership between the University of Liverpool, the Liverpool School of Tropical Medicine, the Kamuzu University of Health Sciences and the Wellcome Trust. In the 25 years since its formation, it has transformed health in the country with particular impact on malaria, pneumonia, childhood diarrhoea, typhoid, HIV and TB. The oxygen plant installed by the partnership has been estimated to generate a million litres of oxygen per day for more than 100 beds at the hospital while other oxygen is filled in gas cylinders to be supplied to district hospitals in the surrounding region. The plant will have a lasting legacy within Malawi, as beyond the COVID-19 pandemic oxygen will be vital in the treatment of patients suffering from respiratory illnesses such as pneumonia.

With limited supply of oxygen in the health system in March 2020, the plant has made a tangible difference to patient outcomes. The plant is funded by an extraordinary grant from MLW partner, the Wellcome based in the UK, which provided the programme with over £2m to support the national response to COVID. This grant was also used to provide PPE, so that the risk that hospital staff faced from becoming infected with COVID-19 was reduced. The partnership has assisted the Malawi Ministry of Health in providing a COVID diagnostic service to support both contact tracing and testing in the country and has provided a diagnostic service to the largest government referral hospital in Southern Malawi.

"The oxygen plant installed by the partnership has been estimated to generate a million litres of oxygen per day for more than 100 beds at the hospital while other oxygen is filled in gas cylinders to be supplied to district hospitals in the surrounding region"

Informing the evolving policy response

The pandemic has highlighted that our understanding of science is never exhaustive but that it evolves continuously as we gather greater evidence. Responding to a pandemic, often described as a 'once in a century event' is a complicated task that requires global collaboration and consultation from experts across a variety of professions.

The case studies in this section demonstrate examples of how universities are helping to inform the ongoing policy response to COVID-19. From how we restart mass participation events to understanding transmission through national testing schemes, this work is not only essential to how we respond to the current pandemic, but it also will help us understand what future actions may be needed to protect public health.

COVID-19 mapping and mitigation in schools
University of Bristol

I n partnership with Bristol City Council, Bristol Schools and Public Health England (now the UKHSA), the University of Bristol is leading a large-scale study to understand the determinants and consequences of COVID19 infection in schools. The COVID-19 Mapping and Mitigation in Schools Study (CoMMinS) is informing the public health response and mitigation measures being implemented in schools, with longer term insights into waning of immunity, and long term health and educational consequences for school children.

"To date CoMMinS has fulfilled its dual aim of providing real-time support to schools throughout the pandemic as well as establishing a platform from which to gain insights into the determinants and consequences of COVID-19 infection in the school setting"

Funded by a £2.75m grant (as a UKRI/NIHR Urgent Public Health study), CoMMinS set out in September 2020 to work in partnership with schools to help them to manage the challenges faced in delivering continuity in education and managing COVID-19 infection in the school setting.

Bristol researchers have been working throughout the last school year with 17 schools across the city of Bristol, to undertake monthly saliva sampling and collect questionnaire data. PCR testing for active infection as well as antibody testing for seroprevalence have both been rolled out. The study has necessitated close linkage with NHS Test and Trace and the local city Health Protection Team. Realtime support has also been provided, for example, in establishing lateral flow testing at short notice in participating schools. Test data, including seroprevalence, is currently being linked to the NHS systemwide data set (all health records). Analysis will focus on the determinants and consequences of symptomatology and infection in children and adults working in the educational setting.

In a reactive arm of the study researchers are testing multiple members of the same household where an index case has been identified, twice weekly for 4 weeks, to try to better understand within household transmission patterns.

Further efforts to help to mitigate the impact of the COVID-19 pandemic include working with school staff to recognise mental wellbeing issues, developing and evaluating app-based health behaviour interventions, development of digital tools to enhance contact tracing and liaison with the Department for Education to gain a better evidence base to inform policy to mitigate against lost learning.

To date CoMMinS has fulfilled its dual aim of providing real-time support to schools throughout the pandemic as well as establishing a platform from which to gain insights into the determinants and consequences of COVID-19 infection in the school setting. Data have been informative with respect to model construction and gaining a deeper understanding of the mental wellbeing of children as they have navigated the pandemic.

Lead researcher: Caroline Relton

National REACT study helps monitor the spread of COVID-19 in England

Imperial College London

Imperial College London is leading a major programme of home testing for COVID-19 to track the progress of the infection across England. Named the Real-time Assessment of Community Transmission (REACT) Study, the programme was commissioned by the Department of Health and Social Care and is being carried out in partnership with Imperial College Healthcare NHS Trust and Ipsos MORI.

The REACT study is England's largest, most significant piece of research looking at the population prevalence of COVID-19. REACT takes two main approaches to track the virus in the population, looking for both current and past infection. The REACT 1 programme is monitoring coronavirus infection levels over time and the REACT 2 programme is assessing antibody finger-prick tests and using these to estimate how far the virus has spread.

> **"The REACT study is England's largest, most significant piece of research looking at the population prevalence of COVID-19"**

Since July, the REACT team have produced a series of reports to highlight the fast-changing patterns of COVID-19 infection nationally, thus directly informing government policy. These reports have included antibody surveys, symptom reporting, infection trends and tracing variants in the community.

**Lead researchers: Paul Elliott, Graham Cooke, Helen Ward, Ara Darzi**

Expanding sewage wastewater testing to identify coronavirus spikes in Ireland

Queen's University Belfast, University College Dublin

By measuring SARS-CoV-2 concentrations in sewage, researchers at Queen's University Belfast and University College Dublin have played an important role in estimating the infection rate on the island of Ireland, enabling the public health authorities to quickly detect local COVID-19 outbreaks and identify new variants of concern.

The detection and monitoring of microbial pathogens in sewage and wastewater treatment systems is an effective strategy to study the epidemiology and distribution of bacterial and viral pathogen loads in a population. As SARS-CoV-2 is shed in high levels in faeces, wastewater testing has become a complementary, early-warning strategy for outbreaks of COVID-19, aiding governmental decision-making around future infection prevention/control policies.

