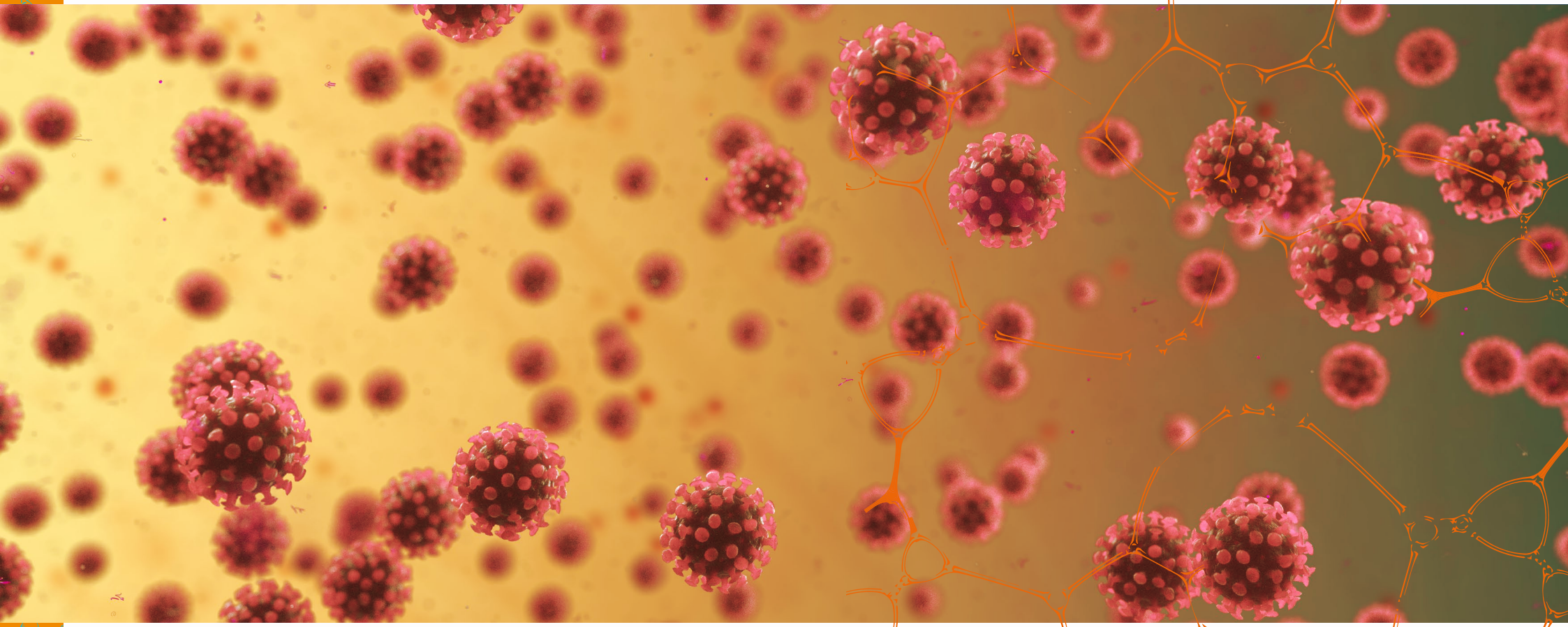
Medical Research Council

MRC community COVID-19 response: Impact, Legacy and Lessons Learned



Contents

Executive summary

The response from the UK academic community to address the 2020 SARS-CoV-2 pandemic was a highly impressive demonstration of how research can address the most pressing societal challenges. From the early months of 2020, the Medical Research Council UK Research and Innovation (MRC UKRI) received thousands of research applications to combat the pandemic challenge.

Over the course of the first year of the pandemic (2020-21), MRC UKRI provided £252m in funding and support for these projects. A total of 7,896 named researchers, academics and others, applied for MRC funding.

The 1,213 researchers who succeeded in gaining funding came from every biomedical research-intense UK academic institution and all four nations of the UK, as well as 28 countries around the globe. 197 new projects were funded (with a commitment of £222m). In addition, 116 (~£29.9m spent) existing MRC-funded projects and programmes were redirected/repurposed to target academic expertise nationally and internationally to address the COVID-19 threat (see additional details in the MRC COVID-19 Response Interim Report).

Early 2020 saw the immediate roll out of:

- **The world's largest trial of treatments for COVID-19: RECOVERY.**
- **The development of the Oxford/Astra Zeneca vaccine.**
- **A UK-wide virus sequencing platform: COVID-19 Genomics UK Consortium (COG-UK).**
- **COVID-19 population impact modelling.** Live data on the epidemiology of COVID-19 across UK from research platforms including MRC-University of Glasgow Centre for Virus Research (CVR), MRC Human Immunology Unit (HIU), MRC Biostatistics Unit (BSU), the Early Assessment of COVID-19 epidemiology and Vaccine/anti-viral Effectiveness study (EAVE II), and the UK Longitudinal Linkage Collaboration (UK LLC).
- **The COVID-19 toolkit.** Refocused work within the Department of Signal Transduction at the MRC Protein Phosphorylation Unit in Dundee and the MRC CVR provided a standardised set of COVID-19 molecular research tools enabling consistent comparable COVID-19 research around the world.
- **Global pandemic response through the MRC International Units**. MRC The Gambia and MRC Uganda Virus Research Institute (UVRI) and London School of Hygiene & Tropical Medicine (LSHTM) Uganda Research Unit and researchers around the world.

The many staff within the MRC PPU labs who worked on generating and characterizing reagents for the Covid-19 Toolkit
Image credit: MRC Protein Phosphorylation Unit

The rapid pivoting of UK biomedical research resulted in a great breadth of outputs and life-saving interventions.

Some key examples are shown below:

- The development of the **Oxford/Astra Zeneca vaccine** for global use. It was validated in clinical trials around the world within one year and was used in more countries (178) across the globe than any other vaccine: 25% of all doses of COVID-19 vaccines administered globally were the Oxford/Astra Zeneca vaccine. Its rapid development led on to initial vaccination of >90% of the UK 70+ year old adults by January 2021 (>85% of over-12-year-old children were double vaccinated by the end of 2021).
- World leading modeling of viral transmission**, infection and impact of interventions.** Regular, updated and accurate modelling data on the pandemic spread and impact was tirelessly provided by the researchers at the MRC Centre for Global Infectious Disease Analysis (GIDA), MRC BSU,Joint UNiversities Pandemic and Epidemiological Research (JUNIPER modelling consortium) based in London, Bristol, Cambridge, Exeter, Lancaster, LSHTM, Manchester, Oxford and Warwick Universities. The modelling also provided critical insight into the likely impact of proposed interventions.
- The most extensive SARS-CoV-2 tracking programme**.** COG-UK was able to track UK virus transmission and mutations in real-time. The data and techniques were shared globally and informed government decisions on lockdown, population testing strategies, transmission reduction strategies (travel restrictions), and COVID-19 variants of concern. The consortium provided a legacy of increased expertise, for example, a 70-fold increase in genome sequencing capabilities was developed in the UK.
- Identification of the first effective treatment for severe COVID-19 through the **RECOVERY trial**. Dexamethasone use was assessed to have saved 22,000 lives in the UK and an estimated 1 million globally by March 2021. Other beneficial treatments include tocilizumab and baricitinib, which were also anti-inflammatories. RECOVERY informed the clinical community of the lack of effectiveness of many unsuccessful treatments which were being used. The rapid establishment of the RECOVERY trial was the result of pandemic planning developed over the previous decade through the International Severe Acute Respiratory and emerging Infections Consortium (ISARIC), the MRC Clinical Trials Unit, the MRC Clinical Trials Services Unit and others.
- Established novel templates for delivering pandemic data for real-time policy development.
- Translated existing expertise and infrastructure into effective diagnostic tools virtually overnight
- More than 3,307 publications.
- More than 260 COVID-19 datasets and databases; 4 linked Trusted Research Environments (soon to be 5) covering the four-nations; more than 36 new data handling, analysis and management techniques
- More than 15 new medical products (including the vaccine, treatments, and clinical care protocols)

See details of these and other impacts arising from the UKRI response below and in the report and annex of the Impact Evaluation of UKRI's R+I Funding Response to COVID-19.

Projects

1,255
applications within MRC remit

313
projects supported

197
new, dedicated C19 awards

116
existing awards repurposed to pandemic

People

7,896
applicants

5,522
unique named individuals

1,299
new to UKRI

1,213
researchers supported

Pounds

£222m
newly committed

£29.9m
repurposed (of £185m award spend)

Places

1,057
UK based awardees

156
international awardees

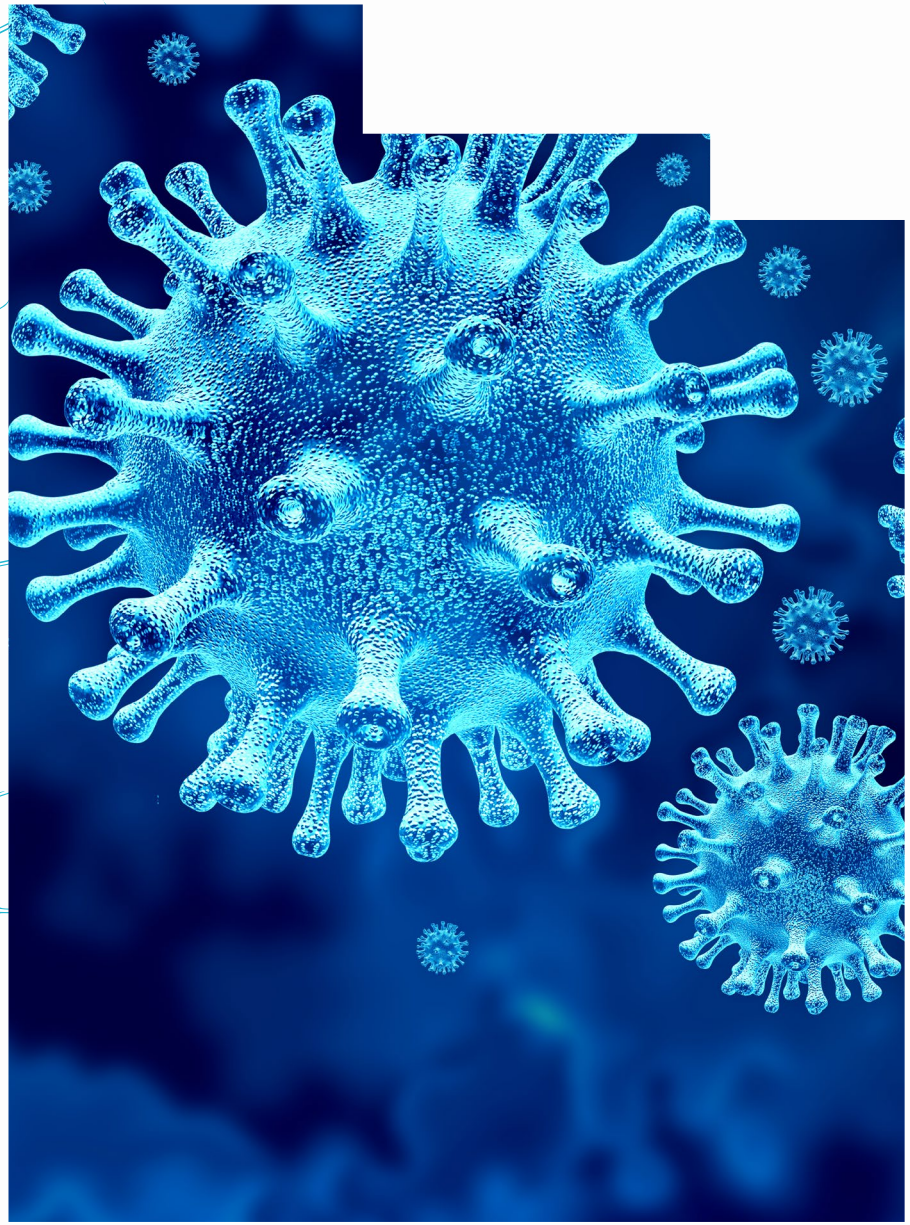
From **28** countries

UK Places

PI in every UK region

100%
of biomedically research intensive universities funded

134
Awards to the largest HESA registered HEIs



Introduction

Over the first months of 2020, with support from MRC URKI and other government and charitable agencies, the UK biomedical research community established a collaborative, pan-UK effort to address the public health and well-being challenges imposed by the COVID-19 pandemic.

