Oxford University Hospitals
NHS Foundation Trust

Cover Sheet

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Title:	**Research & Development Governance and Performance Report 2020/21**

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Board Lead:	**Chief Medical Officer**
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Key Purpose:	**Performance**

Executive Summary

1. This paper presents the Oxford University Hospitals NHS Foundation Trust's (OUH) Research and Development Governance and Performance Report for 2020-21.
2. The COVID-19 pandemic presented both opportunities and challenges for clinical research at OUH during 2020-21. The majority of ongoing non-COVID-19 studies had to be paused during this period, to enable rapid expansion of COVID-19 research and to facilitate flexible redeployment of research staff and facilities to address clinical care demands.
3. The strength of the OUH partnership with the University of Oxford (OU), especially the NIHR Oxford Biomedical Research Centre (BRC) and the support of the Joint Research Office (JRO), underpinned Oxford's rapid and world-class response to the COVID-19 pandemic across a broad range of areas, which has benefitted millions of people.
4. New systems, processes and structures were implemented to ensure appropriate oversight and review of requests to set-up new studies and to resume studies that had been paused during this period. These have enabled R&D to work highly effectively with local stakeholders and some will remain in place as a positive legacy of the pandemic.
5. With the support of the Oxford Academic Health Partners (OAHP), the JRO has initiated discussions with colleagues in the other partner organisations – Oxford Brookes University and Oxford Health NHS FT – to explore opportunities to align operational processes. This should help to improve the quality and consistency of the support provided to Oxford researchers, many of whose projects span at least of two of the partner organisations. This, in turn, should increase the opportunities for our patients to benefit from participating in a greater variety of high quality research studies.

Recommendation

The Trust Board is asked to

- Receive this report and note the content.

Contents

Research & Development Governance and Performance Report 2020/21

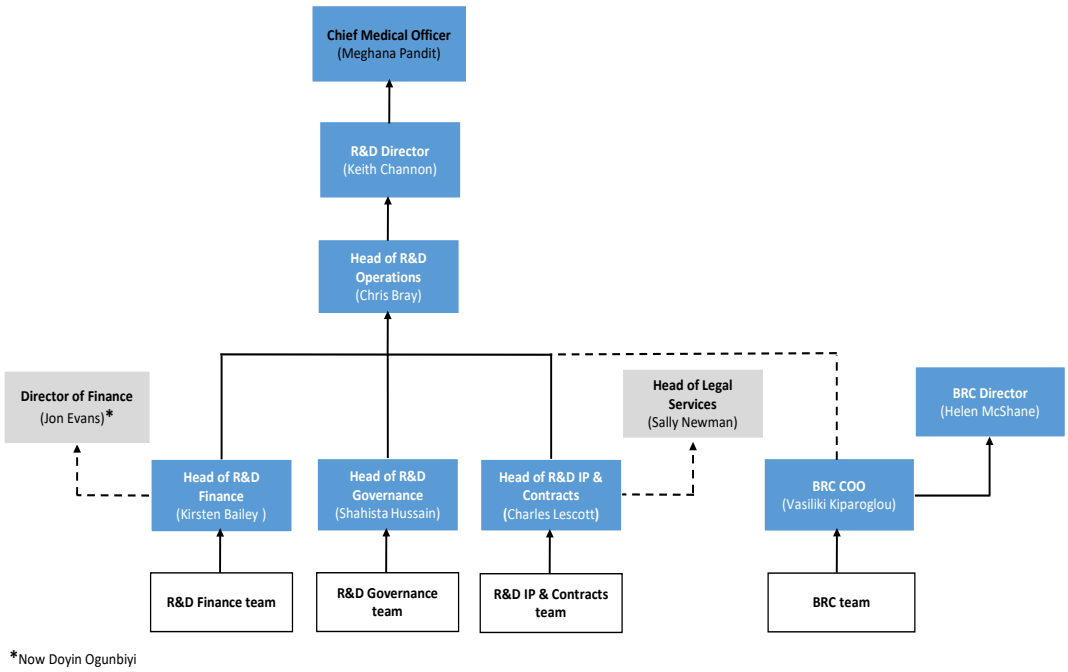
1. Introduction

Structure and Organisation

1.1. Research and Development (R&D) is part of the Corporate Division of Oxford University Hospitals NHS Foundation Trust (OUH), reporting via the Director of R&D to the Trust's Chief Medical Officer, who is an Executive member of the OUH Board.

1.2. Within R&D there are specialist teams responsible for Governance, IP and contracts, Finance and BRC management.

Figure 1. OUH R&D Organogram



1.3. In addition to this annual report to the Trust Board, R&D provides formal reports to the following committees and boards:

- Joint R&D Committee (JRDC) 4 times/year
- Trust Management Executive (TME) 3 times/year
- Strategic Partnership Board (SPB) 3 times/year

1.4. Two of these (the JRDC and SPB) are joint committees/boards between OUH and the University of Oxford (OU). The Trust's longstanding partnership with the University is fundamental to the delivery of high-

quality research at the Trust. The University benefits from access to the Trust's patients and data to further its research, meanwhile the Trust's patients and staff benefit from the contributions of world-leading academic clinicians and the advances in diagnosis and treatment that stem from world-leading research. However, the organisations' different priorities, processes and systems mean that maintaining and developing these opportunities requires careful and active management.

1.5. A programme of work has been initiated with OU's Medical Sciences Division to update the basis for joint research work involving OUH clinical data, including governance, intellectual property (IP) and infrastructure aspects.

1.6. In the coming months OUH will also be working in close partnership with OU on preparing a bid which OUH will submit in the quinquennial competition for NIHR Clinical Research Facility designation and funding (2022-27).

The Joint Research Office

1.7. The OUH R&D teams are part of the Joint Research Office (JRO), a partnership with the University of Oxford established in 2011 to help deliver medical research in Oxford by improving communication and streamlining processes through shared knowledge and expertise between the University and the Trust. There are currently around 125 staff in the JRO, divided roughly 40:60 between the Trust's R&D teams and University teams. The JRO's Co-leads (one for the Trust and one for the University) meet regularly with the Heads of the seven JRO teams to oversee and develop this important relationship. The combined efforts of the JRO's teams play a critical role in underpinning the continued success of the NIHR Oxford Biomedical Research Centre (see Section 3). The JRO is overseen by the JRDC.

1.8. Further information about the activities of the JRO, including plans to work more closely with Oxford Health NHS Foundation Trust and Oxford Brookes University, is provided in Section 7 of this report.

2. Clinical Research Activity During the COVID-19 Pandemic

2.1. The COVID-19 pandemic has dominated clinical research activity at OUH throughout 2020-21. The vast majority of ongoing non-COVID-19 studies were paused during this period, enabling COVID-19 research to expand rapidly, and to facilitate flexible redeployment of research staff and facilities to address clinical care demands. New systems and processes were put in place to assess requests to set-up new studies,

including expedited processes to set-up urgent COVID-19 studies, and to resume studies that had been paused.

2.2. The *Studyline* research portfolio management system, developed at OUH and shared by OUH and OU (as well as the other four NHS Trusts in the Thames Valley and South Midlands Local Clinical Research Network (LCRN)), has been invaluable in helping track at study level the additional processes put in place during the pandemic as well as the production of regular management reports for review by key stakeholders.

Non-COVID-19 Clinical Research

2.3. The OUH plans for managing non-COVID-19 clinical research during the pandemic (summarised below) represent a practical approach that was consistent with the Restart Framework and subsequent Guidance published by the NIHR. This included the formation of an Assessment & Prioritisation Panel (APP), whose members represented the key stakeholders locally, including Principal Investigators (PIs), research nurses, R&D, relevant Clinical Support Service Directorates, OU and the LCRN. The APP has met every 1-2 weeks since early June 2020, to enable rapid responses as well as effective decision making and communication.