Researchers in the Faculties of Medicine, Health and Life Sciences, and Engineering and Physical Sciences, at Queen's University Belfast, along with colleagues in University College Dublin, have developed viral wastewater testing protocols and Geographical Information Reporting Tools to integrate public health data with environmental surveillance for the community monitoring of SARS-CoV-2 levels. Although wastewater monitoring is not accurate enough to identify how many people are infected with COVID in any given area at any given time, it can be
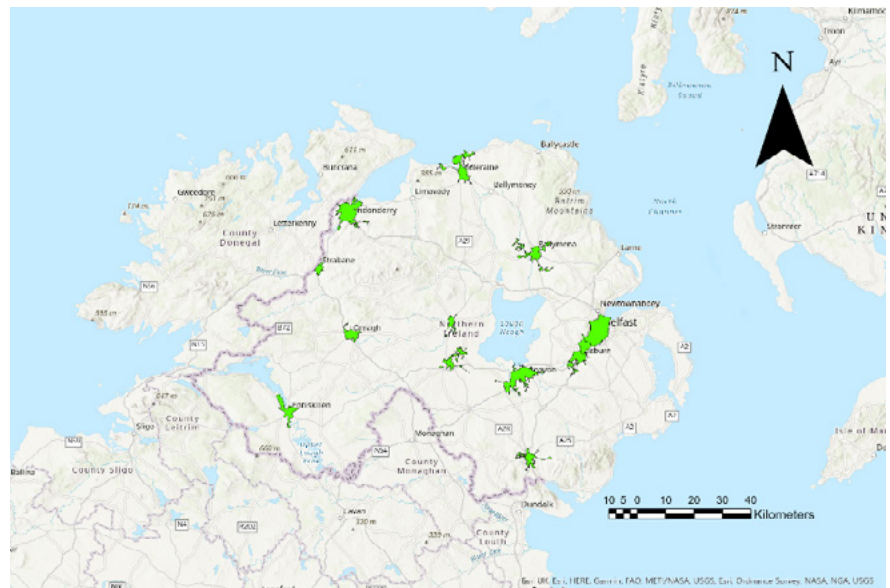
> "As SARS-CoV-2 is shed in high levels in faeces, wastewater testing has become a complementary, early-warning strategy for outbreaks of COVID-19"

effectively used alongside population testing to understand where specific variants are circulating, and to provide an early warning of escalating cases in specific geographical areas.

The success of this pilot study, funded by Science Foundation Ireland and the Northern Ireland

Department of Agriculture, Environment and Rural Affairs, has led to the development of a wider SARS-CoV-2 wastewater monitoring programme within Northern Ireland. In this £3m expansion researchers at Queen's University Belfast are currently monitoring 14 wastewater treatment works across the province, covering 35% of the population: this will be further expanded throughout 2021 to approximately 40 treatment sites, providing ca. 65% population coverage. In addition to links with the Irish wastewater surveillance programme, the NI monitoring effort is also embedded within the wider UK wastewater testing programme, through collaboration with, for example, the Joint Biosecurity Centre.

Lead researchers: John W. McGrath, Deirdre Gilpin, Jennifer McKinley

Researching COVID-19 risk-mitigation, from mass testing to reopening mass events

University of Liverpool

Public health experts at the University of Liverpool have led the way in developing and understanding data-driven, population-wide mitigation of COVID-19 risks for reopening society. This work delivered the world's first study of voluntary, city-wide rapid antigen testing for people without symptoms of COVID-19 and the first reopening of live music events in the Northern Hemisphere. It's data science engine, the Combined Intelligence for Population Health Action (CIPHA) system also leaves a legacy of science embedded in population health management across NHS, local government and public health data sources, and an efficient way of networking action-research across regional health systems.

From November 2020 to April 2021, people living or working in the City of Liverpool were invited to get tested for the COVID-19 virus whether they had symptoms or not. Rapid antigen asymptomatic testing centres were deployed, initially with support from the British Army, and adapted and coordinated across NHS, local government, public health, and academic organisations in near-real-time using the CIPHA intelligence system, which had been initiated by the University six months earlier. COVID-19 case detection increased by a fifth and infection rates fell by a fifth up to mid-December after the introduction of 'mass testing', enabling earlier reopening of the city, before the Alpha variant surge.

Half of Liverpool's economy depends on visitors, hospitality, and events, so plans for reopening of the sector were developed with the University during the national 'mass testing'

Liverpool's Sefton Park was one of the government's official trial events to research how large gatherings can safely take place again.

pilot – informing the wider DCMS Events Research Programme. Around May Bank Holiday weekend, 13,262 people from Liverpool City Region attended four live events in Liverpool – a business festival, two nightclub events and a music festival. Eventgoers took rapid antigen tests beforehand, and their test results were automatically linked with tickets via CIPHA – enabling rapid outbreak control measures. There were 12 associated COVID-19 cases, half of whom were known to each other and mixed outside events. At the same time there was an outbreak of >40 linked cases around a swimming pool in the region. The zero-sum goal of mitigating at least as much risk as the events added was achieved. The research indicated how to further improve COVID safety around events with better testing regimens, symptom surveillance, transport arrangements and ventilation at venues.

> ## "The research indicated how to further improve COVID safety around events"

The UK Government has published two reports from this work and is expanding the CIPHA system. Internationally, the work has helped clarify for policymakers, the utility of rapid antigen testing alongside RT-PCR testing, showing that useful sensitivity can be greater from a rapid antigen test giving results 24-48 hours earlier than a RT-PCR test despite the latter being more sensitive. The work has also provided evidence of substantial socio-economic inequalities in COVID-19 risk mitigations.

Lead researcher: Iain Buchan

Monitoring changes in health behaviours reported in UK national lockdowns

University of East Anglia

In rapid response to COVID-19, lead researchers from across the Faculty of Medicine and Health at the University of East Anglia launched a ground-breaking nationwide longitudinal study to identify and track the secondary impacts of the pandemic by monitoring changes in health behaviours reported over the course of the UK national lockdowns.

The team used innovative 'ecological momentary assessment' (EMA) methods to track changes in health behaviour daily, by asking participants to complete a brief survey each evening. Participants contributed daily reports on smoking, drinking, substance use, diet, exercise, and wellbeing. Detailed daily data were collected every day over the first lockdown, from April to July.

Following the initial data collection, follow-up surveys were distributed three, six and twelve months later to collect additional health resource data and self-reported diagnosed clinical conditions of the cohort. Researchers successfully collected detailed contextual data throughout the study, including policy changes and key announcements. In-depth interviews and innovative photo diaries were collected from a sub-sample of the cohort to generate a more detailed qualitative understanding of the impact of the pandemic on people's health behaviours.

Based on current analysis, key results show that lockdown saw people in the UK eating less fruit and

"Overall, the findings indicate that on average, people's health behaviours worsened in the early stages of the UK's COVID-19 pandemic measures"

vegetables, getting less exercise and drinking more alcohol. Researchers observed a decrease in cardiovascular activity but a slight increase in strength training. When it came to the increase in alcohol consumption, the team found women drank more frequently but men drank greater quantities per drinking occasion. Overall, the findings indicate that on average, people's health behaviours worsened in the early stages of the UK's COVID-19 pandemic measures, and that worsening unhealthy

behaviours were associated with being younger, female and having a higher BMI. Qualitative data revealed how those with existing social assets fared better, being able to adapt and respond to lockdown conditions, while those living in difficult social circumstances found it much harder to positively respond.