Strategic planning began in MRC and UKRI head office in January 2020 to address the potential gravity of the emerging SARS-CoV-2 pandemic.

Well established global relationships in the UK academic community, including with academics in Wuhan, China, had tracked the nascent pandemic's level of transmission and rising lethality. The virus first emerged in China in October 2019. Early data evidenced a potential 5.3%- 0.15% fatality rate in COVID-19 patients with a very high level of transmission. The earliest cases were recorded in China in mid-November 2019 with cases appearing in every region of the world by the end of March 2020. The combination of these factors created the real possibility of 420m-12m deaths globally, unless rapid and effective interventions were identified and implemented.

Agile pivoting to COVID-19 directed research

There is extensive evidence that MRC past investments played a significant role in nurturing and enabling an academic research landscape that could agilely respond from the outset of the pandemic. The Impact Evaluation of UKRI R+I Funding Response to COVID-19 determined that the governance and management structures of MRC-funded Units and Centres enabled whole institutions to pivot from the 'day job' to 'fighting the pandemic'. This agility was an important feature of the success of their COVID-19 research contributions. *"'It was a key policy insight; university centres behaving in a manner more typical of a national laboratory or government research establishment. This ability to pivot towards a national emergency echoes the behaviour of UKRI itself".* The staff from MRC UKRI research Units and Centres utilised their well-established networks and relationships, identified sources of relevant existing data, and developed methods for rapid acquisition of new data to conduct a substantial volume of research. These networks included researchers from all corners of the UK; approximately half of the grant holders who were interviewed said that pre-existing relationships were the strongest enabling factor in achieving impact at pace.

While the rapid response to COVID-19 focused research was evident across the biomedical community, notable examples of this agility were demonstrated by the MRC/University of Glasgow Centre for Virus Research (CVR), MRC Centre for Global Infectious Disease Analysis (MRC GIDA), and the newly established Coronavirus Genomics Consortium (COG-UK). By March 2020, the CVR, with world leading expertise in virology, pivoted all staff (>240 research personnel) towards fighting the pandemic. Likewise, MRC GIDA had redirected the full-time research focus of 70 disease outbreak experienced staff to COVID-associated modelling. The COG-UK executive team had put their 'day jobs' on hold to focus on SARS-CoV-2 sequencing with researchers from 16 academic institutions, the UK's four public health agencies, the Wellcome Sanger Institute, the Lighthouse labs, and 79 National Health Service Trusts redirecting their efforts to join them over the year. In addition to pivoting research focus, the Francis Crick Institute supported the local hospital and NHS trust through provision of COVID-19 testing and transformed the Crick building into a vaccination centre, manned by 300 Crick staff in support of UCL Hospital staff, providing more than 80,000 vaccinations over 8 months.

Tackling an unknown virus

The realisation of the high transmission, hospitalisation and mortality rates associated with the SARS-CoV-2 virus necessitated rapid intervention. However, all components of treating and containing the virus were unknown at the time, as were the implications for a population living with a global pandemic. The limited understanding of how the virus behaved made it difficult to develop treatments, as well as infection prevention protocols at the individual and population levels. Beyond those, the additional factors of diagnosis, differential susceptibilities, care, mental health, and social impact also had to be considered as immediate concerns.

The extent of the ignorance was a strong argument for the need for basic discovery science as a basis for others to design interventions e.g. how the virus entered cells at the molecular level. To initiate research to address these components, as well as the more directly health related research areas, MRC UKRI and National Institute of Health Research (NIHR) launched the NIHR/UKRI Rapid Response (RRI) Call 1 in February 2020. The call focused on vaccination and treatment, followed by a rolling call to harness the breadth of the relevant academic expertise.

These projects were focused toward 15 different heath-focussed areas of the pandemic response[1]. In parallel, UKRI launched the Rapid Response Agile rolling call to engage the expertise of all disciplines (see MRC COVID-19 Interim Report for details)

The MRC UKRI Executive Chair at the time, Professor Fiona Watt, and colleagues noted in August 2021:

> *"The Rapid Response rolling call engaged the entire research community. There was representation on the panels, which met weekly, from across England and the devolved nations, and the call was able to respond to shifting priorities as the pandemic evolved. We worked closely with the community, including through targeted nested highlight calls, to address the issues being thrown up by the disease. To some extent we could be seen as moving into 'contract research."*

Adapting funding mechanisms

The challenges imposed by the pandemic also motivated a significant change in funding mechanisms to generate knowledge that could be rapidly translated into policy and clinical interventions to benefit population health. All Rapid Response projects were funded on the understanding that they would provide data or products to impact on societal health or well-being within the 12-18 month duration of the award. This approach was a complete departure from the normal funding process, which is designed to support the development of break-through discoveries or knowledge aggregation whose contributions to societal wellbeing and prosperity would be translated over subsequent years or decades.

A similar change in funding mechanism was employed in the pan-UKRI Rapid Response call to support COVID-19, addressing projects across the breadth of academic expertise with similar expectations of immediate impact. Additionally, MRC UKRI supported COVID-19 research in international MRC Units in Uganda and The Gambia to monitor and investigate COVID-19 in their communities and led on a variety of international programmes to engage with COVID-19 research across the globe. For example, MRC UKRI galvanised international COVID-19 research through the Global Effort on COVID-19 Health Research funding call (GECO), as well as a joint research call with India.

As well as the shift in emphasis on rapidty of impact, MRC UKRI support was also focused on 'platform funding' – programmes designed to be a linkage or intersection of expertise and data. Platform funding was used to provide data to reveal the actions of this unknown disease and facilitate response to shifting understanding and knowledge priorities as the pandemic evolved. Many of the grants funded in the first wave of funding (Feb -Sept 2020) were co-developed with MRC UKRI head office or arose from community response as platforms, in contrast to the usual project grant funding. The names of the platforms funded through the RRI (some are listed page 10) exemplify the diversity of knowledge priorities that were identified, funded, and investigated through these platforms.

1. Candidate Therapeutics R+D, Clinical Characteristics, Diagnostics, Epidemiological Studies, Ethics Consideration for Research, Ethnicity, Health Care Service Management, Immunology, Mental Health, Modelling, Pregnancy, Social sciences in the Outbreak, Transmission, Vaccines, and Virus

Examples of RRI platform logos

www.opensafely.org

www.phosp.org

www.co-connect.ac.uk

www.commins.org.uk

www.principletrial.org

www.condor-platform.org

www.ucl-virus-watch.net

www.ed.ac.uk/usher/eave-ii

www.uk-reach.org/main

www.arc-yh.nihr.ac.uk/what-we-do/mental-health/owls

www.isaric.org

- COVID-19 multi-arm, multi-stage adaptive clinical trial: **CoV-MAMS**
- Secure platform across 55 million patients' full-linked primary care records: **OpenSAFELY**
- Post-hospitalisation COVID-19 study: a national consortium to understand and improve long-term health outcomes: **PHOSP-COVID**
- COVID - Curated and Open aNalysis aNd rEsearCh platform: **CO-CONNECT**
- COVID-19 Mapping and Mitigation in Schools: **CoMMinS**
- Platform Randomised trial of INterventions against COVID-19 In older people: **PRINCIPLE**
- A UK underpinning platform to study immunology and immunopathology of COVID-19: The UK Coronavirus Immunology Consortium: **UK CIC**
- COVID-19 National DiagnOstic Research and Evaluation Platform: **CONDOR**
- Understanding community incidence, symptom profiles, and transmission of COVID-19 in relation to population movement and behaviour: **Virus Watch**
- Investigating incidence, severity and risk factors for COVID-19 in BAME and Migrant groups to inform public health action.
- Early Assessment of COVID-19 epidemiology and Vaccine/anti-viral Effectiveness: **EAVE II**
- United Kingdom Research study into Ethnicity And COVID-19 outcomes in Healthcare workers: **UK-REACH**
- Liverpool COVID-19 Drug Interactions
- A global registry of women affected by COVID-19 in pregnancy: **nCoV**
- Strengthening & Accelerating the Global Research Response to COVID-19 by Sharing Methods and Knowledge Between Countries, Networks and Organisations
- Controlling COVID19 through enhanced population surveillance and intervention: a platform approach: **Con-COV**
- Serum Testing Of Representative Youngsters: **Coronavirus STORY**
- The COVID-19 Clinical Neuroscience Study: **COVID-CNS**
- Transmission of COVID-19 in kids: **TraCK**
- Optimising Well being during Self-isolation: **OWLS**
- COVID-19 symptom tracker: **ZOE**
- Coronavirus Clinical Characterisation Consortium: **ISARIC-4C**

National Core Studies platforms

As the first year of the COVID-19 pandemic progressed, policymakers, led by Sir Patrick Vallance (Government Chief Scientific Adviser), determined that a larger form of the platform model seen within the RRI portfolio of awards was needed to rally the UK expertise more effectively. It was evident that although knowledge about this new disease was growing across many public sector organisations, it was siloed; with the rapid pace of the work, there was insufficient knowledge permeability between the groups. The National Core Studies (NCS) platforms were intended to bridge those gaps, bringing together the academic and government department expertise, knowledge and capabilities. In autumn 2020, the UK government funded the initial phase of six NCS platforms to respond to near term strategic, policy and operational needs relating to the COVID-19 pandemic.

The NCS programme was launched to provide data within very tight timeframes for the government's immediate decision-making needs. The programmes were broadly successful in achieving their objectives, and specifically with engaging government agencies such as the Office of National Statistics (ONS) and UK Health Security Agency (UKHSA) who were not traditional partners for the academic biomedical research community.

> *"These novel and vital connections were facilitated by an empowerment derived from the government appointment of NCS leads[2]".*

As they were aligned with MRC UKRI strategic objectives, MRC UKRI adopted oversight of the three NCS programmes within the biomedical research sphere: Longitudinal Health and Wellbeing, Data and Connectivity and Immunology. [See National Core Studies COVID-19 response: Objectives, Impacts and Legacy for details].

The data provided by the MRC UKRI portfolio of COVID-19 awards informed government health and societal decision making around many key areas, including:

- lockdown procedures and implications
- vaccination strategies across ethnic, age, and socio-economic diversity
- clinical policy on health care and interventions
- tracking transmission
- evolving variants of the virus

The COVID-19 response projects also provided significant support for all researchers at the time, through robust networking, cross discipline working, research tool and data sharing, and existing data accessibility. Much of that progress will carry forward into the future, through additional linking of existing UK data assets and the availability of new datasets. These efforts have made UK networks of biomedical and population databases more accessible, powerful, and informative than ever before.

2. Observation from Patrick Chinnery, Chair of UK CTAP, Lead on NCS Clinical Trials Infrastructure and Clinical Director for MRC.