Date	Stage
11 March 2020	Escalation plan announced, along with notification of Stage 1 (prepare)
17 March 2020	Stage 2 (limit research activities)
24 March 2020	Stage 3 (essential research activity only)
28 May 2020	Resumption plan announced, with notification of Stage A (enabling partial resumption of non-essential paused research)
16 September 2020	Stage B (expedited pathway for resuming non-interventional studies)
29 December 2021	• Temporary suspension of new approvals for resuming studies and for setting-up non-COVID-19 studies – necessitated by 'second wave' of OUH patients with COVID-19. Studies already approved to continue during the pandemic able to active, provided they still meet the necessary conditions, consistent with NIHR Guidance
9 March 2021	• Removal of temporary restrictions introduced on 29 December

2.4. These plans were approved by OUH's Chief Medical Officer (CMO) and Director of R&D, who were also jointly responsible for deciding when to implement each stage and for communicating this to the PIs for the ~2200 active clinical research studies hosted by OUH. The design and timing of implementation of the OUH plans were aligned with parallel processes in the University of Oxford's Medical Sciences Division, whose staff are responsible for leading and/or running a high proportion of the clinical research hosted by OUH.

2.5. Between 11 March – 27 May 2020, a 3-stage escalation plan was followed to ensure OUH could deliver COVID-19 related clinical research as quickly and efficiently as possible, whilst continuing to provide clinical care for all of our patients, including those who may be participating in research studies. The only non-COVID-19 research active during Stage 3 was 190 studies where patient care was dependent on the research protocol.

2.6. On 28 May 2020, this was succeeded by a new staged plan to support the resumption or set-up of clinical research studies that had previously been considered to be non-essential, subject to specific conditions being met.

- On moving to Stage A on 28 May 2020, PIs were able to request support to resume paused clinical research studies and to set-up new studies.
- The move to Stage B on 16 September 2020 introduced an expedited pathway for PIs to resume non-interventional studies, which are generally lower risk and less demanding in terms of OUH support.

2.7. On 29 December 2020, due to the increase in COVID-19 cases, the consequent pressures on OUH's clinical services and the Government's Tier 4 restrictions, the decision was taken to pause all new non-COVID-19 clinical research activities – both the resumption of paused studies and the set-up of new studies – in order to reduce the number of hospital visits and clinical interactions between staff and research participants. Studies already approved to continue during the pandemic could however remain active, provided they still met the necessary conditions. This temporary restriction was lifted on 9 March 2021.

2.8. Since OUH moved to Stage A on 28 May 2020, the Assessment & Prioritisation Panel has supported requests from PIs to resume activity for an additional 516 studies which had been paused on 24 March 2020 (Figure 2a). The total number of resumed non-COVID-19 clinical research studies on 31 March 2021 (the end of the period covered by this report) was 706. By the same date the APP had also supported a total of 283 requests to set-up new non-COVID-19 studies (Figure 2b).

Figure 2a. Resumption of non-COVID-19 clinical research studies – for recruitment and/or follow-up

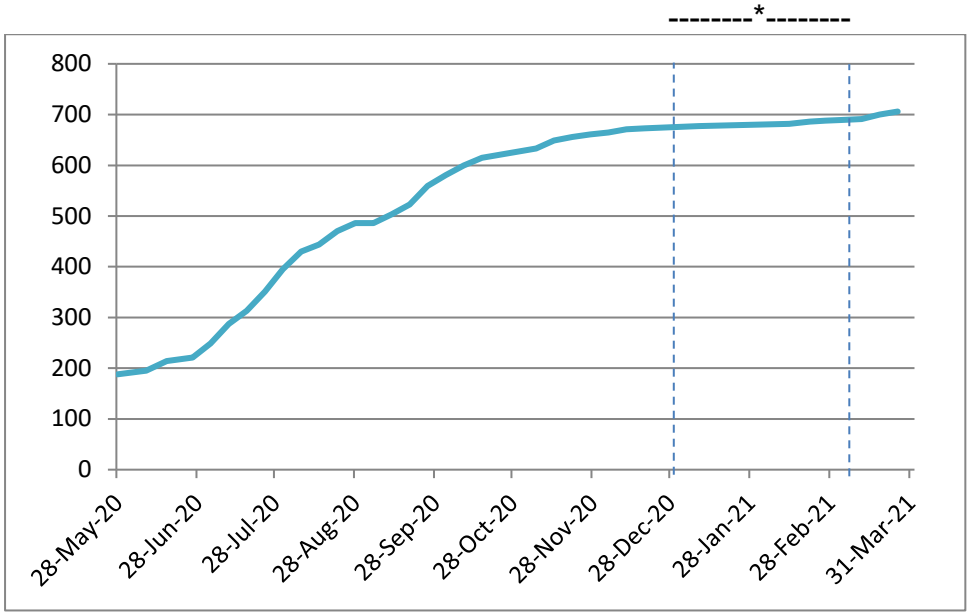
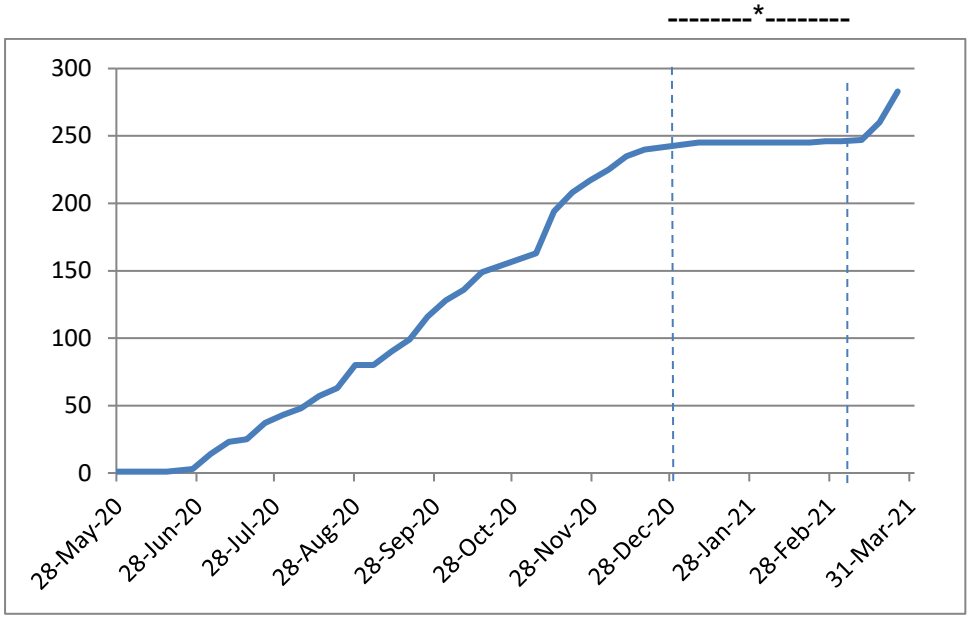


Figure 2b. New non-COVID-19 clinical research studies approved for set-up



--------*-------- all new clinical research activities were paused between 29 December 2020 – 9 March 2021

2.9. PIs' requests to resume paused studies, or to set-up new non-COVID-19 studies were initially reviewed by one of eight Local Research Oversight Groups (LROGs), which represent the most research-active

areas at OUH. Six of these LROGs were set-up from scratch after the start of Stage A. Each LROG is chaired by a PI from that area and its members include other PIs, representatives from OU and from the LCRN. The LROGs were responsible for confirming that the pre-conditions for resuming research during the pandemic have been met and that they consider the research to be a priority. Once approved by the LROG, requests were forwarded to the APP for final review and sign-off.

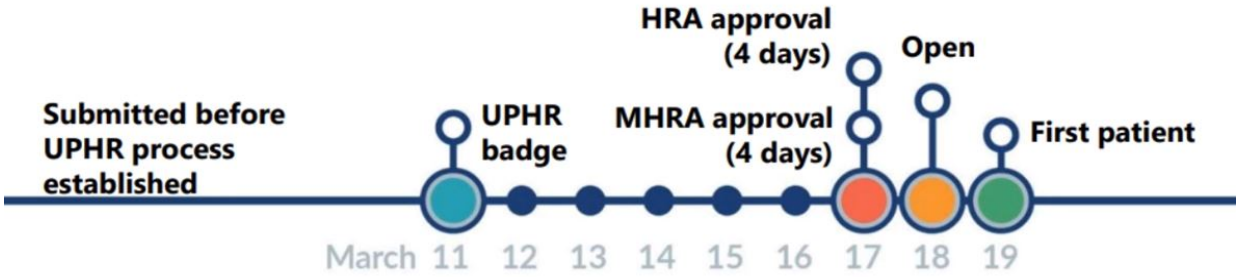
2.10. The LROGs and APP have proven to be highly effective. There is considerable enthusiasm for them to continue to operate after their role in managing research during the pandemic has ended, but their remit will be amended to enhance the model for coordinating and supporting research across OUH under more normal conditions.