The study gained widespread media attention in relation to eating behaviours during lockdown and early findings of nutritional data were released, on request, in order to be included in the DEFRA National Food Strategy report. Its findings were significant as they showed that if these short-term changes become longer term habits then people's health could be compromised as a result. As younger people in general displayed more unhealthy changes than older people, the net impact on health outcomes of any long-term changes in habit would be greater as younger people have more life years ahead of them. Additionally, the fact that people with higher BMI showed more unhealthy behaviours is concerning because excess body weight is associated with a more severe COVID-19 prognosis.

Lead researchers: Caitlin Notley and Felix Naughton

Ethnicity and COVID-19 outcomes in healthcare workers

University of Leicester

A recent PHE report highlighted how 63 per cent of healthcare workers who died from COVID-19 were from a Black, Asian or Minority Ethnic background. It is therefore important that we understand the differences between COVID-19 diagnosis and clinical outcomes, professional practices, and wellbeing among ethnic minority healthcare workers to inform the responses and support that these staff receive. UK-REACH aims to address this gap in our understanding.

Researchers at the University of Leicester are investigating why people from ethnic minority backgrounds have a higher risk of becoming infected with SARS-CoV-2 and also developing severe COVID-19, with twice the risk of death compared to the White population. The University of Leicester-led UK-REACH study (UK Research study into Ethnicity And COVID-19 outcomes in Healthcare workers) is jointly funded by UK Research and Innovation (UKRI) and the National Institute for Health Research (NIHR).

"Researchers at the University of Leicester are investigating why people from ethnic minority backgrounds have a higher risk of becoming infected with SARS-CoV-2 and also developing severe COVID-19"

The study includes a number of sub-studies but one key sub-study will follow a group of healthcare workers from ethnic minority backgrounds for a period of 12 months to see what changes occur in their physical and mental health, how they have changed their professional and social behaviours in response to COVID-19, and how risky their jobs are. The study will also include non-clinical staff integral to the day to day running of healthcare institutions, including cleaners, kitchen staff and porters. This is the first UK study to be conducted on a large scale investigating why ethnic minority healthcare workers could be at greater risk of COVID-19 and it is hoped that findings will help to inform the development of risk reduction and support programmes. Ultimately, this will reduce health inequalities and improve the long-term health outcomes of healthcare workers.

A stakeholder group of major national organisations including the General Medical Council, the Nursing and Midwifery Council, General Dental Council, NHS Employers and the Professionals' Associations will help to conduct the research and provide evidence to policymakers so that decisions can be made in near real-time.

Lead researchers: Manish Pareek and team

Supporting education and training

During the first wave of the pandemic, universities and medical schools followed government guidance to cancel in person teaching. The impact on medical education was vast. In order to graduate and join the NHS workforce, medical students are required to complete clinical placements where they take part in the treatment of real patients under supervision. With these placements cancelled and teaching moved online, medical schools had to quickly adapt to ensure that students were able to continue their learning and meet the requirements expected of them by the regulator and the public.

While this section provides a few examples of how medical schools adapted to this new environment, from innovative virtual wards to online assessments, it should be noted that all of the UK's medical schools have examples of creativity in their delivery of education during this period and worked tirelessly to ensure the pipeline of doctors was not disrupted in the midst of a global health crisis. In addition to undergraduate education, another case study in this section explores how a London medical school is supporting primary care workers treat patients with coronavirus through online learning.

Medical students also played a huge role in supporting the NHS, particularly during the first wave of the pandemic. Thousands of students volunteered to help, from aiding vulnerable communities that were shielding to helping relieve hospital pressures by undertaking health care assistant roles. As well as volunteering, over 4500 final year medical students graduated early and began work in the NHS in order to provide extra support for front line staff.[5] Their contribution and commitment were essential to support the health service in a time of need.

5. General Medical Council, The state of medical education and practice in the UK (2020), p.57 https://www.gmc-uk.org/about/what-we-do-and-why/data-and-research/the-state-of-medical-education-and-practice-in-the-uk

The world's first mixed reality undergraduate bedside teaching

Imperial College London

Patient interaction is essential to medical education however during the peak of the first wave of the pandemic, all clinical placements were cancelled. Imperial College London School of Medicine piloted the world's first mixed reality undergraduate bedside teaching to give medical students an immersive clinical teaching experience from home.

"The mixed-reality technology enables the clinical live stream to be supplemented visually with digital information"

Wearing Microsoft HoloLens, clinicians were able to share a live feed of hospital inpatients with medical students watching on their devices from home. The mixed-reality technology enables the clinical live stream to be supplemented visually with digital information, such as the patient's drug charts or radiographs, which can be superimposed as holograms onto the environment. The bi-directional sound enabled students to interact directly with the patient as well as the clinician. The HoloLens allows the wearer to record their teaching sessions, ensuring the medical school can offer an ever-expanding library of cases and clinical interactions accessible to students at any time. Educators also acted as simulated patients to understand the experience from the patient perspective.

Dr Louis Koizia at St Mary's hospital, one of Imperial College NHS trust's sites, wearing a HoloLens headset used to examine patients. Photograph: Thomas Angus/Imperial College London

Professor Amir Sam piloting the use of mixed reality technology as a simulated patient with holograms of a chest radiograph and a faculty facilitator. Photograph: Imperial College London

Historically, Grand Rounds saw a patient wheeled into a lecture theatre where their case would be presented to an audience of clinicians and students. The reversal of education delivery with Hololens enables a teacher to take large groups of students virtually to a patient's bedside and offers a novel opportunity for the provision of clinical education.

Lead researchers: Amir Sam and Risheka Walls

New online course launched to support primary care workers treating patients with coronavirus

St George's, University of London

With healthcare practitioners receiving a huge amount of new information every day about COVID-19, academics from St George's, University of London created a free online course to extract key information relevant to healthcare workers treating patients in primary care settings.

Primary care services form the largest part of most people's experience of health care, providing the first point of contact in the health care system and acting as the 'front door' of the NHS. During the pandemic it was therefore essential that general practice was equipped to plan, risk assess, and provide care for COVID-19 patients and the accumulating backlogs of patients with other acute and chronic diseases. With new advice emerging daily about how to manage COVID-19 infections, academics at

> **"The course allows learners to explore the epidemiology, clinical symptoms and signs, and current management of COVID-19"**

St George's, University of London recognised the need to compile and take users through the most useful and up-to-date research and guidance.