Honours for COVID-19 researchers

The high proportion of honours recipients (2020, 2021, and 2022) acknowledges the extensive contribution of the biomedical academic community, listed below. Each of these individual honours represents impact that was made possible by extensive networks of scientists, clinicians, fellows, analysts, technicians, and students who put aside their own projects to work on the COVID-19 research data needs. The strategic and administrative work done by staff at MRC UKRI head office was also recognised with honours awarded to Joanna Jenkins (then Head of the Infections and Immunity Board) and Jonathan Pearce (MRC Director COVID-19 Response). There has also been acknowledgement of MRC UKRI staff for the heavy workload undertaken (e.g. MRC UKRI staff workload doubled in 2020) to ensure that the highest quality, most needed research was funded at speed.

Honours received across Biomedical community for COIVD-19 research (2020-2022):

- Wendy Bickmore *CBE NY21*
- Wendy Burn *CBE NY21*
- Adrian Hill Knighthood BD21
- Teresa Lambe *OBE BD21*
- Masimo Palmarini *OBE BD21*
- Sarah Gilbert *Damehood BD21*
- Kate Binbgham *Damehood BD21*
- Abdul Sesay *OBE NY22*
- John Stageman *CBE NY22*
- Nick Lemoine *OBE NY22*
- Chris Whitty *Knighthood NY22*
- Gregor Smith *Knighthood NY22*
- Frank Atherton *Knighthood NY22*
- Jonathan Van-Tam *Knighthood NY22*
- Jenny Harries *Damehood NY22*
- Pascal Soirot *Knighthood BD22*
- Aziz Sheikh *Knighthood BD22*
- Ewen Harrison *OBE NY23*
- Nish Chaturvedi *OBE NY23*
- Emma Thomsom *OBE BD20*
- Sara Elizabeth McDonald *OBE BD20*
- Catherine Sudlow FRSE *OBE BD20*
- Stephen Townley Holgate *Knighthood BD20*
- Paul Elkington *OBE BD20*
- Ann Sarah Walker *OBE BD20*
- Timothy David Spector *OBE BD20*
- Gideon James Rubin *OBE BD20*
- Graham Francis Hassell Medley *OBE BD20*
- Antony Vivian Cox *OBE BD20*
- Julia Rose Cog *OBE BD20*
- Catherine Tracey Moore *OBE BD20*
- Christian Delles *OBE BD20*

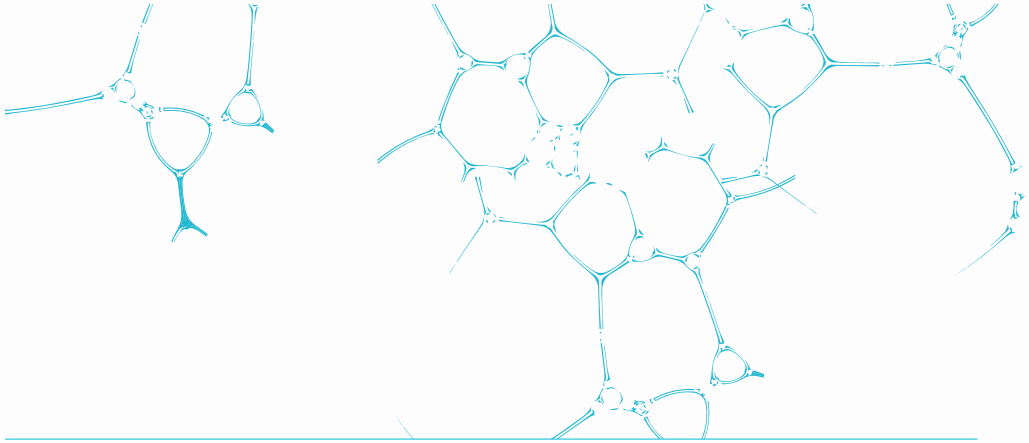
Faster dissemination of research outputs

Prior to the pandemic, new academic research was traditionally communicated via published journal articles or conference presentations. The entire publishing timeline from submission to acceptance was estimated to take approximately 6 months in the life sciences sector.

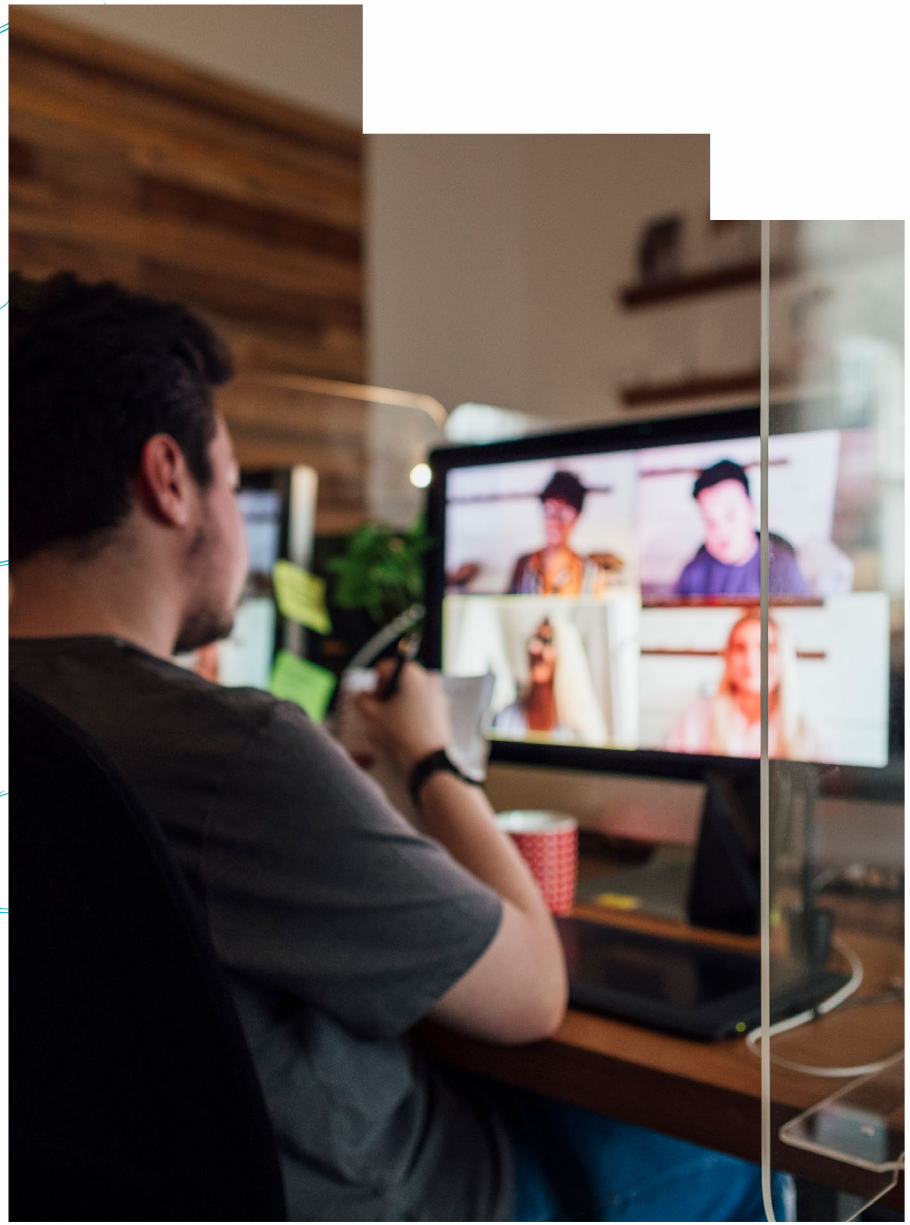
A study analysing publications during the first 10 months of the pandemic, between January 1 and October 31, 2020, found that preprint servers hosted almost 25% of COVID-19–related science, and that these COVID-19 preprints were being accessed and downloaded in far greater volume than other preprints on the same servers. The study demonstrated the practice of rapidly and openly sharing science in the context of a global pandemic and the essential role of preprints in this endeavour.

The researchers funded through the MRC COVID-19 response embraced this practice, releasing data through publication faster while still attracting high levels of global interest.[3] While this approach of 'doing science by press-release' has been criticised due to the lack of appropriate peer review before public release, it has proven useful where the rapid dissemination of new evidence changed clinical practice and, as a result, saved lives.

A notable example of this was the June 2020 pre-print publication of the RECOVERY trial results, showing the life-saving benefit of dexamethasone in severely ill patients with COVID-19.



3. See 'speed of publication data' (Figure 3 on Page 20)



Connectivity of UK response

The UK biomedical community rapidly realised the breadth and complexity of the COVID-19 pandemic threat. They immediately began to fashion plans to apply their expertise to the challenge. They formed research programmes and networks with new colleagues and existing collaborations.

Some of these were developed in collaboration with MRC UKRI staff and government advisors, some entailed a repurposing of existing resource and research infrastructure within MRC-funded institutions and others were brought forward to respond to MRC COVID-19 funding calls. The 197 new awards made by MRC UKRI supported 1,095 named researchers from 91 organisations across the UK (see Figure 1). This includes a project lead in every region of the UK, with funding to all 26 of the 'biomedically research intensive' universities[4]. Using the HEIs in the HESA database, MRC UKRI supported COVID-19 research across 95%[5] of the HEI investment in the UK (134 organisations). In addition, these UK-based researchers were joined in their COVID-19 efforts by 156 international applicants from 28 countries. These applicants were assisted by an army of unnamed individuals in MRC Units and Institutes, NHS laboratories, and research centres across the four nations of the UK.

4. Defined as research organisations receiving at least 0.35% of MRC UKRI total expenditure for the past three years.
5. Based on HESA expenditure from 2015/16 to 2020/21.

Figure 1: Distribution of COVID-19 awardees (lead and co-researchers) across the UK by city

Researchers' Dunkirk spirit

Beyond the newly supported COVID-19 funding, researchers showed an inspiring 'Dunkirk spirit' in bringing what they could to support the pandemic response, from donations of PPE and equipment to the creation of novel pandemic-relevant resources from disciplines outside of immunology.

Senior MRC UKRI colleagues observed in August 2021 how "*perhaps surprisingly, scientists with no research interests of direct relevance to COVID-19 have stepped in to support testing, whether by donating equipment or carrying out the tests, have volunteered to process blood samples for the COVID-vaccine trials and become trained to deliver vaccines. This could lead to a profound change in research culture, with an intermingling and mutual understanding of discovery and applied medical research.*"

Given the scale of the response and limited MRC UKRI resource not all information was captured on grant management systems. Of the 5,522 unique applicants to MRC's COVID-19 funding schemes, we were able to identify the majority (76%) through pre-existing UKRI records. This left 1,299 applicants unmatched to our systems, so without linkage to past UKRI application history. It is likely that many were new applicants to UKRI as they were predominantly from organisations in China, private sector companies not in our organisation data or were members of the public, acting as lay representatives in Patient and Public Involvement and Engagement (PPIE) roles. While only 58 of these 'new-to-UKRI' applicants were on successful applications, it is indicative of how broadly researchers sought to collaborate.

To assess these collaborative efforts, we compared the information available on co-applicants on newly funded COVID-19 awards (n=160)[6] to those of other non-COVID-19 MRC UKRI awards (n=346, from 'business as usual' funding in the same start date timeframe: 01 March 2020 to 31 March 2021)[7]. COVID-19 awards were, on average, significantly shorter in duration and higher in value than these comparator MRC UKRI awards.

6. The availability of applicant details was limited for 37 of the 197 newly funded COVID-19 awards, including the strategic support funding to MRC university units and MRC's contributions to large national platforms. These awards were made to the unit director or platform lead, but data on research teams behind them is absent or incomplete. These programmes were excluded from the analysis.
7. The total commitment of these 346 comparator awards was £283m, with expenditure of £119m to end of FY 2021/22.

Figures 2a & 2b – Comparisons of research project structure

Figure 2a: Team size' by mean number of applicants per award (left) and value per person (right) ± standard error.