COVID-19 Clinical Research

2.11. 69 COVID-19 clinical research studies had been approved to take place at OUH by the end of March 2021. 33 of these are sponsored by OU and four by OUH. 26 were on the UK Government list of Urgent Public Health (UPH) studies and 43 were 'local priority studies'. 47 were new studies, that have been set-up from scratch since March 2020. The other 22 were pre-existing studies that had been amended to address COVID-19 research questions or, in a few cases, were essential to support the delivery of COVID-19 research. Examples of these studies are included in Section 3 and a complete list is available online here.

2.12. More than 5000 participants were recruited to these studies at OUH during 2020-21 (with some patients being recruited into more than one study). This included 400 patients recruited to RECOVERY, the largest randomised controlled trial of potential COVID-19 treatments in the world, which has made a series of significant discoveries that have helped save many lives around the world during the pandemic. One of the keys to the success of RECOVERY was the speed with which it was set-up at the start of the pandemic (see Fig. 3). Joint Research Office teams played a significant role in this achievement – the study sponsor is OU and OUH was the first site to complete set-up activities (on 18 March 2020) and recruited the first participant the next day.

Figure 3. RECOVERY Trial set-up timeline



2.13. All COVID-19 studies which involve OUH patients and/or staff have been reviewed and approved by the OUH/OU COVID-19 Clinical Research Review Group (CRRG). The remit of this group is to ensure the portfolio of COVID-19 studies (including Long-COVID studies) at OUH is complementary, that resources are used efficiently and that any local priority studies do not impede OUH's commitment to running UPH studies. The CRRG has met weekly since the start of the pandemic. It is co-chaired by the Director of R&D and the Director of the NIHR Oxford BRC. Other members include research nurse managers, R&D and senior clinicians who are actively involved in research as well as patient care in the most relevant parts of OUH (ED, ICU and respiratory).

3. NIHR Oxford Biomedical Research Centre (Oxford BRC)

3.1. The 20 NIHR BRCs in England, including the Oxford BRC, have been awarded an eight-month costed extension, to 30 November 2022. The competition for the next round of BRC designation and funding, from 2022-2027, is expected to be launched in early 2021-22. Preparations for the next Oxford BRC bid are underway. The prospective themes have already been identified and an internal OUH/University of Oxford competition has been run, with PIs being asked to submit a Pre-Qualifying Questionnaire (PQQ). The Oxford BRC will be working closely with colleagues from the Oxford Health BRC, with frequent oversight from the Board of the Oxford Academic Health Partners (OAHP), to ensure their renewal bids are complementary but distinct. A series of joint workshops have been held online to facilitate and promote collaboration in specific area.

3.2. The 20 Oxford BRC themes have published 931 papers in 2020/21 in peer-reviewed journals, including *Nature*, *Nature Genetics*, *The Lancet*, *BMJ* and *New England Journal of Medicine*.

3.3. The Oxford BRC includes 21 NIHR Senior Investigators, 24 NIHR Emeritus Senior Investigators, 202 NIHR Investigators

funded/supported by the BRC, 378 NIHR Associates and 27 NIHR Academy Members with specific BRC funding.

3.4. During 2020/21 the NIHR Oxford BRC attracted more than £330m of external funding, representing a leverage ratio of nearly 14-fold. This includes over £114m from research councils; more than £40m from research charities; £43m from the DHSC and NIHR; £50m from other non-commercial sources; £58m from industry collaborative and £24m from industry contracts.

COVID-19 Research

3.5. The Oxford BRC, supported by the Joint Research Office teams, has been at the forefront of Oxford's – and the UK's - rapid response to the COVID-19 pandemic across a broad range of areas, working in close partnership with OUH and OU to deliver translational research with global impact. Twelve of the 26 OUH-hosted nationally prioritised Urgent Public Health studies were sponsored by OU and some 4,300 patients were recruited into them. In many cases, the Oxford BRC provided the enabling infrastructure that facilitated and expedited this research. Early repurposing of contingency funding for 2020-21 allowed the Oxford BRC to provide crucial COVID-19 pump-priming funding, prior to projects securing external funding. The Oxford BRC has published more than 150 articles on COVID-19 that have been cited more than 23,365 times.

3.6. COVID-19 studies supported by the Oxford BRC that have had 'World-Class Impact' (one of OUH's five Strategic Themes) include the RECOVERY trial, the Oxford Vaccine Trial and related studies, staff testing studies and Long-COVID studies. Examples of these are provided, along with summary descriptions, in Appendix A.

Other research (non-COVID-19)

3.7. Whilst COVID-19 has attracted most attention during 2020-21, there has also been a large number of other diverse research advances which have been led or enabled by the Oxford BRC. These include improvements in the diagnosis of several cancers and of Parkinson's disease, the development of a new malaria vaccine, a better understanding of the genetic basis of hypertrophic cardiomyopathy and of motor neuropathy, and the development of a machine learning algorithm that could help identify hospitalised patients requiring intensive care. Further information about these and other research studies are provided in Appendix B.

Pump-priming of new strategic initiatives

3.8. Following a competitive call overseen by the Oxford BRC Steering Committee, eight proposals, many covering a number of themes, have been awarded Research Capability Funding (RCF), to take forward key areas of research:

- Developing a research centre devoted to urgent and acute care
- The creation of a state-of-the-art imaging centre
- The creation of a new cell and gene therapy centre
- Developing a new model for neurological MRI that improving the linkage between research and clinical practice
- Expanding the number of endoscopy patients taking part in research
- Developing a nursing, midwifery and allied health professional clinical academic pathway
- Developing a new informatics infrastructure to investigate how major bleeding is treated
- Developing new cancer treatments based on 'liquid biopsies'.

Oxford BRC Director Prof Helen McShane said the funding was used "*to look ahead to where we want to be as a BRC in the coming years and pump-prime strategic new initiatives that will help us to transition to the next round of NIHR funding for BRCs*."

As part of one of these projects, the Oxford BRC has appointed four Nursing, Midwifery and Allied Health Professionals (NMAHPs) to take part in a pilot programme to develop their research skills and knowledge.

Further information about RCF is provided in Section 6 of this report.

People, Leaders and Awards

3.9. Four academics supported by the Oxford BRC were named as NIHR Senior Investigators in March 2021. They are:

- Prof Peter McCulloch, of the Nuffield Department of Surgical Science, who founded the QRSTU research group, dedicated to studies of quality and safety interventions in surgery
- Prof John Powell, of the Nuffield Department of Primary Care Health Sciences, who advises NICE on the safe adoption of surgical and other interventional procedures.
- Prof Jonathan Rees, of the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, whose research is

focused on improving orthopaedic patient outcomes and treatment delivery.

- Prof Matthew Snape, of the Department of Paediatrics and Oxford Vaccine Group, whose research focuses principally on vaccines against meningococcal, pneumococcal, influenza, RSV and Ebola virus disease.

3.10. The Oxford BRC and local NIHR partners announced the appointment of seven new Senior Research Fellows, the second cohort of emerging research leaders to receive the accolade.

Those named from the Oxford BRC were:

- Sarosh Irani, associate professor and honorary consultant neurologist specialising in autoantibody-mediated diseases of the central nervous system.
- Graham Collins, a consultant haematologist and OUH lymphoma lead. He is chair of the National Cancer Research Institute Hodgkin Lymphoma Study Group.
- Bethan Psaila, a Cancer Research UK Advanced Clinical Scientist working on megakaryocyte/platelet biology and bone marrow fibrosis in cancer.
- Helen Dakin, a senior researcher in the Health Economics Research Centre.

Public Involvement and Engagement in Research

3.11. A travelling NIHR photography exhibition showcasing ground-breaking NHS research taking place across the Thames Valley has visited Oxford city centre, Didcot, Newbury and the John Radcliffe Hospital. 'The Body Unlocked: How Research is Changing Lives' aims to engage with members of the public to encourage greater participation in research.

3.12. During the pandemic, the BRC has been unable to host its regular face-to-face public talks. It has, however, organised a number of successful public talks online:

- In June 2020, Prof Sir Martin Landray explained the background to the RECOVERY Trial and the latest developments. Watched live by 220 people, the talk has been seen over 2,000 times since.
- In July 2020, Prof Sir Andrew Pollard discussed the development of the Oxford vaccine the progress the trial was making. The talk was watched live by around 600 people and the video has subsequently been viewed nearly 5,500 times.