Designed for front-line clinicians, healthcare workers and professionals tackling the large volume of patients in the current COVID-19 pandemic within the UK primary care sector, the course allows learners to explore the epidemiology, clinical symptoms and signs, and current management of COVID-19. Participants also learn how to complete a safe assessment of suspected COVID-19 cases and discover the best protocol to protect themselves and others going forward.

The course is relevant to healthcare practitioners around the globe and learners are encouraged to share their experiences and best practice in order to support each other. Thus far, over 27,000 people have enrolled on the course, demonstrating its necessity and applicability to the healthcare practitioners dealing with COVID-19 in primary care settings.

For more information about this course, see FutureLearn – Managing COVID-19 in General Practice.

Lead researchers: Mohammad Razai, Pippa Oakeshott, Shamez Ladhani

Virtual Primary Care: working together to enhance primary care education across the UK

University of Leeds in partnership with the Medical Schools Council

The need for innovative approaches to undergraduate teaching in general practice was brought starkly into focus by the onset of the COVID-19 pandemic. The delivery of primary care had fundamentally changed during the pandemic as GP practices rapidly adopted digital approaches towards triaging and consulting patients. This change meant that there was an urgent need for learning resources which could be used to support undergraduate teaching based upon in-person consultations in primary care.

Following a conversation with a medical student about the Channel 5 documentary, GPs: Behind Closed Doors, Dr Jane Kirby realised the unique potential of the series' back footage for supporting teaching in general practice. In partnership with the TV production company Knickerbockerglory, work was undertaken to identify footage which could be used for training purposes. The Medical Schools Council and the Society for Academic Primary Care Heads of GP Teaching Group worked together to build a secure platform which could house the consultations,

"The resource was created as a result of unprecedented collaboration between medical schools, GPs and patients"

with learning objectives and discussion points appearing on screen.

The resource was created as a result of unprecedented collaboration between medical schools, GPs and patients. Over thirty contributors came together through the Society of Academic Primary Care Heads of GP Teaching Group to map the consultations to undergraduate medical curricula, tag them for clinical and educational content, and produce educational guides to accompany the consultations. In this way, the diagnosis, clinical management and decision-making skills which are observed in general practice could be taught in a guided virtual environment relevant to undergraduate medical students.

Learning through GP experiences has been made possible throughout the pandemic by the Virtual Primary Care platform. In the nine months which have passed since the resource was launched in October 2020, the consultations have accrued over 1 million minutes' viewing time. The resource has reduced pressure on GP practices to provide in-person clinical placements and has ensured that NHS services could devote more time to patient care during the most critical periods of the pandemic.

Lead researchers: Dr Jane Kirby and Professor Joe Rosenthal.

Partners: The Medical Schools Council, The Society for Academic Primary Care Heads of GP Teaching Group, Knickerbockerglory TV.

Contributing authors: The project began at and benefited from support by the School of Medicine at the University of Leeds. Since it started, academics from over 30 institutions from across the UK and Ireland have contributed to Virtual Primary Care.

Improving student knowledge, attitudes and empathy towards people with dementia and their family carers

Brighton and Sussex Medical School

Medical schools, like many institutions, had to quickly adapt to new modes of teaching while ensuring medical students still met the learning outcomes expected of them. This example explores how Brighton and Sussex Medical School (BSMS) educators were able to redesign an innovative education programme that allowed medical students to continue their learning. It also provided opportunity to conduct research on the impact of COVID-19 on the quality of life of people with dementia and their families.

Time for Dementia is a longitudinal education programme in which medical students visit a person with dementia and their carer in their own home over a two-year period. The purpose of the programme is to enhance knowledge, skills and positive attitudes towards those with dementia.

Due to the pandemic, the programme's delivery was changed from paired face-to-face home visits to group virtual sessions which preserved the vital longitudinal element of the programme along with direct, albeit virtual, contact with families (people with dementia and their carers) over this period. This involved developing a new system for delivering the programme, collaboration with the Alzheimer's society, the development of structured session guides, and teaching the families how to use

video conferencing. Over 65 virtual sessions were run over the last academic year.

Pre-pandemic data was also used from an on-going research study into the impact of participating in Time for Dementia to investigate changes in quality of life, disease severity, and social functioning in the families taking part in the programme.

"The purpose of the programme is to enhance knowledge, skills and positive attitudes towards those with dementia"

Assessments were repeated during the pandemic and researchers were able to generate a dynamic picture of the impact of COVID-19 on the lives of people with dementia and their carers. Working with the established relationship between BSMS and the Time for Dementia families allowed researchers to engage and recruit participants (n=250) into this new study which has helped NHS services understand in 'real time' the impact of the pandemic on this vulnerable group.

Lead researchers: Stephanie Daley, Juliet Wright, Sube Banerjee

Lending a helping hand: medical students supporting the NHS and local communities

Newcastle University

Since the very start of the pandemic, medical students have not hesitated to rally together to do all they can to assist those most in need of help. During the peak of the first wave thousands of students across all years of study were volunteering within and outside the NHS, providing vital support to people in their local communities.

Within a day of the UK national lockdown starting in March 2020, students from Newcastle University had signed up to a North East voluntary group called 'Newcastle Medical Students Helping Hands' to support NHS staff and vulnerable residents. As the COVID-19 pandemic took hold in the UK, healthcare workers suddenly faced increasing workloads with long hours and last-minute changes to their busy schedules making it difficult for staff to juggle family and caring commitments. Newcastle Medical Students Helping Hands was there to provide childcare, assist with shopping and look after pets for people who needed free and flexible assistance. The initiative has been appreciated by staff in hospitals throughout the North East and was recognised in a virtual visit to the region by HRH the Earl of Wessex.

As part of the First Responder scheme, Newcastle students have also been working with the North East Ambulance Service, attending the most severe categories of emergency calls and responding to immediate life-threatening

"**Scores of medical students from Newcastle University also continue to volunteer on the frontline to support one of the region's largest vaccination hubs**"

emergencies. Providing a uniformed service dispatched by the NHS Trust, pairs of students volunteer their time across shifts throughout the week to provide life-saving support to people dialing 999 in the Tyneside area.

Scores of medical students from Newcastle University also continue to volunteer on the frontline to support one of the region's largest vaccination hubs, ensuring as many people as possible receive their COVID-19 jabs.