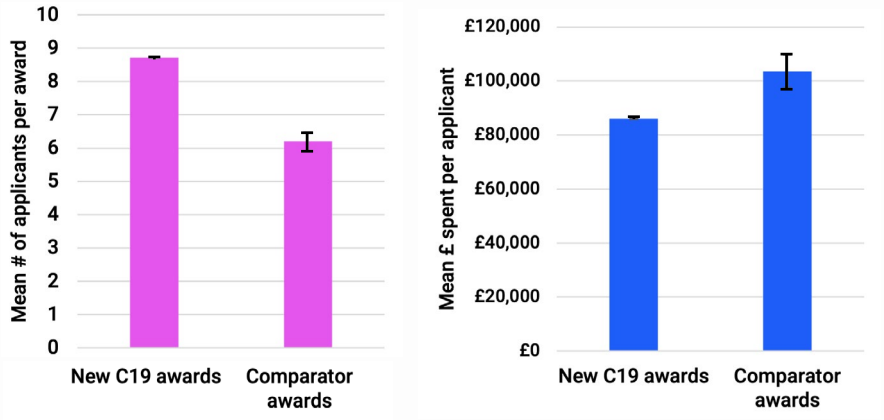
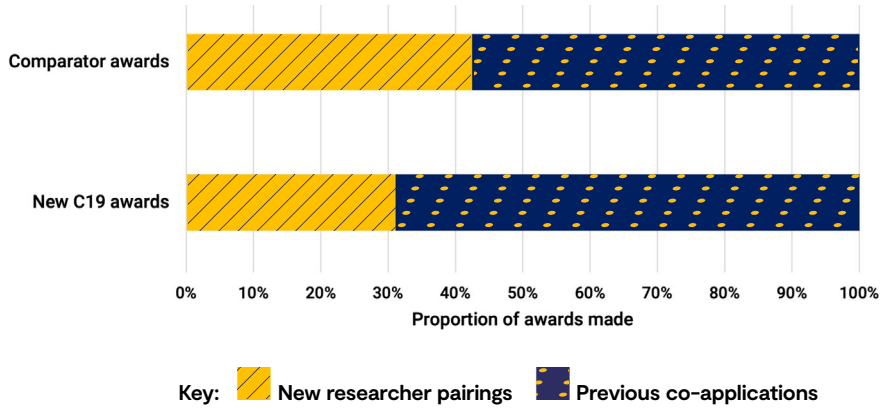


Figure 2b: Proportions of awards with new collaborations using network analytics



The identified research team size of newly funded COVID-19 awards was greater in number than the MRC UKRI comparator awards (an average of 8.7 people vs 6.2, respectively- Figure 2a, left panel, t-test $p<0.01$). While the mean commitment for newly funded COVID-19 awards was higher than the MRC UKRI comparator awards, the average value of the award per applicant was slightly lower but not statistically significant (Figure 2a, right panel).

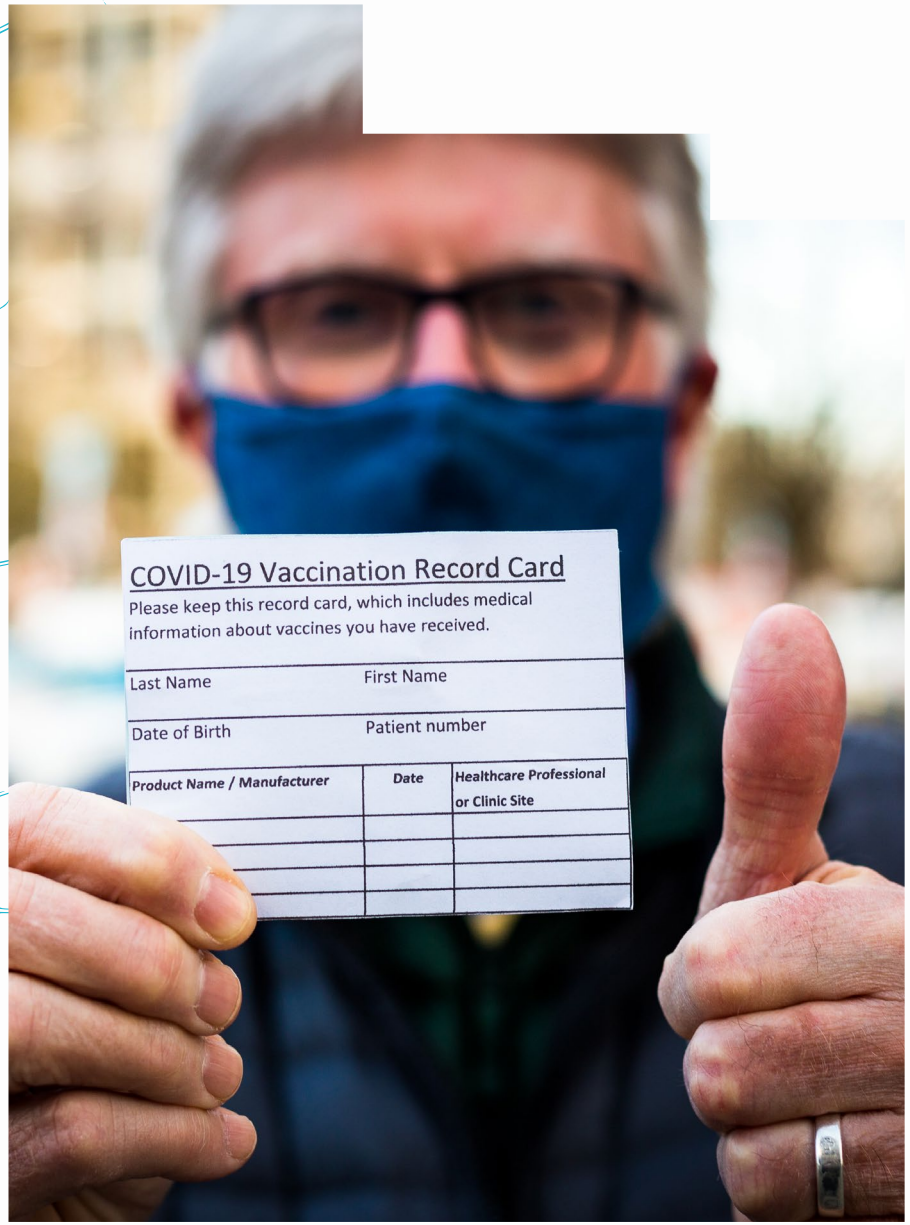
There were similarities between COVID-19 awards and the comparator award in terms of research team sizes (Figure 2a, above) and the forging of new connections between researchers (Figure 2b, right).

To understand whether the COVID-19 awards generated new collaborations, we looked at the applicants on each newly funded COVID-19 awards and compared with participants on awards and applications made since 2015. We examined whether individual researchers had been on applications together before 2020. If the total new applicant pairings are aggregated, we observed proportionally fewer new pairs in the newly funded COVID-19 awards versus our MRC UKRI comparator (Figure 2b).

Throughout this report, we have highlighted many excellent examples of new connections and cross-disciplinary collaborations in the COVID-19 research programmes. We also have some output data from Researchfish showing new collaborations were created post-funding. However, at the point of application researchers on COVID-19 were working with larger than average teams but within previously established collaborations. Given the speed with which the applications and projects were pulled together it is perhaps more likely that researchers would form their projects based on existing networks of collaboration.

In addition to the individual projects and redirected research of the MRC Units, NCS platforms were established to facilitate connectivity between the work being carried out across the public UK health sector: NHS, our universities, and government. Close examination of those connections revealed some room for improvement but there were significant connectivity successes across sectors or organisations that had not been possible prior to the pandemic. Notable examples of this were: 1) the increase in patient recruitment into community clinical trials through data-linkage with NHS Digital and NHS Track and Trace, 2) the rapid establishment of vaccine effectiveness using NHS and non-health datasets and 3) COG-UK success in knitting together the contrasting approaches and different goals of each of the partner members and collaborators (academics, Wellcome Sanger Institute, Lighthouse Labs, public health agencies, NHS Trust laboratories, and others) into a unified sequencing network.

8. Mean duration for COVID-19 awards was 16 months versus 32 months for MRC UKRI comparators, while mean commitment was £1.1m and £0.8m respectively. COVID-19 awards were also 83% spent by end of FY 2021/22, vs only 42% spent by MRC UKRI comparator awards.



Impacts and Outputs

The research outputs from the COVID-19 awards and their subsequent impact are large in number and diverse in their areas of impact. During the first year of the pandemic, the response from the UK academic community was immediate, extensive, and highly effective.

There are countless examples of researchers coming together to bring their expertise to bear on the pandemic challenge. We have published many of them over the past two years and include a few examples below.

Surveillance

The COG-UK consortium was formed in March 2020 to deliver SARS-CoV-2 genome sequencing and analysis to inform public health policy, and to support the establishment of a national pathogen sequencing service. Sequence data is now predominantly generated by the Wellcome Sanger Institute and the Public Health Agencies. Since its launch, COG-UK has sequenced over two million SARS-CoV-2 genomes (reported as of February 2022) which accounts for a quarter of all SARS-CoV-2 genomes shared globally.

Prior to SARS-CoV-2, the largest previous dataset for real-time genomic viral epidemiology during an epidemic was ~1500 genomes from the West African Ebola outbreak, which were sequenced over the course of 2014–2016. By comparison, COG-UK surpassed this total within the first month of its launch and has continued to push viral genome surveillance to an entirely different scale.

Access to a dataset of this scale has allowed researchers to look at the relatedness of the viruses within a health care institution or community and compare to the transmission patterns in the surrounding areas to reveal the patterns linking individual cases. This in turn allows them to spot otherwise unidentifiable opportunities for intervention.

Enabling infrastructure

Several key pieces of infrastructure and enabling discovery research led to the success of COG-UK. For example, the CLIMB project (Cloud Infrastructure for Microbial Bioinformatics), which was funded by MRC in 2014 provided COG-UK with computing infrastructure and bioinformatics analysis capability. The 2013 launch of the Genomics England platform and the associated 100k Genome Project supported one of the first TB sequencing services that offered routine sequencing to rapidly predict drug resistance. This allowed clinicians to provide the correct drugs to patients faster and demonstrated the power of genome sequencing for public health.

Data linkage

COG-UK also facilitated improved data linkage by joining the Health Data Research Alliance in summer 2021. This allowed COG-UK to contribute to creating an ever-more unified approach to the use of health data across the UK as well as to work with partners on issues related to data standards and quality. Data linkage relies on data sharing, which has been prioritised by COG-UK since its inception. Viral genome information being linked with human health data and other datasets such as population health data will open up innovative areas of cross-disciplinary analysis to better understand COVID-19 and how to further improve patient outcomes.

Capacity building and legacy

Data collected by the WHO show that in March 2021, 54% of countries had sequencing capacity. By January 2022, thanks to the major investments made during the COVID-19 pandemic, the number had increased to 68%. Even greater gains were made in the public sharing of sequence data: in January 2022, 43% more countries published their sequence data compared to a year before.

COG-UK consortium team

Image credit: Ikotkas photography

Modelling

The COVID-19 Response Team at the MRC GIDA was instrumental in characterising the epidemiology of the novel SARS-CoV-2 virus, and delivering timely, reliable data to inform policy worldwide.

The MRC GIDA Director was present at the first 'precautionary' Scientific Advisory Group for Emergencies (SAGE) meeting at the end of January 2020. At the second meeting, it was confirmed that representatives from the Response Team, MRC BSU, and JUNIPER would be members of a SAGE subgroup for the duration of the pandemic.

Pathways to policy influence

The COVID-19 Response Team provided the UK government with scientific evidence to support their policy response. The research outputs and analysis fed into advisory committees such as the Scientific Pandemic Infections group on Modeling (SPI-M), New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG), and SAGE. In addition, multiple members of the team have provided evidence in the House of Commons and the House of Lords in several inquiries and committee meetings.