- On 19 November 2020, Prof Julia Hippisley-Cox spoke about her research into risk prediction models for a range of diseases, including COVID-19, and how they can be used to improve healthcare. The video has been viewed more than 500 times.
- On 16 March 2021, Prof Mona Bafadhel outlined her STOIC Study, on treatment with budesonide to reduce hospitalisation for COVID-19. The video of her talk has been viewed over 5,500 times.
- On 22 March 2021, the Oxford BRC hosted a panel discussion: Clinical academic career pathways for nurses, midwives and allied health professionals, chaired by Dr Helen Walthall, OUH's Director of Nursing and Midwifery Research and Innovation. A recording of the discussion is available here.

The BRC also worked with other parts of the local NIHR infrastructure to organise a series of online talks as part of the Oxford IF science and ideas festival. Talks cover topics such as diabetes, sleep and metabolism, endometriosis, childhood anxiety and weight loss.

3.13. The Oxford BRC held a series of PPIE webinars between November 2020 and March 2021 aimed at patient and public involvement volunteers. Topics included why qualitative research matters for healthcare; an introduction to finding and reading a health research paper; and statistics in health and medical research.

3.14. The Oxford BRC has been working with a group that includes teenagers, young adults, carers and people from black, Asian and minority ethnic communities to inform a new patient and public involvement and engagement (PPIE) strategy, with a particular focus on making health research accessible.

3.15. A PPIE lead was recruited to sit within the central BRC management team. This cross-cutting role works closely with the existing PPI staff in the Partnerships for Health, Wealth and Innovation Theme and with the patient representative on the Steering Committee, as well as liaising with individual themes to identify those where more PPI support is needed.

It was also decided that there would be a closer working relationship with the Health Economics Research Centre, whose researchers will work with themes that would benefit from a greater health economics analysis.

3.16. The local health research comms network has begun delivering regular media and social media training to researchers from partner organisations. The Oxford BRC communications manager and his

LCRN counterpart have delivered three free online sessions, attended by a total of around 50 people. Further sessions are planned throughout 2021.

3.17. Twenty-five early and mid-career researchers and health professionals have embarked on a six-month course to give them the skills to become effective leaders in the future. The Next Generation Leaders Programme is commissioned and designed by the Oxford BRC Training and Education team. This is the second such leadership programme that the Oxford BRC has organised.

Following an external audit, the Oxford BRC has again been successfully certified to the internationally recognised ISO 9001:2015 standard.

4. Research Governance

Background

4.1. Research governance refers to the framework in OUH to manage the research process from end to end, to ensure that research is undertaken in a safe, appropriate and ethical manner, in accordance with national guidance and applicable laws to ensure that maximum benefit is derived from research for public and patients. Compliance with the legislation is overseen nationally by the Health Research Authority. This includes:

4.1.1 UK Policy Framework for Health and Social Care 2017 - The UK policy framework sets out principles of good practice in the management and conduct of health and social care research that take account of legal requirements and other standards.

4.1.2 Good Clinical Practice (GCP) – GCP is a set of internationally recognised ethical and scientific quality requirements for designing, conducting, recording and reporting research that involves human participation. Compliance provides public assurance that the rights, safety and wellbeing of participants are respected and protected, and that the data generated are credible and accurate.

4.1.3 EU Directives - *The EU Clinical Trials Directive (EUCTD – 2001/20/EC)* sets out how clinical trials investigating the safety or efficacy of a medicinal product in humans must be conducted. It includes medicinal trials with healthy volunteers and small scale or pilot studies. *The Good Clinical Practice (GCP) Directive (2005/28/EC)* supplements the EUCTD, strengthening the legal basis for requiring member states to comply with the principles and guidelines of good clinical practice. After leaving the EU the UK implemented the EUCTD (which will become an EU Regulation from 2022), into domestic legislation. This is still the

case, although the UK government is consulting about making changes in the future.

4.1.4 Medicines for Human Use (Clinical Trials) Regulations - The EUCTD was implemented into UK law in May 2004, as the Medicines for Human Use (Clinical Trials) Regulations 2004, and has since been amended (2006a, 2006b, 2008).

4.1.5 Human Tissue Act - The Human Tissue Act 2004 repealed and replaced the Human Tissue Act 1961, the Anatomy Act 1984 and the Human Organ Transplants Act 1989 as they related to England and Wales, and the corresponding orders in Northern Ireland. The Human Tissue Authority regulates the removal, storage, use and disposal of human bodies, organs and tissue.

4.1.6 Declaration of Helsinki - The Declaration of Helsinki was developed by the World Medical Association as 'a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data' (Para 1, Declaration of Helsinki).

4.1.7 General Data Protection Regulation (GDPR) - Most clinical research requires the processing and/or storage of personal and sensitive information. The General Data Protection Regulation (GDPR) legislates for the control and protection of personal information relating to living individuals including both facts and opinions about the individual.

4.1.8 Mental Capacity Act - Research studies involving adults aged 16 or over who lack capacity must comply with the Mental Capacity Act 2005. This includes persons with dementia, learning disabilities, mental health problems, stroke or head injuries who may lack capacity to make certain decisions, including consenting to participate in a research study. The act does not apply to studies falling under the Clinical Trials Regulations (CTIMPs).

4.1.9 OUH Frameworks for R&D Governance, Training and Monitoring – Locally, clinical research is governed by a number of OUH Trust policies:

- Safety Reporting in Clinical Research
- Sponsorship of Clinical Research Studies
- Trust Management Approval for Clinical Research
- Monitoring and Audit of Research Studies
- Research Passports, Honorary Research Contracts and Letters of Access

- Management of Intellectual Property
- Integrity in Research
- Consent for use of clinical samples and data in research

These policies are underpinned by a suite of Standard Operating Procedures (SOPs) within R&D. Policies and SOPs are updated in response to national and local developments. The Governance team conducts a wide variety of activities, which are summarised in Sections 4.2 – 4.6. As indicated, many of these involve working in close collaboration with their OU colleagues in the JRO's Clinical Trials Research Governance team.

Oversight of Compliance and Safety

4.2. GCP Monitoring – the purpose of monitoring is to ensure that the safety of participants is assured; that the trial results will be credible and accurate and that the trial is conducted in accordance with the protocol and regulatory frameworks. The governance team undertakes monitoring visits to each OUH-sponsored trial.

4.3. Formal auditing of compliance - An audit is part of implementing quality assurance. It is independent and separate from routine monitoring or quality control functions. The purpose of an audit is to evaluate a system(s) or trial conduct and compliance with the protocol, SOPs, Good Clinical Practice (GCP), and the applicable regulatory requirements. Where OUH is hosting research with an external Sponsor, such trials may be audited by the governance team. These trials are selected through a risk-based approach.

4.4. Compliance checks - The governance team routinely undertakes assessment of compliance with various aspects of clinical research; primarily focussing on informed consent and safety reporting. The brief checks are of great value for oversight of compliance as they are less resource intensive than formal audit and so a greater number of studies can be covered.

4.5. Safety Reporting - As Sponsor, the Trust is responsible for regulatory assessment of Serious Adverse Events (SAEs). As host organisation, the Trust has a responsibility for ensuring that safety reporting processes are appropriate and complaint. The appropriate level of oversight is established by a risk assessment prior to the granting of Trust Management Approval, for both sponsored and hosted trials. All SAEs reported are reviewed by the OUH and OU Joint Trials Safety Group (TSG). The aims of this review are: to pick up any trends, such as increases in un/expected events, and take appropriate action; to identify whether additional advice or information is required from investigators; to evaluate the risk of the trial continuing and take

appropriate action where necessary, including requests for specific audits.

4.6. Consent - As part of the actions identified by the HTA's inspection of the OU's HTA Licence 12217 in 2018, the Trust has identified the need for improved consent processed to ensure that consent given by patients for the use of clinical samples and clinical data in future research studies is clearly recorded and can be retrieved, audited and modified in accordance with patients' wishes. The OUH has undertaken a review of its consent policy and is committed to implementing a digital consent process that integrates consent for both clinical procedures and for use of clinical samples and clinical data in research studies. The work for developing this capability, deployed within the OUH's EPR system, is in progress.