In fact, across the country, medical students have been recognised as playing a significant role in the successful vaccine roll out in the UK. Under the direct supervision of a GP, they have collectively administered tens of thousands of vaccines, improving their clinical and communication skills in the process. They have also played a vital role in raising awareness about the importance of vaccination and in encouraging vaccine take-up among groups who are less likely to be vaccinated.

Running high stakes virtual OSCEs during the COVID-19 pandemic

University of Central Lancashire

The objective structured clinical examination (OSCE) is considered one of the most important modalities in the summative assessment of medical students. It tests clinical skills and comprises a circuit of short stations in which each medical student is examined in the presence of real or simulated patients. While it was not possible to conduct in-person exams, several medical schools set out to explore how OSCEs could be successfully carried out online. This case study explores how the University of Central Lancashire adapted their OSCE's in the midst of the pandemic.

In May 2021 the University of Central Lancashire trialled a six-station hybrid VOSCE/OSCE for 400 students, in which the examiners and actors remained at home while the medical students used facilities on campus. The system was set up on Microsoft Teams, with groups of seven students in socially distanced classrooms using headphones. Students were supplied with information in a paper format; there was a room controller in each of their rooms to ensure time was kept. This method was found to work reasonably well, however, some students reported that they were disrupted by their colleagues in the assessment rooms.

Rising rates of COVID-19 around the main clinical centre threatened summer examinations, so the School of Medicine planned and delivered a 10-station system in which

three stations ran with a simulated mannikin on campus and seven communication stations were held online. Students remained at home for the online examination. They were assigned one of four tracks with their own organisers, actors and examiners. Five circuits ran each day, with organisers communicating via instant messaging services.

The online system with students in their homes functioned more efficiently. Feedback from the students was positive and many pointed out that the examination resembled patient interviews on their primary care placements. Some observed that real human contact, even during an assessment, was of value. However, some students also found it more difficult to prepare for a virtual consultation. Several observed that communicating with just head and shoulders has its limitations.

> **"Importantly, the outcomes have been found to be comparable with the medical school's pre-pandemic assessments"**

Examiners found the system to be effective and fair and received supportive feedback from external reviewers. Importantly, the outcomes have been found to be comparable with the medical school's pre-pandemic assessments. This system offers the opportunity to deliver assessments of a range of skills and the medical school plans to utilise it in future for more limited tasks.

Understanding the wider impact of COVID-19

With the development of vaccines and new treatments it is hoped that some form of normalcy can slowly resume. However, there are wider, long-term health implications of COVID-19 that must be investigated.

A major concern is the impact of 'long COVID' where symptoms can persist weeks or months post-infection. The information on long COVID is currently limited and research in this area is essential to ensure that the health service is prepared to support those affected so that their quality of life can be maintained.

This section also explores further key areas university-led research is helping to understand, from how the virus affects different groups and communities, in particular minority ethnic communities which have been hardest hit by the virus, to investigating how COVID-19 impacts other aspects of healthcare such as mental health and pregnancy.

Understanding the impact of COVID-19 on ethnic minority communities

King's College London

The patterns of morbidity and mortality suggest that individuals from Black, Asian or other minority ethnic backgrounds are being disproportionately affected by COVID-19. Researchers at King's College London are working to understand what lies at the heart of this alarming inequality and to explore to what extent it is related to other underlying, existing, disparities.

Guy's and St Thomas' and King College Hospitals have treated among the largest number of COVID-19 cases in the UK resulting in a rich database on COVID-19 infections. Researchers are using this mine of information to better understand the reasons why Black, south Asian and other minority groups make up a significant cohort in the COVID-19 mortality figures. While socioeconomic and cultural differences may be factors in the disproportionate impact of COVID-19, it is striking in the work from King's that there are marked differences among different ethnic minority groups. Notably, those of south Asian background are significantly more likely to die after admission than other ethnic groups (including Black patients), raising the possibility that underlying biology plays a role in susceptibility of specific ethnic groups to contract the disease and its severity. The King's researchers are looking at genetics, underlying health conditions, such as heart disease and diabetes, and differences between south Asians in the UK and India to determine if these factors could be driving some of the recorded differences in survival.

A new Centre for Population Health, focused on bringing together specialists in human health, data science, law, social science and technology to drive changes in government policy and public behaviour, will explore some of the issues causing health inequality in the UK's COVID-19 epidemic. Researchers will develop a model that will help track the virus and build a picture of the demand for COVID-19 testing, both for active viral infection and immunity. The model will help to identify the communities most at risk. In its first stage the

> **"The King's researchers are looking at genetics, underlying health conditions, such as heart disease and diabetes, and differences between south Asians in the UK and India"**

model is focusing on South London and will then expand to the South of England – a diverse community of over four million people. The model will be shared across the UK and with other countries to support the global fight against the novel coronavirus.

Combined with the work on the underlying biology, this research will provide vital information that will inform global models to help effectively protect more vulnerable communities and individuals from COVID-19.

Lead researcher: Ajay Shah

Understanding the pregnancy and neonatal outcomes for women with COVID-19

Imperial College London

The COVID-19 outbreak will affect thousands of pregnant women globally and evidence is currently limited on its impact on pregnancy and neonates. There is a need to rapidly collect clinical experiences of COVID in pregnancy and the neonates to inform improvements in clinical care and public health, a task that is being led by researchers at Imperial College London.

The Pregnancy And Neonatal outcomes for women with COVID-19 (PAN-COVID) is a database that aims to offer a continuously updated collection of clinical case reports of COVID-19 in pregnant women and neonates (infants less than four weeks old) from around the world. The information is being used to inform the global obstetrics community about the natural history of the disease and guide improvements in maternal care and public health.

The study is a collaboration between Imperial College and Cardiff Centre for Trials Research, with over 180 sites in 16 countries. It was given Urgent Public Health approval and has been adopted by the UK CRN. The team have produced regular reports available for healthcare professionals and researchers

globally and will explore the pregnancy outcomes of COVID-19 infection, including miscarriage, fetal growth, restriction and stillbirth, pre-term delivery and transmission from Mother to Baby.

Data linkage will be undertaken to the NHS X Urgent Public Health common dataset to gain wider value from the collected data. Data will be used to construct risk-reduction models and inform healthcare policy and practice.

Lead researchers: Edward Mullins and Christoph Lees

> "There is a need to rapidly collect clinical experiences of COVID in pregnancy and the neonates to inform improvements in clinical care and public health"

Delaying surgery for seven weeks after testing positive for COVID-19 reduces mortality risk

University of Birmingham

Due to the increased risk of mortality, international guidelines recommend surgery should be delayed for patients testing positive for COVID-19. However there is little evidence regarding the optimal duration of delay. A study led by researchers at the University of Birmingham has found that surgery should be delayed for seven weeks after a patient tests positive for COVID-19.