These pathways to policy impact proved fruitful over the course of the pandemic, both within the UK and globally. For example, the team released a report by end of March 2020 (later published in June 2020), which quantified the impact of non-pharmaceutical interventions in reducing transmission in multiple European countries. This work was used by several European governments to inform their policy responses.

They provided modeling evidence which informed decisions to lockdown, testing strategies, vaccination rollout, surveillance and response to variants of concern, roadmap to recovery, as well as longer term and more global pandemic responses.

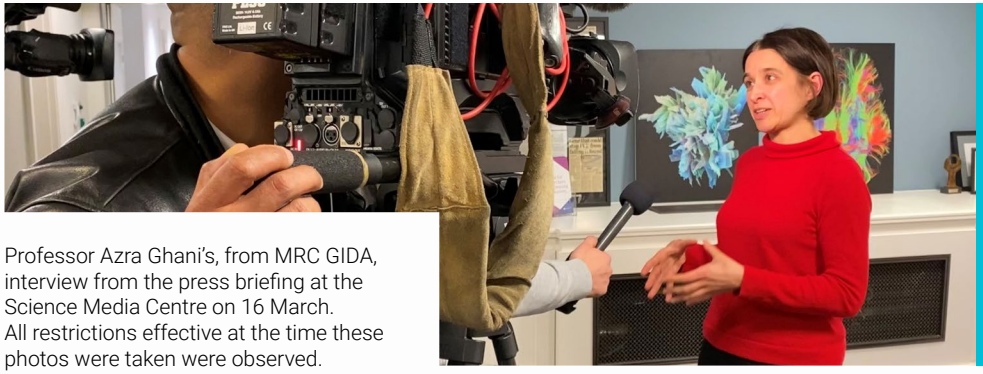
To do this, the team at MRC GIDA mobilised mathematical modelling capacity, pre-existing networks, and knowledge platforms from other outbreak analysis work. For example, previous MRC GIDA collaborations with researchers in Hong Kong during the SARS-CoV-1 epidemic in 2003 established the networks that were vital in the early weeks of 2020, when reports of a novel coronavirus from China began to emerge. Similarly, the 2009 H1N1 'swine flu' pandemic that began in Mexico was useful for developing the mathematical models needed for understanding underlying infection numbers in the early stages of an outbreak.

Global impact through a network of collaborators

The COVID-19 Response Team worked closely with several United Nations agencies, such as the World Health Organisation, World Food Programme, and the International Monetary Fund to produce a global modeling framework and a web page with COVID-19 planning tools, , including a lower and middle-income countries short term forecast dashboard. This is still used by global organisations to feed directly into the WHO COVID-19 essential supplies forecasting tool. This tool is used by many countries to plan the commodities they require based on predictions for the next 30-60 days. These new collaborations extend the application of MRC GIDA's work, and their clear global impact.

Public engagement and open science

Throughout the pandemic, the COVID-19 Response Team provided timely information directly to the press with support from the Science Media Centre. This increase in public engagement put many of the scientists and their work under the spotlight of public scrutiny. However, because the team had moved to open access coding and provided all modelling methodology through GitHub for use by other teams across the UK and globally, this increased attention was not problematic. The approach demonstrates their commitment to reproducibility, data management, and transparency in data and methods. Since emergence of the SARS-CoV-2 virus in late 2019, the team has produced over 60 peer reviewed publications and 42 public online reports, with summaries translated into seven languages and impact reach across 193 countries.



Professor Azra Ghani's, from MRC GIDA, interview from the press briefing at the Science Media Centre on 16 March. All restrictions effective at the time these photos were taken were observed.

Image credit: SL van Elsland

COVID-19 Toolkit

The COVID-19 Toolkit is a resource designed and validated by scientists at the University of Dundee's MRC Protein Phosphorylation and Ubiquitylation Unit (MRC PPU) in partnership with the MRC/University of Glasgow Centre for Virus Research (CVR).

The Toolkit represents a complete set of scientific and diagnostic tools detecting the SARS-CoV-2 virus, including infectious clones, patient isolates, cell lines, and antibodies. These have been made openly available to research groups worldwide to accelerate research through a user-friendly webpage and established biorepositories.

Supporting the global COVID-19 research community

The primary impact of the Toolkit was supplying the UK and global research communities with essential reagents needed to conduct fundamental discovery science. This would in turn enable the rapid development of diagnostics, vaccines, and therapeutics for tackling COVID-19. The existing infrastructure of the MRC PPU Reagents and Services facility, which functions as a not-for-profit facility that provides these resources to the research community at cost, allowed this to happen at speed. This was key, as in the early months of 2020, very few labs within the UK had the capabilities to generate their own viral proteins or antibodies to investigate specific characteristics of the virus, such as transmission or immune escape. The Toolkit, including its reverse genetics system made these materials accessible to other biology labs that were keen to make an impact to further research into SARS-CoV-2. For example, in December 2020, scientists used the Toolkit to understand how protein interaction networks were involved in pan-viral disease mechanisms in coronaviruses. By making the Toolkit available to the global research community, these resources have fast-tracked the investigation of many aspects of COVID-19 research.

Legacy of improving reproducibility

The ability to replicate the results of a scientific experiment is a fundamental tenet of scientific integrity. A large proportion of the reproducibility problems in science are thought to be due to variability within the quality or accessibility of critical key tools and reagents. As the COVID-19 pandemic unfolded and the research community mobilized in response, it was vital to support the reproducibility of the COVID-19 research through access to reliable reagents and tools. The 'Toolkit approach' pioneered by the team at MRC PPU Reagents and Services was therefore vital for addressing the current 'reproducibility crisis' in biomedical research. The MRC PPU Reagents and Services facility's networks of collaborators and capacity for rapid dissemination of these validated tools will be a valuable contribution to the scientific community.

Extending the Toolkit to influenza

The MRC PPU Reagents and Services and researchers at the CVR are also extending this approach to another key virus, by developing the Influenza Virus Toolkit. Although the influenza virus undergoes large amounts of mutations each year, there are also several regions of conservation where the genetic code of the virus does not change across different strains or variants. Recent mortality statistics have revealed that influenza kills more people annually than COVID-19, and therefore a uniform set of standard tools, reagents, and diagnostics for the entire global research community will improve the quality of influenza research and our understanding of the disease.

The many staff within the MRC PPU labs who worked on generating and characterizing reagents for the Covid-19 Toolkit

Image credit: MRC Protein Phosphorylation Unit

Outputs of COVID-19 Awards

The UK biomedical research community instigated 197 new projects and programmes (241 projects[9]) which were funded through the new COVID-19 funding calls and redirected research using their existing funding (110 Unit and Institute programmes and 6 repurposed research projects).

A COVID-19 research publication portfolio[10] can be collected for the entire MRC COVID-19 portfolio while data for other outputs can only be assessed for newly funded COVID-19 awards[11] through researchfish data. Other information on specific areas of outputs and impact were collected through surveys of sub-portfolios of COVID-19 awards. An aggregate review of the MRC COVID-19 newly funded project outputs in April 2023 shows a highly productive period using the usual indicators. The comparator awards[12] are MRC projects starting over the same period as COVID-19 newly funded awards (1 March 2020 through 31 March 2021). These comparator awards covered the full spectrum of the MRC UKRI research remit. They were funded for 3-6 years with no expectation for rapid output.

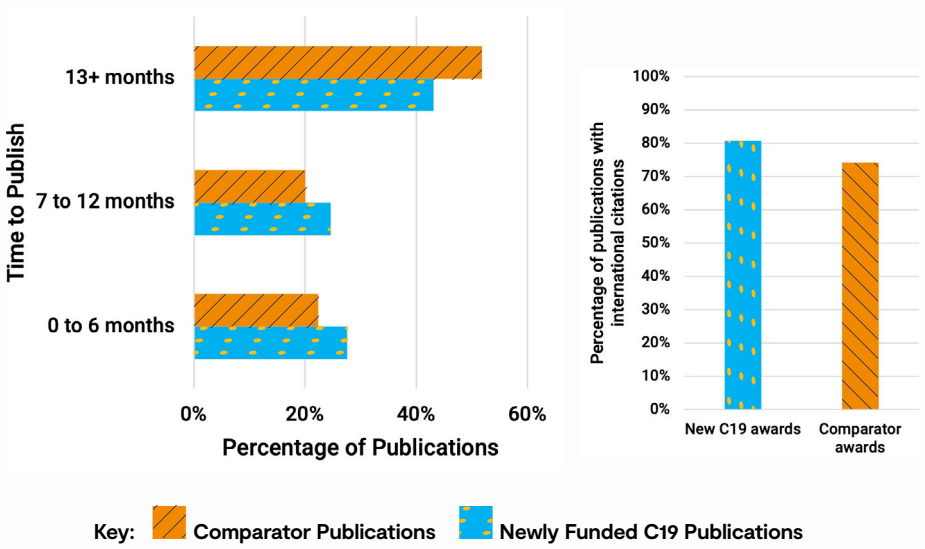
Publications

Typically, the production of research outputs is measured in years, but the pandemic created a pressing need for more rapid dissemination of research findings. The responsiveness of the research community is exemplified by the time to publication data (Figure 3, left chart) for COVID-19 awards where a greater proportion of their publications were published more rapidly (27% were published within six months and 24% in 7-12 months of the award start date (vs 22% and 20% of comparator award publications, respectively). Using citation by an international audience as an indicator of appetite for the data presented, the publications from the newly funded COVID-19 awards show a similarly high level of global interest as a comparable MRC UKRI funding portfolio (81% and 74%, respectively; Figure 3, right chart).

The comparator portfolio of awards (n= 270) produced 17,984 publications between March 2020 and March 2023. Over the same time period, 5,827 publications were produced by the MRC COVID-19 response projects/programmes (n= 182): the newly funded COVID-19 projects (2,094 publications) and the existing projects repurposed to COVID-19 research (3,974 publications).

The data and insights they demonstrated were released more rapidly than the usual publication rate with a comparable level of global interest. This is consistent with an externally commissioned survey of all UKRI newly funded COVID-19 lead investigators, 44% (n=289) said they produced results 'much faster than usual' and 26% said 'a little faster than usual'.

Figure 3: publications by speed of publication (left) and relative rate of international citation (right)



9. 197 awards, some of which were subdivided into separate projects. Of these, 182 provided data on associated publications via researchfish.
10. Publication data extracted from the 2023 researchfish submission period. Corresponding publication dates were taken from Dimensions via Google BigQuery
11. Data on other outputs is collected from researchfish reporting.
12. 346 awards. Of these, 270 provided data on associated publication via researchfish.

Other outputs

There have been many indicators of the collaborative nature of the biomedical community COVID-19 response. This is also reflected in the increase of reported post-award collaborations . Other outputs reported include many new datasets recording COVID-19 impacts on the UK population and on clinical responses as well as COVID-19 targeted products such as the Oxford/Astra Zeneca Vaccine, therapeutics, and clinical care protocols. The high percentage of COVID-19 awards reporting databases and products is consistent with the focus on rapid development of outputs providing data or tools for policy makers. Given the lack of knowledge about the SARS-CoV-2 virus, its transmission and impact on health, datasets were of paramount importance. Creation of hundreds of datasets has been reported with significant development of new databases and analytical tools to facilitate access and linkage of the datasets.

The table below provides a snapshot of awards producing output within two years (2020-2022) demonstrating the faster than usual time to output delivered by the researchers during the pandemic. This efficiency in part reflects the dedication of the researchers but primarily it reflects the highly targeted research questions posed. The usual research project is intended to explore gaps in knowledge rather than the data gathering 'contract research' of the COVID-19 portfolio. The timeframe required for delivering new insights is generally longer.