Training

4.7. Through collaboration with the OU Clinical Trials and Research Governance team (CTRG), training is provided to both Trust and University staff to cover all research related legislation and GCP; courses being designed for both staff new to trials and an update for experienced researchers.

4.8. For CTIMPs there are both online and face-to face GCP courses available, with an online assessment to help experienced researchers assess their need for updating their knowledge. Both are recognised by industry sponsors due to their accreditation by Transcelerate, as well as the Royal College of Physicians.

4.9. An additional training course designed specifically for clinical researchers not engaged in the conduct of a CTIMP is also provided. Informal training is provided in the form of advice and support to researchers and their teams.

4.10. Due to the COVID-19 pandemic it has not been possible to provide face-to-face CTIMP training or non-CTIMP training during the period covered by this report. However, 89 people attended training on Obtaining HRA and Ethics Approval which was delivered online and a further 481 applicants have been accepted onto the online GCP training course.

Research Passports

4.11. The Governance team processed and authorised 30 applications for Letters of Access and four Honorary Research Contracts to enable research activity to take place at OUH. Additionally, the team also validated research passports for Oxford-based researchers planning to perform research activities in other NHS Trusts.

Classification Group

4.12. There are times when it is not clear if a project should be classified as a research study, audit or service evaluation. In order to establish an authoritative and collective opinion on such projects, OUH's R&D Governance team and the Clinical Trials and Research Governance team in OU have established the Classification Group to review project outlines and give a considered opinion. The group meets at least monthly, or more often where there is high demand, and classified a total of 145 projects during the period covered by this report.

5. Research and Development Finance

5.1. The R&D Finance team provides management accounting, costing, and pre and post award financial support to researchers undertaking or applying to undertake research activity within OUH. Responsibilities include managing the finances for the Oxford BRC and the Thames Valley & South Midlands Local Clinical Research Network (LCRN), which is hosted by OUH; costing commercial and non-commercial studies within agreed timelines, and providing and paying invoices for studies once they are active.

5.2. The finances are managed for individual studies from pre-award through to post-award to ensure all costs are considered, reimbursed and accounted for in line with funders guidelines and the Trust's agreed procedures. The pre-award team also work closely with researchers and the LCRN to review the costs and activities included on grant applications to various funding bodies. This activity represents an important area which helps to secure funding opportunities for research projects across all clinical areas of OUH.

Financial Position and activities for year ending 31st March 2021

5.3. For the 2020-21 financial year, the annual income and expenditure budget for R&D was set at £55 million. This included income and expenditure of £43 million from the major NIHR grants (Oxford BRC and the LCRN) as well as other smaller NIHR grants. £12 million of income and expenditure was budgeted for commercial and non-commercial (non NIHR) research projects.

Research Funding by area	2020/21 Expenditure (£m)
NIHR Biomedical Research Centre (BRC)	23
NIHR Local Clinical Research Networks (LCRN)	16
NIHR Research Capability Funding (RCF)	3
Other NIHR grants	1
Other income (commercial & non-commercial)	12
	55

5.4. The COVID-19 pandemic had a significant impact on certain areas of R&D income in 2020-21. As a result of the reduction in overall research activity and in particular the pausing of a high proportion of studies in March 2020, there was a modest reduction in total income from the commercial and non-commercial (non-NIHR) studies at the end of the year..

5.5. The NIHR continued to make payments for the LCRN, Oxford BRC and individual grants, and these grants were fully spent to achieve a breakeven position as in previous years. Some additional funding was made available via the LCRN for the support of Vaccine studies, and due to the impact of COVID-19 on activity, a small number of NIHR grants requested some re-profiling of funds so that they can be spent in a future year.

5.6. R&D finance were involved with the expedited financial review of the Urgent Public Health COVID-19 studies throughout 2020-21. In line with national guidance, this involved the rapid review of the finances available for each trial in order to assist with setting up these trials as quickly and efficiently as possible at OUH.

5.7. Grant applications continued to be very active, with the number of grants with OUH involvement applied for this year exceeding the number of grants applied for in the previous 12 months.

5.8. Due to the pandemic, the National Contract Value Review Process for the single costing of commercial studies is still on hold pending confirmation from the NIHR when this new way of working will be implemented.

Research Capability Funding

5.9. Research Capability Funding (RCF) is awarded to research-active NHS organisations based on the amount of other NIHR income received by that organisation, including the number of NIHR Senior Investigators associated with the organisation. The purpose is to:

- Help research-active NHS organisations to act flexibly and strategically to maintain research capacity and capability.
- Support the appointment, development and retention of key staff undertaking or supporting people and patient-based research.
- Contribute towards the costs of hosting NIHR-funded or 'adopted' research that are not currently fully covered across NIHR's programmes, and that are not met in other ways.

5.10. The OUH received £3.3 million of RCF funding for 2020-21. After making an allocation to Trust overheads for research and a contribution towards the cost of hosting NIHR/DHSC-supported research, just under £1 million was awarded in support of eight BRC RCF strategic projects (see Section 3.8), and in excess of £1.2 million was awarded to support more than 40 smaller awards to support research activities across the OUH and OU.

Financial Planning 2021-22

5.11. For the Oxford BRC, 2021-22 represents the fifth and final year current designation and funding from the NIHR. The budget for this year is £22.7million. The current BRCs had been due to end in March 2022, however costed extensions have been awarded so they can continue until the end of November 2022. Preparations for the next NIHR BRC competition are underway and the R&D Finance team will be working closely with the Oxford BRC Director, COO and proposed themes to develop the budgets that will be submitted as part of the bid.

5.12. For the LCRN, funding levels for 2021-22 were confirmed by the DHSC at the end of March 2020. There was a slight increase to the overall funding for the Thames Valley and South Midlands LCRN to £17.8 million, of which the budget for OUH is £7 million. Budgets for each clinical area were considered and awarded in line with the funding allocation for the year.

5.13. Income from commercial and non-commercial studies may continue to be impacted by reduced activity due to COVID-19 in 2021-22. Therefore, forecast income in this area has been set at a prudent level compared to pre-pandemic financial years. This will be monitored closely throughout the financial year.

5.14. The RCF allocation to OUH for 2021-22 (the next financial year) is £2.3 million, the highest for any Trust. However, this is £1 million less than 2020-21 because of pre-announced changes to the funding formula designed to reduce the amount of RCF provided to Trusts in England. Applications for the new year are invited from the Trust and OU in

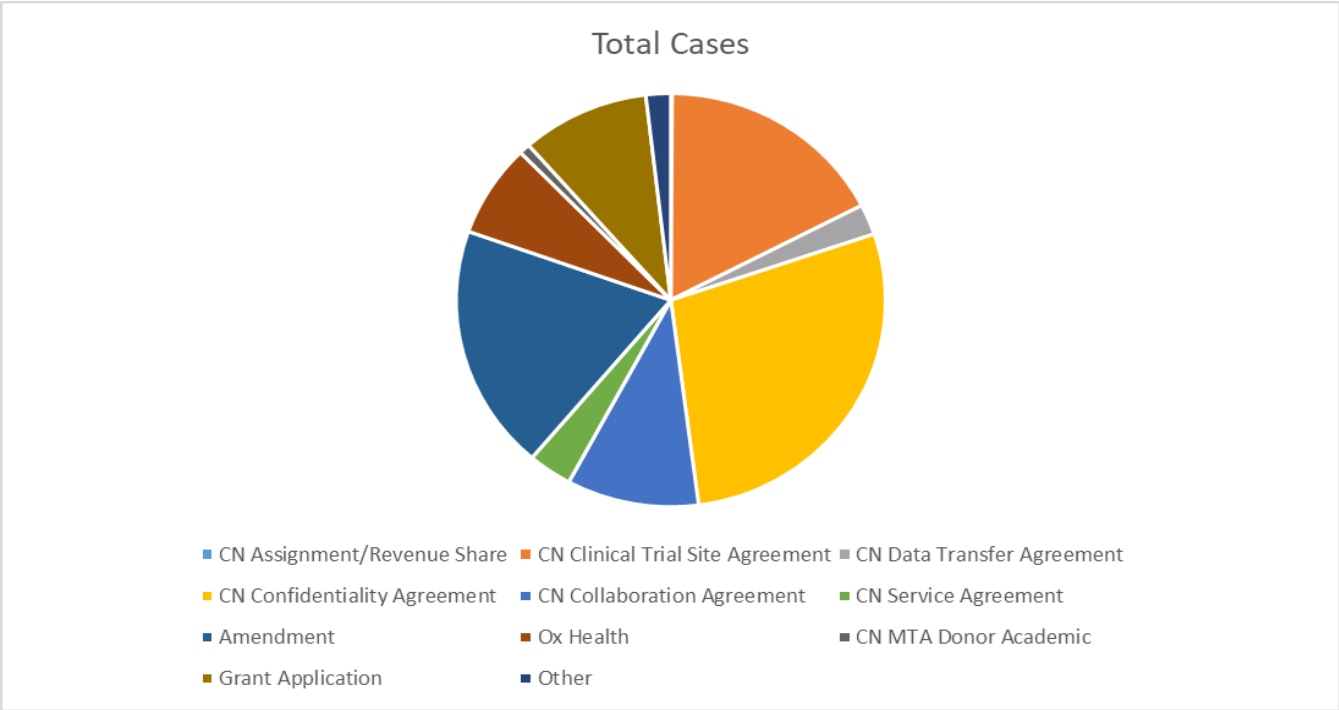
support of research activities in line with the NIHR guidance for this funding.