"Patients are more than two-and-a-half times more likely to die after their operations, if the procedure takes place in the six weeks following a positive diagnosis for SARS-CoV-2"

A global surgery group has discovered that surgery should be delayed for seven weeks after a patient tests positive for COVID-19 – as operations taking place up to six weeks after diagnosis are associated with increased risk of death. Led by experts at the University of Birmingham, more than 25,000 surgeons worked together as part of the COVIDSurg Collaborative to collect data from 140,727 patients in 1,674 hospitals across 116 countries including Australia, Brazil, China, India, the UAE, UK and USA – creating one of the world's largest and broadest studies on surgery.

Researchers discovered that patients are more than two-and-a-half times more likely to die after their operations, if the procedure takes place in the six weeks following a positive diagnosis for SARS-CoV-2. The findings were consistent across age groups, differing severity of the patient's condition, urgency of surgery, grade of surgery and in sensitivity analyses for elective surgery. Following a delay of seven weeks or more, patients with ongoing COVID-19 symptoms also had higher mortality than patients whose symptoms had resolved or who had been asymptomatic.

Lead researchers: Dmitri Nepogodiev and Aneel Bhangu

Exploring experiences of bereavement during the COVID-19 pandemic

University of Cardiff, University of Bristol

Millions of people across the UK have faced bereavement during the COVID-19 pandemic. 'Bereavement during COVID-19' is a national study conducted by researchers from the Universities of Cardiff and Bristol, that is investigating the experiences and needs of people bereaved during the pandemic, and the response of the voluntary bereavement sector to these challenges.

The mixed-methods longitudinal study is investigating the grief experiences, support needs and use of bereavement support by people bereaved during the pandemic in the UK, and the adaptations, challenges and innovation involved in delivering bereavement support. 711 people bereaved between 16 March and December 2020 completed an online survey. Results demonstrated the exceptionally difficult sets of experiences associated with bereavement during the pandemic, with acute disruption to end of life, death and mourning practices, as well as social support networks.

Many participants described the distress caused by being unable to visit and say goodbye to their loved ones in hospitals and other settings. Being unable to host conventional funeral services or wakes, share stories and celebrate their loved ones' lives exacerbated their distress and made it difficult to find closure and begin to grieve.

A substantial number of participants struggled to access support from friends and family and experienced loneliness and social isolation. Reduced in-person contact due to lockdowns, social distancing and quarantining affected the perceived

"Results demonstrated the exceptionally difficult sets of experiences associated with bereavement during the pandemic"

quality of support and disrupted collective mourning practices, while the wider social difficulties of the pandemic compounded feelings of isolation.

The results demonstrated high level needs for emotional support; 51% of participants experienced high or severe vulnerability in grief but most were not accessing formal bereavement services or mental health support. The majority of participants had not tried to access bereavement services, for reasons such as lack of appropriate support, discomfort in asking for help and

uncertainty about how to access services.

The study also highlighted the impact of the pandemic on 147 voluntary and community sector bereavement services. Service providers reported increased demand and more complex needs among clients. Two thirds recognised that there were specific community groups which experienced barriers to accessing their service.

Findings from the study were presented at the launch of the UK Commission on Bereavement in June 2021 which included a public statement by the Minister for Mental Health committing to address the gaps and challenges identified in the study. Further discussion with governmental bodies on this issue is ongoing, enabling real-time consideration of emerging research results at UK policy levels.

Lead researchers: Emily Harrop and Lucy Selman

Combatting depression and loneliness during the COVID-19 pandemic

Hull York Medical School

COVID-19 has highlighted and amplified many health and social problems which existed before the pandemic. One issue which predated the pandemic is the co-existence of depression and loneliness alongside long term conditions in older people. Depression significantly worsens outcomes of multiple morbidities and loneliness increases the risk of dying. The risks of depression among older people with multiple morbidities is around 2-3 time higher, and this is often driven by loss of role and social isolation.

At the beginning of the pandemic researchers at Hull York Medical School (HYMS), based at the University of York, began to investigate the impact of the pandemic on older people. The team specifically explored ways in which depression and loneliness might be prevented among people who were asked to isolate for long periods. The team quickly adapted a strategy known as 'behavioural activation', a type of 'talking therapy' which aims to help people maintain or introduce activities which are important to them. The Behavioural Activation in Social Isolation during COVID-19 (BASIL C-19) study was quickly established between HYMS and the universities of Leeds, Keele and Manchester. A team of researchers and NHS nurses were trained to deliver behavioural activation to ensure that social connections were not lost for older people who were shielding. Older

> **"The team specifically explored ways in which depression and loneliness might be prevented among people who were asked to isolate for long periods"**

people who were self-isolating were contacted by phone on a weekly basis and a schedule was drawn up collaboratively.

The BASIL C-19 trial was one of 92 studies adopted by the National Institute of Health Research's Urgent Public Health (UPH) programme, designed to rapidly establish 'what works' for the NHS in fighting the

pandemic and to mitigate the impact of COVID restrictions. To date the BASIL C-19 trial is the only study to mitigate the psychological impacts of COVID-19 on the UPH portfolio. The results of the pilot trial show that telephone delivered intervention can successfully prevent loneliness. The broader and longer-term impacts are now being tested in 28 centres across the UK. This will be the largest trial ever undertaken of a scalable intervention to prevent loneliness in older people. The results of BASIL C-19 are anticipated in late 2021. The results will be essential in dealing with the long-term impact of COVID and in addressing loneliness after the pandemic has passed.

Lead researchers: Dean McMillan and Simon Gilbody

Connecting patients and their families during a pandemic

King's College London

In early 2020, with the COVID-19 surge approaching the UK, critical care teams needed a solution for the inability of families to visit patients in hospital, particularly the rapidly growing numbers in intensive care units (ICUs), during the pandemic. The Life Lines project, led by Professor Louise Rose from King's College London and Dr Joel Meyer from Guy's & St Thomas' NHS Foundation Trust, was instrumental in supporting virtual visits for patients in ICUs across the UK.

Developed by a multidisciplinary team of clinicians and industry specialists, the Life Lines project grew from an idea to a UK-wide initiative in just four weeks. Professor Rose and Dr Meyer collaborated with Aetonix, a virtual e-platform company, to adapt their secure online platform, aTouchAway™ – already used by hospitals in Canada and the US to connect patients treated at home with their clinical teams – to allow patients in UK ICUs to have virtual visits with their families.