Newly funded C19 Awards			Comparator Awards			
197 awards	**instances**	**% Total**	**346 awards**	**instances**	**% Total**	**Total projects within awards**
75	178	**38.1%**	98	237	**28.3%**	Reporting further funding
127	609	**64.5%**	165	809	**47.7%**	Reporting collaborations
54	218	**27.4%**	37	62	**10.7%**	Reporting databases
15	20	**7.6%**	7	10	**2.0%**	Reporting products

Detailed analysis of progress of impact for two of the MRC UKRI COVID-19 research programmes: NIHR/UKRI Rapid Response Initiative and Agile COVID-19 funding programmes

The initial component of new COVID-19 funding for the biomedical research community was the rapid response funding calls (NIHR/UKRI Rapid Response 1+2 and NIHR/UKRI Rapid Response Rolling: RRI and UKRI Rapid Response Agile calls: Agile). The Agile call funded COVID-19 research (568 projects) across the UKRI portfolio with 30 awards falling within the biomedical research remit which were administered by MRC URKI. As the names suggest, these projects were tasked with providing data and information rapidly and disseminating it to appropriate policy makers, researchers, or the public.

Call	No. of Projects	Start dates	Duration	£m
RRI 1+2	28	Feb – May 2020	12-18 months	25.9
RRI Rolling	52	May – Nov 2020	12-18 months	47.1
UKRI Rapid	30	May '20 – Apr 2021	12-18 months	16.6

Projects were funded for 12-18 months with extensions determined on the basis of continuing pandemic-data need. The researchers were surveyed[14] on progress and outputs throughout the lifetime of their award. This enabled head office to monitor the research progress, assess areas requiring additional resource, and identify opportunities for administrative support. Additionally, the data provides an indication of progress to impact[15] arising from the research (data below was extracted from survey responses through June 2022).

14. The survey gathered information, quarterly, on project progress: what had been produced, how and to whom the information was disseminated, who was integrated into the project. The response rate was good with 90% of projects reporting at least once and the majority providing multiple responses. The intent of the project was assessed to determine if the research was targeted at clinical or government population health policy and if PPIE was appropriate. The RRI data provided was considered generally robust; 81% of projects providing 3-4 survey responses on average and with only 7 programmes providing data rated 'poor' (AGILE survey data quality was not assessed).
15. Reported by survey.

NIHR/UKRI Rapid Response (80 projects – surveyed September 2020 to June 2022)

Analysis of the survey data documented the researcher response to the urgency of the pandemic through rapid provision of research outputs. Most projects had established links or been provided links to government or clinical policy makers as appropriate for their research topics: 75% of projects focused on data relevant for public policy evidenced direct reporting to government policy makers and 65% of projects focused on clinical insight evidenced direct reporting to clinical policy makers. There is also evidence of uptake and integration across the wider community.

63% of the projects evidenced impact in the areas of their key objectives (targeted data/information provision) within 12 months of project start (34% within 6 months). However, this time scale may have been more challenging for some areas of research under the working restrictions and multiple demands of the pandemic. The RRI funding was classified into 15 theme areas to cover a breath of topics prioritised. It is worth noting that some of these research areas were also being addressed in other larger COVID-19 programmes.

- **Evidenced impact within 12 months:**
  - 4 of 4 Ethnicity projects
  - 1 of 1 Ethic consideration projects
  - 4 of 4 Immunology projects
  - 8 of 9 Epidemiological Studies projects
  - 4 of 5 Clinical Characterisation projects
  - 6 of 7 Social Sciences in the Outbreak projects
  - 3 of 5 Modeling projects
  - 7 of 9 Transmission projects
  - 1 of 2 Diagnostics development projects
  - 3 of 6 Candidate therapeutics assessment projects
  - 4 of 10 Health care management projects
  - 2 of 6 Mental health projects
  - 2 of 6 Vaccine candidate projects
  - 1 of 2 Implications for Pregnancy projects
  - 0 of 4 Virus mechanisms projects
- **Only 5 projects had reported no impact by June 2022**
- **A review of the common output metrics for the RRI projects:**
  - 631 publications were reported from 64 projects with 16 projects reporting no publications (March 2020- March 2022)
  - 20% developed industry involvement
  - 72% of appropriate projects integrated PPIE into their research design

The uncertainty of the exact approach needed to address research questions was evident in the percentage of RRI projects which required some or significant changes to timetable or methodology as they progressed. This was exacerbated by the difficulty in carrying out both lab-based and clinic-based projects during the pandemic. Only 20% of the projects were able to progress as planned with 80% requiring adjustments and changes in timetable or experimental plan.

Agile Rapid response (30 biomedically focused Projects)

The survey for the Agile projects was not as detailed as that for the RRI projects but covered many similar areas and showed a similar focus on rapid impact. Reviewing the survey data through June 2022, 53% of the biomedical Agile projects evidenced impact in the areas of their key objectives (targeted data/information provision) within 12 months (30% within 6 months). 12 projects had reported no impact by June 2022 (this includes 6 of the 9 projects which were still live). Uptake indicators were also at similar levels to that of the RRI projects: 71% of projects focused on data relevant for public policy evidenced direct reporting to government policy makers and 42% of projects focused on clinical insight evidenced direct reporting to clinical policy makers.

The majority of the biomedical Agile project began later than the RRI projects. While there were still significant instabilities in the research environment, the Agile projects were slightly more able, than RRI projects, to adjust in their planning before application; 30% progressed as planned with 70% reported the need to adjust their research plans over the lifetime of the project. Slightly more than half of these projects have received funding to further the research. The funding amount for RRI awards were generally greater than Agile projects. 201 publications were reported from 18 of the biomedical Agile projects with 12 reporting no publications by March 2022.

	RRI	Agile
No. of Projects	80	30
Impact in 6 months	34%	30%
Impact in 12 months	63%	53%
Clinical policy linkage	65%	42%
Government policy linkage	75%	71%
Publications/project	631	201
Projects revised in flight	80%	70%

Legacy of the COVID-19 response

The legacy from the hard work of researchers, analysts, strategists, and policy makers who were active in the COVID-19 response during 2020-2023 is a rich one. Review of the community response has revealed the personal commitment of researchers and underscored the crucial importance of long-term funding for underpinning biomedical research and supporting infrastructure

Additionally, the efforts made during the COVID-19 pandemic have extensively expanded our science knowledgebase, enriched the quality and accessibility of databases, and firmly established networks for collaborative working. The additional experience has advanced future preparedness plans and work is ongoing to further explore ways to improve future responses. The report on the UK government response to the COVID-19 pandemic articulates many areas to consider.

Future pandemic readiness preparations

For decades, many infectious disease specialists around the world anticipated that the next global pandemic would be a new strain of influenza such as the H7N9 'bird flu' virus, rather than a novel coronavirus.

The emergence of the SARS-CoV-2 coronavirus in late 2019 has not lessened the likelihood of this scenario, and several research groups in the MRC UKRI community are applying the lessons learned from this pandemic to be better prepared for the next. For example, the MRC PPU Reagents and Services and researchers at the CVR are extending their COVID-19 Toolkit approach to develop the Influenza Virus Toolkit. A uniform set of standard tools, reagents, and diagnostics for the entire global research community will improve the quality of influenza research and our understanding of the disease.

Long COVID and its impact on society

Long COVID is a condition where people continue to experience symptoms for weeks or months after initially contracting COVID-19. In the UK, the REACT study which uses data from over half a million adults in England found in April 2022 that one in 20 had persistent COVID-19 symptoms. This could mean that over two million people in England could have long COVID.

The burden of long COVID on society is significant, as it can lead to long-term disability and affect people's ability to work, study, and carry out their daily activities. The impact of long COVID on the workforce is substantial, as it can result in prolonged absences from work or reduced productivity. In November 2022, the ONS reported that between June and August 2022, around 2.5 million people reported long-term sickness as the main reason for economic inactivity, up from around 2 million in 2019.

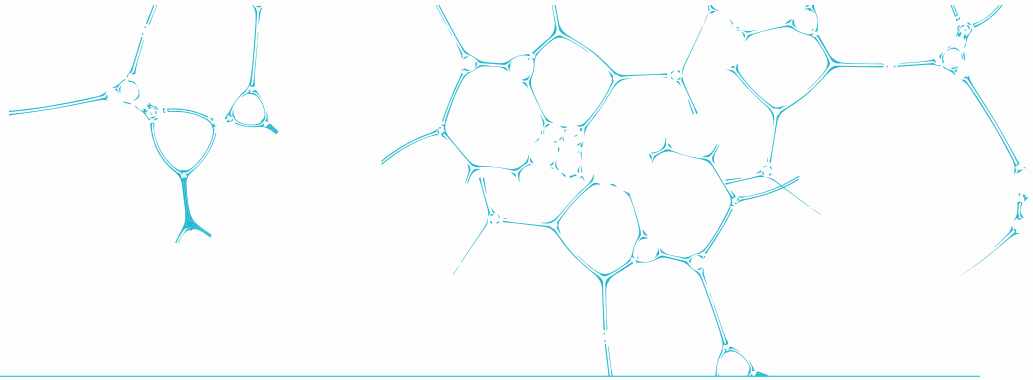
Long COVID can also put a strain on national healthcare provision, as it may require additional resources and healthcare workers to manage the ongoing care of patients with long-term symptoms of COVID-19. The emergence of long COVID underscores the need for continued research into the SARS-CoV-2 virus and the importance of ensuring that national healthcare systems are adequately prepared to manage the ongoing care of patients with long-term symptoms of COVID-19.

As MRC's funding approach returns to a pre-pandemic format for funding knowledge development, initiatives to better understand the COVID-19 pandemic and prepare for future pandemics are supported through continuing research in several key areas. These include the four Long COVID four-year programmes which were funded January 2021 and 11 additional COVID-19 research projects supported via research boards, panels and fellowships. In February 2021, UKRI and NIHR announced £18.5 million to fund four four-year new research studies into long COVID in the community.

The four awards are:

- REACT Long COVID (REACT-LC), a population study to better understand, diagnose and treatment the longer-term impacts of contracting a SARS-CoV-2 infection
- Therapies for Long COVID in non-hospitalised individuals: From symptoms, patient-reported outcomes and immunology to targeted therapies (The TLC Study)
- Characterisation, determinants, mechanisms and consequences of the long-term effects of COVID-19: Providing the evidence base for health care
- Non-hospitalised Children & young people (CYP) with Long COVID (The CLoCk Study)

These four awards and continued research from the NCS, including the population cohorts of LHW, will provide increasing understanding, care protocols and interventions for long COVID to support the millions of people who suffer continued symptoms of long COVID.



Collaborations and capacity-building

A national and international legacy of this pandemic is the establishment of partnerships and collaborations for improved data linkage, data sharing, and capacity building. From the outset of the pandemic, HDR UK helped researchers make COVID-19 databases available on the Health Data Research Gateway. Facilitated by HDR UK, the data community held iterative workshops to agree and establish best practice in data sharing, access, and analysis to make database linkages more efficient. This collaborative working also resulted in development of better analytical tools. COG-UK joined the Health Data Research Alliance in summer 2021, facilitating improved data linkage. This has allowed COG-UK to contribute to creating an ever-more unified approach to the use of health data across the UK as well as to work with partners on issues related to data standards and quality. These networks established linkages across the Trusted Research Environments (TRE) of the four nations which continue to be enriched. Alongside increased data access has been an extensive programme of data scientist training, which will continue improving the pan-UK network.