5.15. The expectation is that NIHR will continue to reduce, or phase out, RCF to NHS Trusts over future years. This trend will have significant implications for OUH R&D funding to meet both OUH infrastructure costs and project-specific research capacity and pump-priming.

6. Research Contracts and IP

6.1. During the year to 31 March 2021, 894 research and IP related cases were finalised on behalf of OUH. This is a 20% increase on the previous year, despite the pause in a large proportion of OUH research activities due to COVID-19. Confidentiality Disclosure Agreements (CDAs) continue to make up the largest category (271). Compared to 2019/20 there was a 24% reduction in the number of clinical trial agreements (167) and a 23% increase in the number of amendments (185), many of which were for Urgent Public Health COVID-19 studies. The team continued the contracting service it provides to Oxford Health NHS Foundation Trust, closing 71 cases over the year, an increase of 70% compared to 2019/20.

6.2. The remaining smaller categories include Material Transfer Agreements (MTAs), Service Agreements (SAs), Collaborations, Data Transfer Agreements (DTAs) and IP related agreements. A breakdown of the Research Contracts and IP team's main activities in 2020-21 is provided in Figure 4.



6.3. Together with other JRO colleagues, the Head of IP and Research Contracts has continued to refine the application of the Overarching Clinical Trial Agreement (OCTA). This agreement streamlines the financial and contractual processes for trials hosted by OUH which are dependent on the provision of services and/or staff by OU.

6.4. The Head of IP and Research Contracts has also joined JRO colleagues and other teams from OUH and OU to review and improve processes to support the smooth conduct of research which involves the sharing of data between both organisations.

7. Joint Research Office

7.1. The JRO has played a key role in enabling Oxford's world-leading response to the COVID-19 pandemic in 2020-21, described elsewhere in this report. The ability to set-up such a significant portfolio of studies, in record time, was only possible because of the established relationships between OU and OUH's research support teams and the trust they have in each other.

7.2. With the support of the Oxford Academic Health Partners (OAHP), the JRO has initiated discussions with colleagues in the partner organisations – Oxford Brookes University and Oxford Health NHS FT – to seek to align operational processes, taking full advantage of the *Studyline* research portfolio management system which is already used by all the partners. The expectation is that many improvements can be

implemented organically and in advance of a proposed new four-party Joint Working Agreement.

7.3. The first documented Terms of Reference for the JRO were approved by the Joint Research & Development Committee (JRDC) in November 2020. These will help to improve the JRDC's oversight, direction and support of the JRO. The development of the JRO will be focussed on a number of objectives, each accompanied by a clear operational plan, including deliverables. The initial JRO Objectives were discussed and approved by the JRDC in January 2021.

7.4. The JRO Away Day that had been planned for 27th April 2020 had to be cancelled, due to the pandemic. A virtual Away Day took place instead, on 2nd July 2020. This featured discussions involving senior executives and presentations from high profile COVID-19 researchers from OU and OUH. It was attended by over 100 JRO staff who gave positive feedback.

7.5. All the JRO's teams – both OUH and OU – have been working from home since mid-March 2020, due to the pandemic. They are looking forward to resuming some on-site working, but this experience is providing valuable insights into alternative models for working together as a joint office in the future. A primary physical hub for the JRO teams, in close proximity to the researchers they support, is still considered to be a fundamental requirement. However, by taking advantage of the team members' proven ability to work more flexibly, such a facility could be based around meetings rooms and hot desks. This means it would not need to be as large as would have been envisaged prior to the pandemic.

8. Recommendation

8.1. The Trust Board is asked to receive this report and note the content.

APPENDIX A. COVID-19 research supported by the Oxford BRC

9.1 Oxford vaccine trials

Work on a COVID-19 vaccine began almost as soon as reports of the virus emerged from China, and its genetic sequence was available. The Oxford BRC-supported teams at the Jenner Institute and Oxford Vaccine Group had already used ChAdOx1 vaccine technology to produce candidate vaccines against a number of pathogens, coronaviruses like MERS, and begun work on preparations for 'Disease X'. The Oxford COVID-19 vaccine team - led by Prof Dame Sarah Gilbert, Prof Sir Andrew Pollard, Prof Teresa Lambe, Dr Sandy Douglas, Prof Catherine Green and Prof Sir Adrian Hill – began the phase I trial in healthy adult volunteers in April 2020. Results of phase II – looking at the immune response to the vaccine in people of different ages – were published in July 2020, while the peer-reviewed findings of the phase 3 trial, which had found the vaccine to be safe and effective, were published on 8 December. The pooled analysis of the trial, published in the Lancet, showed the overall vaccine efficacy at least 14 days after the second dose was 70.4%. In the meantime, an agreement between the University and AstraZeneca had been reached ensuring the mass production and distribution of the vaccine.

Following approval from the MHRA on 30 December, the first doses of the vaccine were given to patients at the Churchill Hospital on 4 January 2021, just a few hundred metres from where it was developed. The first person to receive the vaccine was an 82-year-old dialysis patient, followed by Prof Pollard, the Oxford BRC investigator who has played a key role in developing the vaccine.

The vaccine trial group has continued its research and published papers on the effect of dosing interval on efficacy; the effectiveness of the vaccine against emerging variants; and the potential benefits of a third dose of the vaccine. In mid-February, the team announced it was launching the first study to assess the safety and immune responses in children and young adults of their ChAdOx1 nCoV-19 vaccine.

9.2 RECOVERY trial

The RECOVERY Trial, the world's largest randomised trial of potential COVID-19 treatments, has already identified three treatments that are effective for people hospitalised with COVID-19. The first of these was the cheap and widely available steroid dexamethasone, in June 2020. In February 2021, a second treatment, the anti-inflammatory drug tocilizumab was found to reduce the risk of death and shorten the time to discharge In COVID-19 patients with hypoxia and significant inflammation, treatment with a combination of dexamethasone and

tocilizumab reduced mortality by about one third for patients requiring simple oxygen and nearly one half for those requiring invasive mechanical ventilation. Assessment of an antiviral drug 'cocktail' developed by the US company Regeneron, initiated during 2020-21, concluded in June 2021 that this reduced deaths for hospitalised COVID-19 patients who have not mounted their own immune response. The trial is supported by the Oxford BRC and jointly led by Prof Sir Martin Landray, the BRC's Theme Lead for Clinical Informatics and Big Data, has to date recruited over 42,000 participants across 186 sites.

9.3 PRINCIPLE trial

In parallel to the RECOVERY trial, the PRINCIPLE trial is an urgent public health study looking at potential drug treatments for COVID-19 in older people in primary care. The trial is being led by the University of Oxford's Nuffield Department of Primary Care Health Sciences, which is headed by the BRC's Theme Lead for Multimorbidity, Prof Richard Hobbs.