Support from the True Colours Trust, Gatsby Charitable Foundation, Google, BT, and King's Health Partners rapidly provided Life Lines with 4G-enabled Android tablets pre-loaded with the bespoke version of aTouchAway™ and in April 2020, Life Lines began delivering tablets to ICUs. For the first time, this enabled virtual visiting for the families of COVID-19 patients. The project has provided a secure space for patients

Medical students who supported virtual visits during the first wave of the pandemic at Guy's and St Thomas' Hospital.

"For the first time, this enabled virtual visiting for the families of COVID-19 patients"

and their families to connect and has allowed people to say their goodbyes to those at the end of life.

To date, the project has successfully delivered more than 1,400 devices to 180 NHS hospitals spanning the UK from Cornwall to the Orkney Islands, resulting in more than 100,000 virtual visits. The initiative has recently expanded to India to connect international clinicians with healthcare staff working on the frontline in ICU. Life Lines has also expanded their work to use aTouchAway™ to develop a digital ICU recovery pathway for ICU survivors once they move from ICU on to wards, and then return back home. This digital ICU recovery pathway, facilitated by a dedicated recovery coordinator (ICU specialised occupational therapist) enables patients to set and monitor their recovery goals, provides recovery resources, and addresses the fragmentation and fracture points in the healthcare system currently facing ICU survivors.

Lead researchers: Louise Rose, Joel Meyer, Michel Paquet

Developing an app to support patients with long COVID

University of Leeds

Long COVID refers to persistent symptoms that last for four weeks or longer after contracting COVID-19, and include breathlessness, fatigue, brain fog, psychological distress, pain, and a general decline in quality of life. Researchers at the University of Leeds have developed an app to help build our understanding of the condition, its impact on daily life and the natural course of the illness.

"C19-YRS is now widely used across the NHS and has been recommended for routine use by NHS England in their national guidance for post-COVID syndrome assessment clinics"

Figures from the Office of National Statistics have revealed that during four weeks in February and March 2021, more than one million people in the UK were experiencing long COVID – including 697,000 people who had experienced symptoms for at least 12 weeks. A new app developed in partnership between the University of Leeds, Leeds Teaching Hospitals and Leeds Community Healthcare NHS Trusts, and the digital health company ELAROS, will enable patients to self-report their symptoms, rate the severity and the impact they are having on daily living. The app is initially available to patients in 27 NHS trusts from June 2021 and can be extended to others.

The information that a patient puts onto the app will be relayed to a secure web portal which can be accessed by the NHS clinical team involved in their care, to monitor their progress and evaluate treatment options. The digital system will not only allow healthcare staff to rapidly assess and triage patients but importantly it will enable patients to view the progress they are making towards recovering their health.

The app uses a version of the COVID-19 Yorkshire Rehabilitation Scale (C19-YRS), the world's first long COVID patient reported outcome measure, a questionnaire developed by clinical academics at the University of Leeds during the first wave of the pandemic to aid the diagnosis and management of long COVID symptoms.

C19-YRS is now widely used across the NHS and has been recommended for routine use by NHS England in their national guidance for post-COVID syndrome assessment clinics. Guidelines from the National Institute for Health and Care Excellence (NICE) also support its use for comprehensive assessment of patients.

Lead researcher: Manoj Sivan

Leading the largest national research study into the long-term health impacts of COVID-19

University of Leicester

Researchers at the University of Leicester are leading on a national study exploring the long-term health impacts of COVID-19 on hospitalised patients. PHOSP-COVID is the first UK-wide study to assess the health impacts of COVID-19 on patients and their rehabilitation.

Following the first wave of the COVID-19 pandemic, clinicians were able to gain insight into the acute phase of the disease. However there is still very little information concerning the long-term effects of COVID-19 and the ongoing medical, psychological and rehabilitation needs of these patients. For those who were hospitalised and have since been discharged, it is not yet clear what the health needs for people diagnosed with COVID-19 will be, to enable them to make as full a recovery as possible.

The PHOSP-COVID research study seeks to address this knowledge gap and aims to understand why some people recover more quickly than others, why some patients develop other health problems later on, which treatments received in hospital or afterwards impact longer term recovery, and how patient care can be improved after they have been discharged from hospital.

One of the first patients recruited to the PHOSP-COVID study with the nursing team.

"The PHOSP-COVID study will draw on expertise from a national consortium of leading researchers and clinicians"

Over the next 18 months the PHOSP-COVID study will draw on expertise from a national consortium of leading researchers and clinicians – involving 20 universities and associated NHS trusts. The COVID-19 consortium of researchers and clinicians includes the Universities of Oxford, Manchester, Sheffield, Birmingham, Liverpool, Edinburgh, Nottingham, Imperial College London, and King's College London.

The study is expected to recruit 10,000 patients who were admitted to UK hospital sites with confirmed or suspected COVID-19.

Lead researchers: Chris Brightling, Louise Wain, Rachael Evans

Keeping athletes on track and aware of their heart health during lockdown

St George's, University of London

Researchers at St George's UoL have created an algorithm to guide athletes, club doctors and sporting bodies as to when evaluation by a heart specialist is necessary to ensure that athletes can safely return to training after becoming infected with COVID-19.

The impact of the COVID-19 pandemic on the global sporting community has been immense, disrupting fixtures, contracts, training schedules and those mass-participation events once thought to be immovable and untouchable, such as the London Marathon and the Olympic Games. For elite athletes returning to competitive sport there was initially a lack of guidance about the impact of COVID-19 infection on their health for physicians and coaches involved in their care. During the early stages of the pandemic several high-profile athletes had become infected with COVID-19, and at the time it was not known what impact this could have on their subsequent sporting performance.

Effective guidance was needed as it was recognised that despite being well accustomed to exercising more intensively than the general population, rigorous exercise causes stress on the body, leading to it becoming more run down and more prone to infections. Cardiac involvement is a recognised complication of becoming infected with COVID-19 and has potential implications for athletes, who push their cardiovascular system to the limit on a regular basis to maintain their fitness. The research team at St George's found that there is no current evidence to suggest that athletes are especially susceptible

"The paper gave clear guidance for those with myocarditis to cease exercising for three months in order to rest the heart"

to becoming infected with COVID-19, but that they should not try to exceed the intensity of their usual training programme in parts of the world where the pandemic is still at its peak.

The publication was influential in providing guidance on what to do when athletes infected with COVID-19 display signs of inflammation of the heart muscle – a condition known as myocarditis. Myocarditis has been identified as occurring in a small percentage of COVID-19 patients admitted to hospital and is diagnosed by measuring levels of cardiac troponin in the blood, which is released by the damaged heart muscle. The condition can lead to permanent damage of the heart, especially if the person continues

to exercise. The paper gave clear guidance for those with myocarditis to cease exercising for three months in order to rest the heart. Depending on the results of the individual's follow-up heart scan, it was advised that the cardiologist responsible for their care could prescribe medications or recommend a further period of rest.