COG-Train is an international educational initiative providing open-access learning in SARS-CoV-2 genomics. It aims to facilitate an increase in global genome sequencing and analysis capacity, reduce sequencing inequality and enhance pathogen surveillance. Outputs thus far of COG-Train include a series of Massive Online, Open-access Courses (MOOCs) on all aspects of SARS-CoV-2 sequencing, as well as week-long intensive virtual training courses, short expert workshops and concurrent distributed Classrooms.

Data linkages

Improved data linkages are a key legacy of the UK research community's pandemic response, particularly as developed by the National Core Studies (NCS) programmes. The linkages between databases established by the NCS have made the UK a world leader in mobilising the power of national electronic health record platforms. For example, the use of population cohorts linked to health data will allow researchers to conduct statistically powerful population scale research with large numbers of outcomes. Likewise, the establishment of patient cohorts with specific immune profiles (e.g., cohorts of immunocompromised patients) and the increased use of mobile apps to engage the public in understanding and tracking respiratory disease symptoms in real-time (e.g., ZOE symptom tracker) will enhance public involvement in infectious disease research.

Photo taken by the Malawi Liverpool Wellcome Programme team during a 'Viral Variant Conversations' training session

The Administrative Data Research UK (ADR UK) programme (funded by ESRC UKRI) was created to provide safe access to good quality, de-identified data held by different parts of government to support policy-focused research.

Linking administrative data to the large number of health databases has been a long-existing gap. The UK Longitudinal Linkage Collaboration (UK LLC) was established as a TRE to directly support the Longitudinal Population Studies research through bridging that gap. With funding from MRC URKI, ESRC UKRI, and support from NCS, ADR, and the ONS, the UK LLC makes available, for the first time, systematic linkages between non-health administrative records (employment, earnings, social benefits, pensions and education) and wider determinants of health data, within a TRE.

To ensure patient privacy, NCS teams have developed new methods of data security which allow this unprecedented scale of data access. This is key to understanding effectiveness in public policy, and was vital during the pandemic to enable health, economic and social science research findings to be used to save and improve lives.

While data open access has long been in practice in the UK, pandemic data sharing needs made it a standard operating procedure. As related earlier, MRC GIDA used open access coding and provided all modelling methodology through GitHub for use by other teams across the UK and globally. This practice was common in the data community throughout the pandemic.

Lesson Learned

Interviews[16] with MRC UKRI staff who were engaged in leading and managing the MRC UKRI response to COVID-19 were used to develop this section. This includes their insights on what MRC UKRI, and the global research community, might learn from this pandemic and covers the initial plans that have been put in place.

16. Patrick Chinnery Chair of UK CTAP, Lead on NCS Clinical Trials Infrastructure and Clinical Director for MRC UKRI, Steve Oakeshott Head of MRC Infections and Immunity, Anna Kinsey MRC Virology lead in 2020, now Head of Epidemic Preparedness, Jonathan Pearce MRC Director of COVID-19 Response now MRC Director of Strategy and Planning, Fiona Watt MRC Executive Chair in 2020 now EMBO director.

A need for better coordination

The experience of the recent pandemic has honed our understanding of the key elements needed to respond to a global health emergency. The complexity of addressing a pandemic requires rapid coordination of the multifaceted response, nationally, locally, and globally. This entails the convening of a national oversight group with the appropriate expertise and rapid access to sufficient resources. In addition, there must be cooperation and collaboration across the public institutions and available infrastructures from which to build a coordinated response. In the COVID-19 response, the research community rapidly mobilised to address the emerging threat. They were supported by years of previous investment in infrastructure and capacity building which should continue to maintain readiness for future emergencies. The establishment of the UKCDR provided a first step in supporting a global coordinated research response.

However, there are several elements that could have benefited from further preparedness and coordination. These areas include infrastructure capability; for example, in the areas of vaccine manufacture and distribution, along with global cooperation and collaboration. International cooperation can help to ensure that medical countermeasures are developed and distributed fairly and equitably, regardless of a country's economic status or political influence.

The enthusiastic response of the clinical research community instigated a flood of clinical studies which initially overwhelmed capacity. However, for investigations into COVID-19 treatments, a prioritisation of research and rationalisation of the coordination between researchers, NIHR, and NHS was initiated through by UK CTAP (UK COVID-19 Therapeutics Advisory Panel) and carried through by the formation of the NCS Clinical Trials Infrastructure. Additionally, stockpiling of essential medical supplies, including personal protective equipment (PPE) can help to ensure that healthcare workers have the necessary tools to protect themselves and others from infection. There have been issues with surpluses and wastage of COVID-19 vaccines, such as the Oxford/AstraZeneca vaccine. The UK National Audit Office (NAO) has suggested that the Vaccine Taskforce, NHS, and the UK Health Security Agency, working with local partners, should set out a clear strategy to manage this issue in the future and review the overall expected wastage to ensure lessons have been learned from the write-offs required for the Oxford/AstraZeneca vaccine.

Cross-discipline working

Integration of social science expertise has been of clear benefit in the development and roll out of individual and population health interventions. During the COVID-19 pandemic, the CoMix study was a social contact survey, collecting data on epidemiologically relevant social interactions from two panels of 2500 individuals. The data provided direct insights into contact patterns in the community and were used to estimate changes in the viral reproduction number some weeks ahead of epidemiological data, enabling the impact of non-pharmaceutical interventions to be inferred.

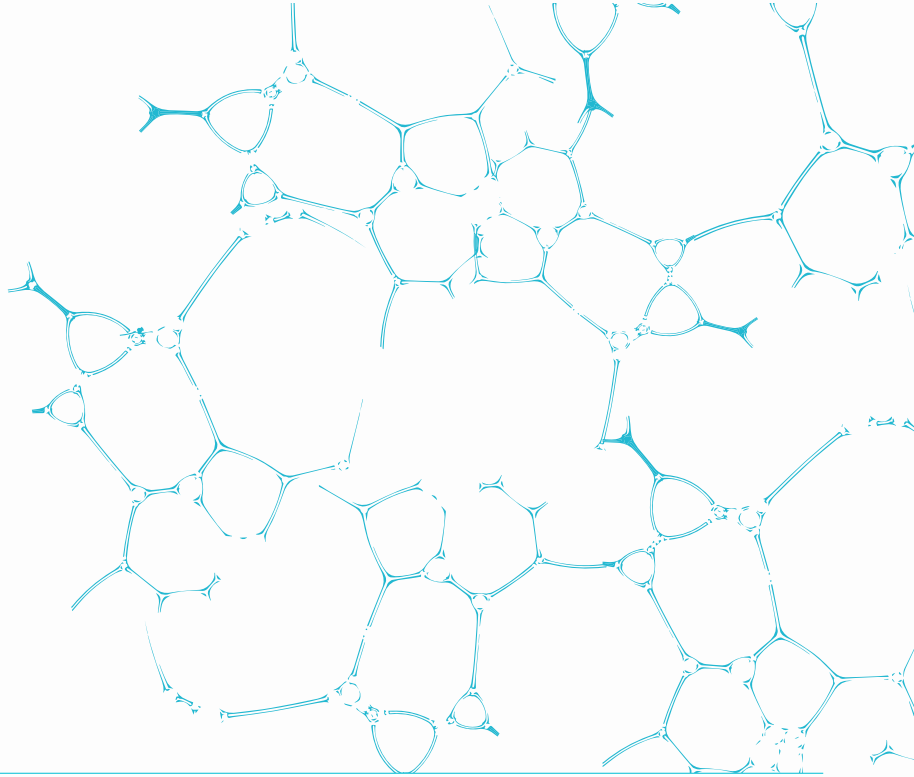
The insights provided by this study highlighted the need for better, richer integration of social sciences research to make all-population interventions more effective and efficient.

In a March 2023 interview, the MRC Director of COVID-19 Response reflected:

> *“Previous pandemic experience is that vaccines and treatments are what get you out of the hole in the end, but that the first lever deployed are non-pharmaceutical interventions (e.g. travel bans, quarantine, lockdowns, etc). In light of this, we would have benefited from a clearer focus on social sciences in the initial phases of the R&I response, including an emphasis on behavioural science as being critical for non-pharmaceutical intervention implementation and why it is important to be able to gauge both health and non-health impacts (e.g. economic, mental health, education, etc), in order to be better able to make cost-benefit analyses of the interventions.”*

It may have been helpful to have given this facet of response more consideration in early 2020. The COVID-19 pandemic highlighted a key role for social science investigations to fully consider the economic and psychological implications of policy responses that would impact public actions. This would be important for non-pharmaceutical interventions such as lockdowns, social distancing, and mask usage as well as the public engagement with vaccines.

Understanding the mechanisms of population behaviour change, and whether punitive policies such as fines for breaking COVID-19 restrictions are actually effective in practice, is important to being better prepared for the next pandemic. Social sciences may better inform how policies can be developed most effectively, and then evidenced and implemented within communities across the population.



The public health measures of the COVID-19 response, including lockdowns and other restrictions, had a significant impact on the population's mental health.

A review of the societal impacts arising from the UK COVID-19 response highlights the importance of a careful consideration of the balance of benefits and disbenefits that might arise from the necessary interventions and efforts to ameliorate the disbenefits. While investigations into differential health vulnerabilities were conducted, the assessment of the impact of COVID-19 interventions on different populations was slower to develop. For example, there was limited consideration for how general well-being in groups such as children, students, isolated individuals, and those of differing socioeconomic backgrounds or cultures would be affected by COVID-19 restrictions. Many people experienced increased levels of anxiety, depression, and stress due to the uncertainty, isolation, and economic hardships caused by the pandemic.

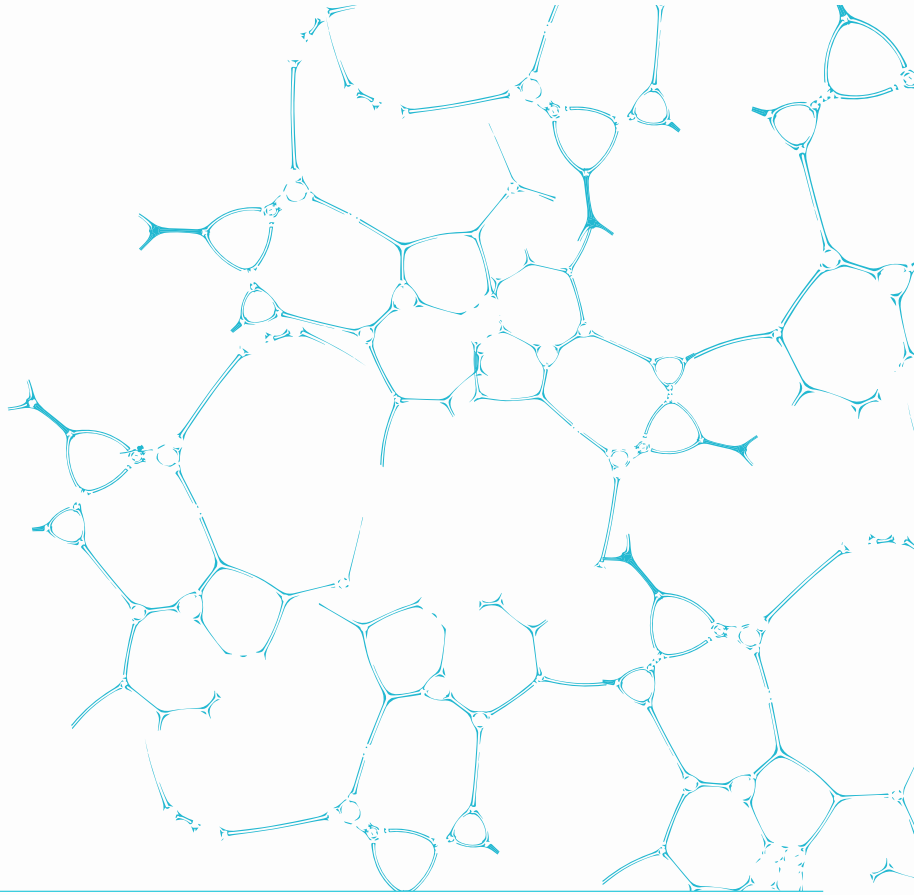
Lockdowns have particularly affected mental health by limiting social interaction and disrupting daily routines, leading to increased feelings of loneliness and isolation. Young people have been heavily affected by school closures and interruptions in education as well as the mental health issues arising from the uncertainty.