9.4 COVID-19 infection survey

The Oxford BRC's Co-theme Lead for Antimicrobial Resistance and Modernising Microbiology, Prof Sarah Walker, is the Chief Investigator for a major ongoing government study with the Office of National Statistics to track the extent of COVID-19 infection in the UK through measuring antibodies in a representative cross-section of the population. Every month, a new group of 11,000 households is tested to find out how rates of infection and immunity are evolving, and so help inform strategies to manage the pandemic. This is particularly important as more people have been vaccinated. Survey results were able to show in Spring 2021, for example, that a single dose of the Oxford-AstraZeneca or Pfizer-BioNTech vaccines had significantly cut COVID-19 infections, and that vaccination was equally effective in people aged over 75 or with underlying health conditions. More than 740,000 people from some 220,000 households across the UK have taken part in the study.

9.5 ELISA test to detect COVID-19 antibodies

The Oxford BRC's Theme Lead for Antimicrobial Resistance and Modernising Microbiology, Prof Derrick Crook, coordinated research by the National COVID Testing Scientific Advisory Panel into developing a reliable COVID-19 antibodies test. Prof Crook's team found that an immunological assay commonly used to measure antibodies, antigens and proteins in biological samples can be specifically adapted to detect and quantifying COVID-19 antibodies - an enzyme-linked immunosorbent assay (ELISA) could be calibrated to be specific for detecting and quantifying SARS-CoV-2 (COVID-19) IgM and IgG

immunoglobulin. The assay was highly sensitive for IgG immunoglobulin from 10 days following the onset of symptoms. With support from the BRC Gastroenterology and Mucosal Immunity theme, the test was adapted into a high-throughput assay. The automated system, which can deliver 50,000 tests a day, has received CE Mark certification and been commercialised by Thermo Fisher Scientific, and is being used by Prof Walker's national COVID-19 Infection Survey.

9.6 QCOVID risk assessment tool

The Oxford BRC provided crucial early funding to the development of the QCOVID coronavirus risk prediction model, which has been used by NHS Digital to develop a population risk assessment which can inform which groups are prioritised for vaccination. The research, led by Prof Julia Hippisley-Cox from the BRC's Multimorbidity and Long-Term Conditions Theme, combines health and personal factors - like age, ethnicity and BMI, as well as certain medical conditions and treatments – to determine a person's risk from COVID-19.

Another study led by Prof Hippisley-Cox, supported by the BRC, found that ACE inhibitors and ARBs – both common treatments for high blood pressure and heart failure – are not generally linked to an increased risk of severe COVID-19 disease or an increased likelihood of being admitted to intensive care. However, the researchers did find higher risk of severe COVID-19 disease for some BAME groups.

9.7 Staff testing programme

In a major collaboration, researchers and clinicians from OU and OUH have been carrying out a comprehensive staff testing programme to give an accurate picture of the extent of COVID-19 infection in the OUH workforce. More than 13,000 people working at OUH have taken part. The research is supported by the Oxford BRC. The first key finding of the testing was the different levels of risk faced by healthcare workers dealing with the pandemic. The programme was able to

- identify and isolate staff members who had the infection before they developed symptoms, preventing them passing infection on to other staff and patients
- identify in which areas of the hospital staff were at greatest risk
- identify which staff groups were at greatest risk
- record which staff have antibodies to the virus that causes COVID-19, enabling these staff to be monitored to understand if these antibodies provide immunity against repeat infections.

Based on the findings of the testing, OUH was able to implement an infection prevention and control plan to limit transmission of the virus.

The research team, who are supported by Public Health England, also found that two doses of either the Pfizer or Oxford-AstraZeneca vaccine offer similar protection against symptomatic SARS-CoV-2 infection to that coming from natural immunity after infection. They had earlier found that individuals who have previously had COVID-19 were highly unlikely to contract the illness again for at least six months following their first infection.

9.8 PITCH study

Oxford BRC researchers are among those leading the ongoing PITCH (Protective Immunity from T cells to COVID-19 in Health workers) study, which is supported by the UK Coronavirus Immunology Consortium. In March it published findings that 99% of people generate a robust immune response against COVID-19 after just one dose of the Pfizer vaccine, and that after two doses levels of protection were even stronger. The findings supported the decision to delay the second dose and provide protection to as many higher-risk groups as possible by providing more first doses. PITCH is a sub-study of the larger SIREN study, which is looking at whether prior infection with SARS-CoV2 protects against future infection with the same virus.

9.9 Public attitudes to vaccination

Oxford BRC-supported study by OU's Health Economics Research Centre found that there was much greater consistency in public attitudes across a range of countries about who should be prioritised for COVID-19 vaccination. There was strong support in the survey for low income groups, non-health related key workers, and non-key workers unable to work from home to be prioritised.

9.10 STOIC trial

Early treatment with a common asthma treatment appears to significantly reduce the need for urgent care and hospitalisation in people with COVID-19, Oxford BRC-supported researchers have found. The STOIC study, led by Prof Mona Bafadhel, found that inhaled budesonide given to patients with COVID-19 within seven days of the onset of symptoms also reduced recovery time. The findings suggest that inhaled budesonide reduced the relative risk of requiring urgent care or hospitalisation by 90% in the 28-day study period.

9.11 Interferon beta

A new inhaled antiviral drug for COVID-19, interferon beta, has shown positive results in phase 2 trials and has now moved on to a larger

international phase 3 trial of hospitalised patients. The new treatment has been developed by UK biotech company Synairgen and the University of Southampton. The trial is supported by the NIHR Respiratory Translational Research Collaboration (R-TRC), led by the Oxford BRC's Prof Ling-Pei Ho, and locally by Profs Naj Rahman and Duncan Richards. OUH contributed 10% of the patients in the phase 2 trial.

9.12 ATOMIC trial

A clinical trial by Oxford BRC-supported researchers has confirmed that azithromycin has no clinical benefit in people with moderate COVID-19. The ATOMIC2 study, led by BRC Senior Fellow Dr Timothy Hinks, was set up to investigate if this commonly prescribed antibiotic could prevent patients with mild-to-moderate COVID-19 from getting worse. However, the findings confirmed those of other trials in showing no significant difference between patients taking azithromycin and those on standard treatment.

9.13 CATALYST Trial

As part of a UK-wide trial, OU researchers are recruiting OUH patients to investigate whether administering the anti-inflammatory drug infliximab to patients with COVID-19 can prevent progression to respiratory failure or death. The multi-arm, multi-stage CATALYST Trial, is being led from Birmingham, in collaboration with the Oxford BRC and UCL BRC. The overall aim is to guide the selection of new drug interventions for large Phase III trials in hospitalised patients.

9.14 CURIAL AI test

Oxford scientists specialising in infectious disease and clinical machine learning have developed an artificial intelligence test that can rapidly screen for COVID-19 in patients arriving in Emergency Departments. The 'CURIAL' AI test, which was supported by the Oxford BRC, assesses data routinely collected during the first hour in Emergency Departments, such as blood tests and vital signs, to determine in near real time the chance of a patient testing positive for COVID-19.

9.15 Wearable technology

Wearable technology developed by Oxford BRC-supported biomedical engineers and medical researchers was used on the COVID-19 isolation ward at the John Radcliffe Hospital to monitor patients' vital signs. The BRC's Technology and Digital Health theme, led by Profs Peter Watkinson and Lionel Tarassenko had already been developing and testing the concept of a virtual High-Dependency Unit (vHDU). The aims

of this approach are to reduce the burden on nursing staff to improve early detection when a patient's vital signs become abnormal.

9.16 Remote primary care

Prof Trisha Greenhalgh, the Oxford BRC's Theme Lead for Partnerships for Health, Wealth and Innovation, received significant government funding for a study to support GPs to deliver effective remote care to their patients during the COVID-19 pandemic. She was awarded £750,000 from the Economic and Social Research Council (ESRC) to study 'remote-by-default' care in the pandemic. This followed an article Prof Greenhalgh had published in the BMJ outlining the guiding principles on how GPs should conduct remote consultations with patients suspected of having COVID-19.

9.17 COVID Sleep study

Prof Colin Espie of the Oxford BRC's Neurological Conditions Theme was the UK lead for an international study investigating the impact of the COVID-19 pandemic on sleep and daily rhythms in adults. The International COVID-19 Sleep Study (ICOSS) looked at changes in sleep quality in relation to social confinement such as lockdowns or self-isolation, risk of exposure to the virus, and psychological symptoms such as anxiety, depression and post-traumatic stress.