The paper has helped to dispel anxiety among stakeholders in professional and elite sport as to what impact becoming infected with COVID-19 may have on athletes and has helped individuals to effectively and safely prepare for a return to competitive sport following infection. It provides a realistic approach which balances the concerns of the impact of COVID-19 on the heart versus subjecting athletes to unnecessary investigations, taking into consideration available resources for elite athletes but also those available to recreational exercisers.

Lead researchers: Michael Papadakis and Sanjay Sharma

Lockdown associated with the largest drop in COPD attacks ever seen across Scotland and Wales

Swansea University, University of Edinburgh

During the early stages of the pandemic evidence emerged that the UK-wide lockdown was associated with poorer outcomes for non-COVID conditions such as cancer and cardiovascular diseases. However, the pandemic's impact on serious respiratory conditions such as chronic obstructive pulmonary disease (COPD) was initially poorly understood. COPD is the name for a group of lung conditions that cause breathing difficulties, including emphysema (damage to the air sacs in the lungs) and chronic bronchitis (long term inflammation of the airways). It is an incurable condition that can severely limit the sufferer's activity levels and quality of life, making it crucial that the impact of lockdown on COPD outcomes is understood.

The study was undertaken by researchers at Swansea University Medical School in partnership with researchers at the University of Edinburgh's Usher Institute, and colleagues in the EAVE II study;
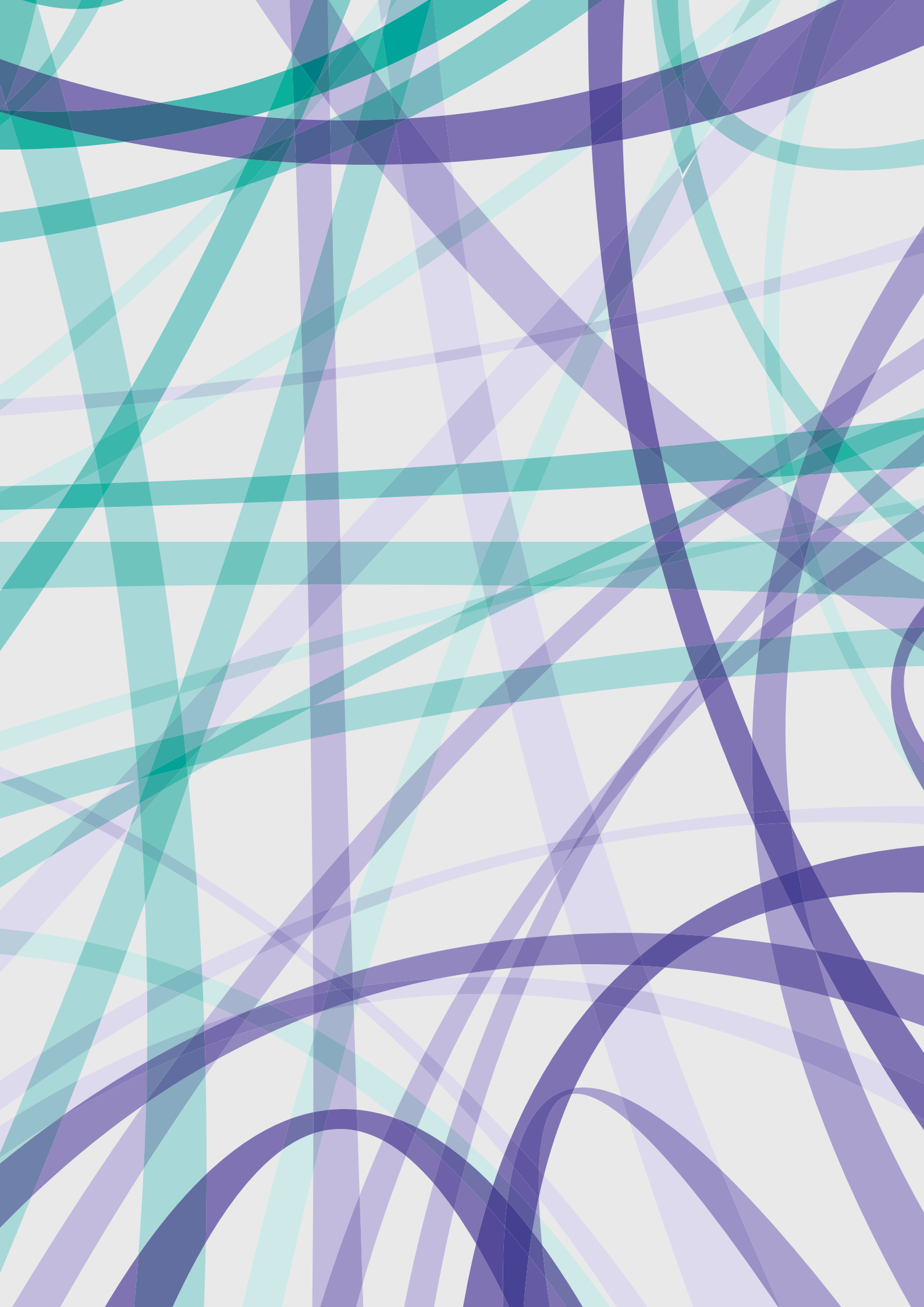
"These findings have far-reaching implications because a reduction in COPD-related attendances increases healthcare capacity and resources to treat people with COVID-19"

a real-time monitoring project of COVID-19 in Scotland. Compared with data from the last five years, the study found a 39% reduction in GP consultations and a 48% reduction in hospital admissions for COPD following the introduction of the first national lockdown. Reassuringly, the study also found no evidence that deaths due to COPD have increased during lockdown. This reduction in COPD exacerbations may have resulted from reduced transmission of non-COVID-19 respiratory infections, reduced

exposure to outdoor air pollution and improvements in COPD self-management through smoking less or by those at risk making other behavioural changes such as improving adherence with prescribed treatments.

These findings have far-reaching implications because a reduction in COPD-related attendances increases healthcare capacity and resources to treat people with COVID-19. Further investigation based on these results could also support the drive to reduce pollution levels. Beyond the pandemic, it is hoped that the findings will support an improved public health message to facilitate effective self-management of COPD and to reduce the transmission of respiratory infections through better hygiene and other precautionary measures.

Lead researchers: Mohammad Alsallakh, Gwyneth Davies, Aziz Sheikh