It is worth noting that research into the impact on mental health, schools and communities did take place during the COVID-19 pandemic. Several UKRI-funded population cohort studies adapted their surveys to better understand these effects within the community. For example, the ESRC funded Understanding Society (UKHLS) survey was adapted to study how the features of the neighbourhood environment moderate the mental health consequences associated with the coronavirus pandemic.

Expanding our consideration of behavioural and social impacts while addressing the biomedical threat will support a more resilient response to future pandemics.

Sustainably harnessing the community response

The recent experience highlighted the need for harnessing the academic and funding staff resource and expertise in a sustainable manner which avoids burnout. Academics took on the burden of reviewing a vast number of COVID-19 relevant funding applications, in addition to continuing their research priorities. MRC UKRI head office staff delivered these funding calls at an unprecedented pace, at significant personal well-being cost. In the future, it will be important to ensure that resource allocation and de-prioritization exercises are undertaken effectively and in a timely manner by MRC UKRI. In addition to readily available funds, MRC UKRI will continue to need experienced funding staff with the appropriate expertise to develop/ administer funding allocations/calls.



Lessons for MRC URKI

For the biomedical research landscape, continuing support will be needed to enable an agile response to the next pandemic. However, each pandemic is unique, many decisions will need to be made rapidly and, at least initially, with little evidence. With the benefit of hindsight, there are areas where lessons can be learned for facing future pandemic threats.

1. Rapid identification of the priority research questions to combat the specific epidemic or pandemic.
2. Creation of an immediately accessible fund to support the primary activities, with a mechanism in place to determine funding streams for subsequent programmes.
3. Co-ordination across government agencies and research funders.
4. Immediate surveillance of the disease-causing organism transmission and morbidity/mortality profile.
5. Maintenance of a highly dedicated staff with the necessary scientific expertise and networks across funders to manage a pandemic response. It is worth noting that with the increased efficiencies in grant management being implemented currently a reduction in staff would be possible but could reduce the potential for rapid, agile emergency response.
6. Determination of the appropriate funding mechanism, which requires a balance between:
    a. the resource-heavy burden on the research community
    b. the funding administration of open research calls ('bottom up') and the more tightly directed convening of research programmes ('top down') recognising and respecting the different characteristics of the outcomes arising from differing approaches
7. Promoting interdisciplinary approaches to understanding and coping with the pandemic threat e.g., researchers in biomedicine, behaviour, population health, psychology, climate, data analysis, engineering, clinical practice, well-being, the humanities, etc.
8. Improving, with policy makers, the facility of communicating research insights
9. Engaging readily with the public, across the full diversity of populations within the UK

While some of these learnings were acted upon during the pandemic, delays in implementation resulted in MRC UKRI head office staff and researcher stress. This in turn delayed start dates, therefore research progress, and potentially led to poorly targeted or under-resourced programmes.

The Executive Chair of MRC UKRI during the initial phase of the pandemic, Professor Fiona Watt, has said that a vital component of the strength of MRC response was:

> *"The depth of knowledge held by MRC staff on SARS and MERS (previous pandemics) which meant, from the start, we had the expertise and necessary connections with other organisations. The willingness of staff to get stuck in was also key."*

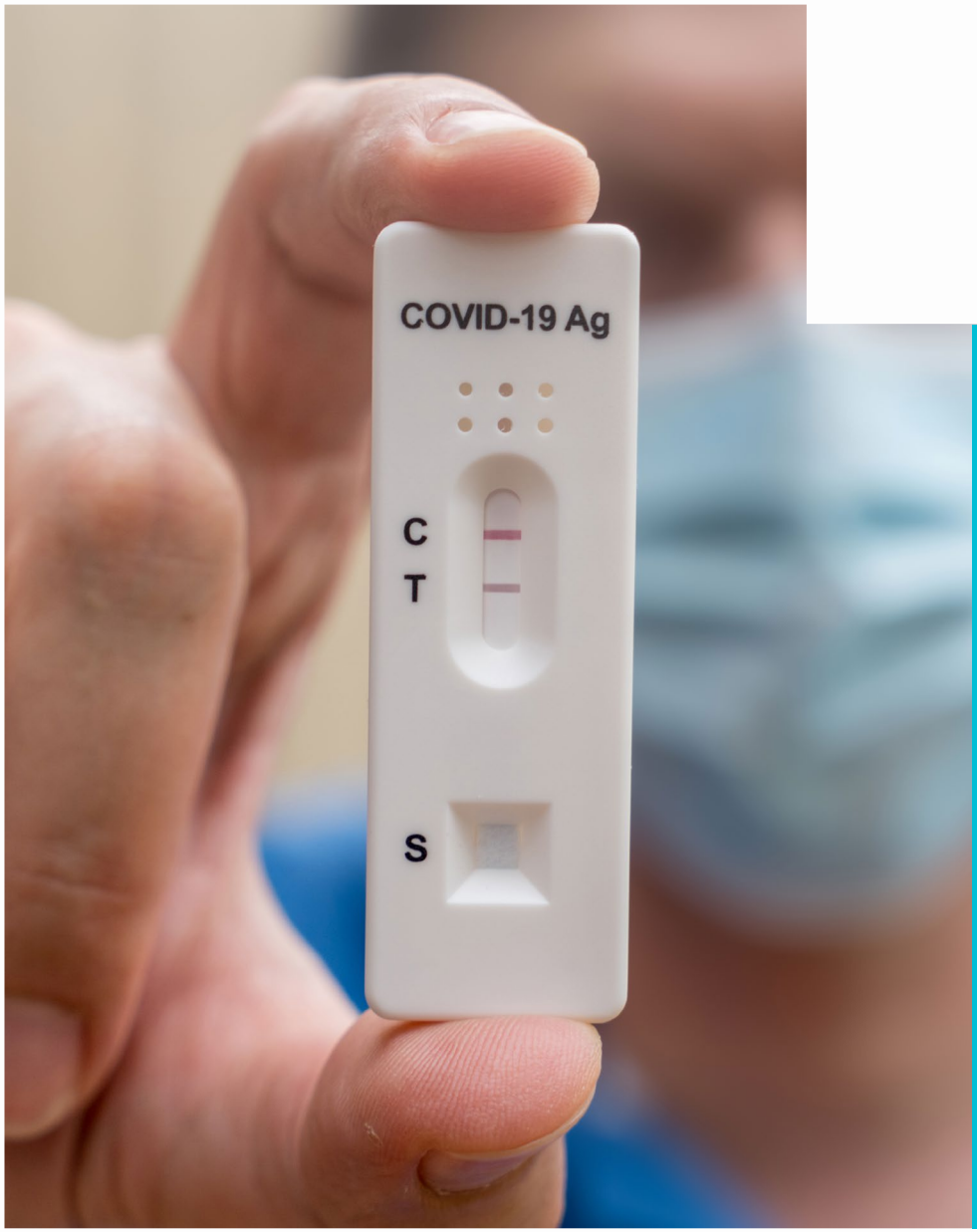
MRC UKRI Pandemic Preparedness Plans

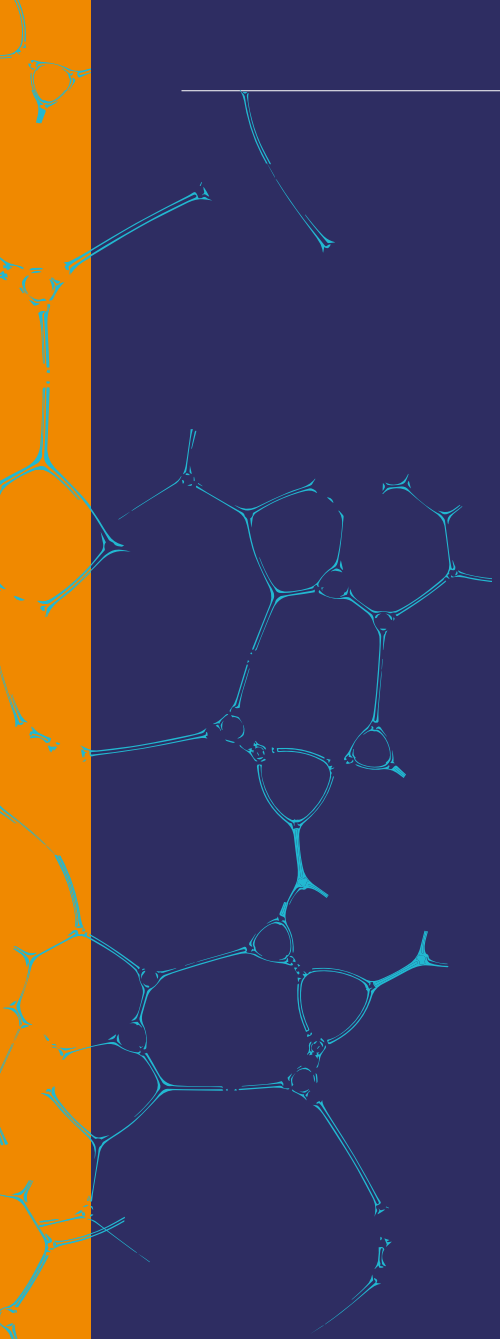
The UK data and networking legacy from the COVID-19 pandemic response, combined with continued support for the infectious disease research landscape will provide a strong base for future pandemic preparedness.

Going forward, MRC and UKRI have initiated a series of programmes to address some of the gaps identified and improve UK preparedness for the next pandemic.

MRC UKRI pandemic preparedness work has four strands:

1. Continuation of highlighting support for research on pandemic preparedness, informed by WHO road map, in the normal Board funding rounds. This highlight notice has been in place since 2016.
2. Participation in the establishment and governance of a Pandemic Preparedness Strategic Oversight Group with representation from UKHSA, DHSC, Wellcome and other UKRI Research Councils. The intent of this group is to rapidly identify when a large, coordinated approach is necessary to respond to an infectious disease threat, to escalate the response as appropriate, and to indicate the priority research questions. Negotiations to identify a rapid response funding source will be progressed by this group. Decisions of the Pandemic Preparedness Strategic Oversight Group will feed into a delivery group to action. MRC UKRI staff are also included in the delivery group.
3. A £20m flagship pan-UKRI programme investing in epidemic preparedness s in development, which builds on a UKRI-AMS-IAP workshop 'interdisciplinary research in epidemic preparedness and response' and lessons learned from the COVID-19 response. A key component of this work will be to engage expertise across the breadth of disciplines which cover the diversity of potential influences on disease emergence. *"'An interdisciplinary initiative to better understand, predict and prevent (re-) emergence of diseases of epidemic potential. Initial investments will seed interdisciplinary teams and research ideas. Larger scale programmatic awards will address research questions and establish a networked, interdisciplinary research community better prepared to address future threats".*
4. A protocol for rapid review of time sensitive research applications has been established in the MRC Infections and Immunity Board. This protocol significantly decreases the time for peer review in emergency situations. Additionally, they have maintained an urgency fund created during the pandemic to fund small sample collection or surveillance projects at speed.





Annex

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Finally, we are immensely grateful to the UK biomedical research community that stepped up during an unprecedented global emergency to contribute to a collective effort that supported the pandemic response. None of this would have been possible without their commitment and dedication.

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