9.18 Haematology

As part of the international REMAP-CAP trial, researchers from the BRC's Haematology theme launched the first national randomised trial looks at potential anti-coagulant therapy for patients with thrombotic complications of COVID-19 infection. The aim of the study, led by Prof Simon Stanworth, is to test whether full therapeutic anticoagulation with heparin improves outcomes in patients with severe COVID-19 infection.

Prof Stanworth also led a study looking at how blood transfusion services have coped during the COVID-19 pandemic. The aim of the study was to develop guidance on transfusion practice and blood supply in times of potential or actual shortage.

9.19 Long COVID studies

A study looking at the longer-term impact of COVID-19 has found that at two to three months after the onset of the disease, 64% of patients continued to experience breathlessness and 55% reported fatigue. The C-MORE study researchers said MRI scans revealed abnormalities in the lungs of 60% of participants, in the hearts of 26%, in the livers of 10% and in the kidneys of 29% of patients. The was the first peer-reviewed paper to be published on the impact of COVID-19 on multiple organs using imaging. The study is supported by the Oxford BRC and the Oxford

Health BRC, as well as the BHF Oxford Centre for Research Excellence and Wellcome Trust. The study is a key part of the national PHOSP-COVID platform, led by the University of Leicester, which itself published its first findings in late March – that a majority of survivors who left hospital following COVID-19 had not fully recovered five months after discharge.

Another Oxford BRC-backed study looking at long-term damage caused by COVID-19 is the C-MORE-POST study. Using hyperpolarised xenon MRI (XeMRI) scans, Prof Fergus Gleeson's team, with colleagues in Sheffield, identified persistent damage to the lungs of hospitalised COVID-19 patients at least three months after they were discharged. This damage was not detected by routine CT scans and clinical tests. Prof Gleeson is now expanding his research to people who were not hospitalised but who have been referred to long COVID clinics.

Another national study involving Oxford researchers is investigating the long-term effects of lung inflammation and scarring from COVID-19. The UK Interstitial Lung Disease Long-COVID19 (UKILD-Long COVID) study, launched with £2 million of funding from UK Research and Innovation (UKRI), is investigating whether post-COVID-19 lung damage will improve or worsen over time, how long it will last, and the best strategies for developing treatments.

Oxford researchers from the BRC's cardiovascular and imaging themes are playing a key role in the multi-centre COVID-HEART study, a partnership involving the NIHR and BHF. The study aims to assess the demographic, multi-morbidity and genetic impact on cardiac involvement and its recovery

APPENDIX B. Other (non-COVID-19) research supported by the Oxford BRC

10.1 Advances in cancer

OUH ovarian cancer specialist Professor Ahmed Ahmed published a paper outlining a new classification which categorises different subtypes of cells and determines which ones can lead to more severe cancer outcomes. In 2020, using single cell RNA sequencing, Prof Ahmed's team identified new types of fallopian tube cells that are origin for the majority of ovarian cancers. His approach, dubbed the 'Oxford Classic' (Oxford Classification of Carcinoma of the Ovary), will provide more accurate predictions for disease outcome in patients, as well as helping researchers to develop targeted therapies for each type of cancer. Prof Ahmed's work is supported by the Oxford BRC.

University of Oxford researchers have developed new clinical prediction models for use in primary care with the aim of accelerating the diagnosis of myeloma. Earlier diagnosis improves survival rates, but delays in myeloma diagnosis are common, in part because symptoms, such as back pain, are non-specific and relatively common in people without cancer. The research team had previously identified certain abnormalities in blood test results that indicate a higher risk of myeloma. Now they have developed new clinical prediction models that incorporate both symptoms and blood test results.

Non-invasive home-based tests that detect blood in patient stool samples offer an accurate and appropriate triaging method for GPs, according to an OU study, which has already informed a redesign of the colorectal cancer pathway at OUH. The development could prompt primary care services nationally to reprioritise symptomatic patients for urgent referral to hospital-based investigation of colorectal cancer. The study, supported by the Oxford BRC, is the first to robustly demonstrate that a positive test of 10 micrograms or more of haemoglobin per gram of sample, as recommended by NICE as a threshold for urgent referral, would detect 91% of underlying cancers in the one in 10 people with symptoms who receive a positive test.

10.2 Malaria vaccine progress

Researchers from the Jenner Institute, supported by the Oxford BRC, have reported that a malaria vaccine they are developing is the first to meet the World Health Organization's goal of at least 75% efficacy. The findings of the Phase IIb randomised, controlled, double-blind trial show the candidate vaccine, R21/Matrix-M, demonstrated 77% efficacy over 12 months of follow-up with no serious adverse events. The trial was conducted in Burkina Faso with 450 participants, aged 5-17 months. Recruitment has now started for a Phase III licensure trial to assess

large-scale safety and efficacy in 4,800 children across four African countries.

10.3 Breakthrough for genetic heart condition

A team led by the Oxford BRC Theme Lead for Genomic Medicine Prof Hugh Watkins has discovered a new type of genetic change in the DNA of people with the inherited heart condition hypertrophic cardiomyopathy (HCM), the leading cause of sudden cardiac death in young people. Until now, cardiologists had been unable to explain why the condition was so varied amongst family members who have the same rare mutation and why some people without these mutations still go on to develop HCM. The discovery, the biggest advance in our knowledge of the genetic basis of the disease in 25 years, will help doctors better predict which family members need to be monitored for the condition and which can be ruled out from further tests or treatment.

10.4 Ancient gene mutation found

Geneticists and clinicians from the University of Oxford and University College London have found that a novel disease gene is responsible for a rare form of hereditary motor neuropathy (HMN). The research was supported by the Oxford BRC. Ten participants from the 100,000 Genomes Project were identified as having VWA1 gene mutations – an unusually high number for a newly-described genetic condition. It is believed that one in 500 people of European origin carry the primary gene mutation, and around one in a million are affected by the condition.

10.5 Spotting deterioration

Oxford researchers have developed a machine learning algorithm that could significantly improve clinicians' ability to identify hospitalised patients whose condition is deteriorating to the extent that they need intensive care. The HAVEN system was developed as part of a collaboration between OU's Institute of Biomedical Engineering and the Nuffield Department of Clinical Neurosciences, with support from the Oxford BRC. The system combines patients' vital signs – such as blood pressure, heart rate and temperature – with their blood test results, comorbidities and frailty into a single risk score, giving a more precise indication of which patients are deteriorating when compared with previously published scores.

10.6 Cartography collaboration

OU has entered into the strategic 'Cartography collaboration' with Janssen Biotech to develop a cellular map of genes and proteins implicated across a range of immune-mediated inflammatory disorders

and to develop relevant new therapies. The work of this collaboration overlaps considerably with and complements the interdisciplinary research being carried out by the Oxford BRC's Gastroenterology and Mucosal Immunity Theme.

Researchers at the MRC-Human Immunology Unit, Weatherall Institute of Molecular Medicine, have used an 'atlas' of immune cells in the human colon to find evidence of the role of CD8 T cells in inflammatory bowel disease (IBD). The findings could lead to a better understanding of how cells behave and interact in people with IBD, and could pave the way for more targeted treatments for this chronic disorder. The study was supported by the Oxford BRC.

10.7 Early detection of Parkinson's disease

Research supported by the Oxford BRC has led to the development of a new way to test for Parkinson's disease before the main symptoms occur, potentially allowing clinicians to identify patients who would benefit from precision therapies that are currently at clinical trial stage. The study was led by George Tofaris at the Nuffield Department of Clinical Neurosciences.

10.8 STEP CHANGE

A three-year European Commission project to fund citizen science projects, including one run by the NIHR Oxford BRC to research metabolism, has got under way. The €2.2m STEP CHANGE project will develop five citizen science initiatives in the areas of energy, environment, health and infectious diseases. The Oxford BRC, which has received more than €270,000 as part of the initiative, and the Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM) will carry out research into the role of steroid hormones in the treatment of non-alcoholic fatty liver disease (NAFLD), obesity and type 2 diabetes. It is the first study to use a citizen science approach in this area.

10.9 Gender equity research

Researchers in the Oxford BRC's core management team have conducted a number of studies around gender equity in research. They found, for example, that linking research funding to Athena SWAN action plans was associated with a rise in the number of women in mid-level leadership positions and the proportion of funding going to women. They have conducted research into the proportion of women authoring the BRC's scientific papers, and have developed a tool to rank and identify new gender equity markers specific to NIHR BRCs.