Oxford University Hospitals
NHS Foundation Trust

Trust Board Meeting in Public: Wednesday 13 July 2022

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Title:	**Research & Development Governance and Performance Report 2021-22**

Status:	**For Information**
History:	**TME 30 July 2022; Annual Reporting**

Board Lead:	**Interim Chief Medical Officer**
Author:	**Dr Chris Bray, OUH Head of R&D Operations**
	Professor Adrian Banning, OUH Director of R&D
Confidential:	**No**
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 2021-21.
2. OUH is one of the largest and most productive research-active university hospital NHS Trusts nationally. The University of Oxford benefits from access to OUH's patients, data and other resources to further its research, meanwhile the Trust's patients and staff benefit from the contributions of world-leading clinical academics and the advances in diagnosis and treatment that stem from their research.
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), has continued to underpin Oxford's achievements during the COVID-19 pandemic, maintaining its research leadership in many aspects of COVID-19, and delivering other high-impact research as the pandemic has waned.
4. A thorough review of OUH's portfolio has identified a large number of studies judged unlikely to be able to deliver due to the impact of the COVID-19 pandemic and which were therefore closed. OUH currently hosts around 1500 active clinical research studies.
5. In common with other NHS Trusts nationally, OUH experienced an unprecedented demand to set-up new research studies in the summer of 2021, as pandemic restrictions were eased. A renewed focus on streamlining set-up activities, coupled with researcher-led prioritisation of new studies for set-up, has already resulted in a 60% increase in set-up capacity compared to the period before the pandemic.
6. With the support of the Oxford Academic Health Partners (OAHP), which includes senior executives from both Universities and both NHS Trusts in Oxford, the JRO has expanded to include research support teams from Oxford Brookes University and Oxford Health NHS FT. Opportunities to align operational processes across the partnership will be identified 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 patients receiving care in Oxford – and beyond – to benefit from participating in a greater variety of high quality research studies.

Recommendation

The Trust Board is asked to

- Receive this report for information.

Contents

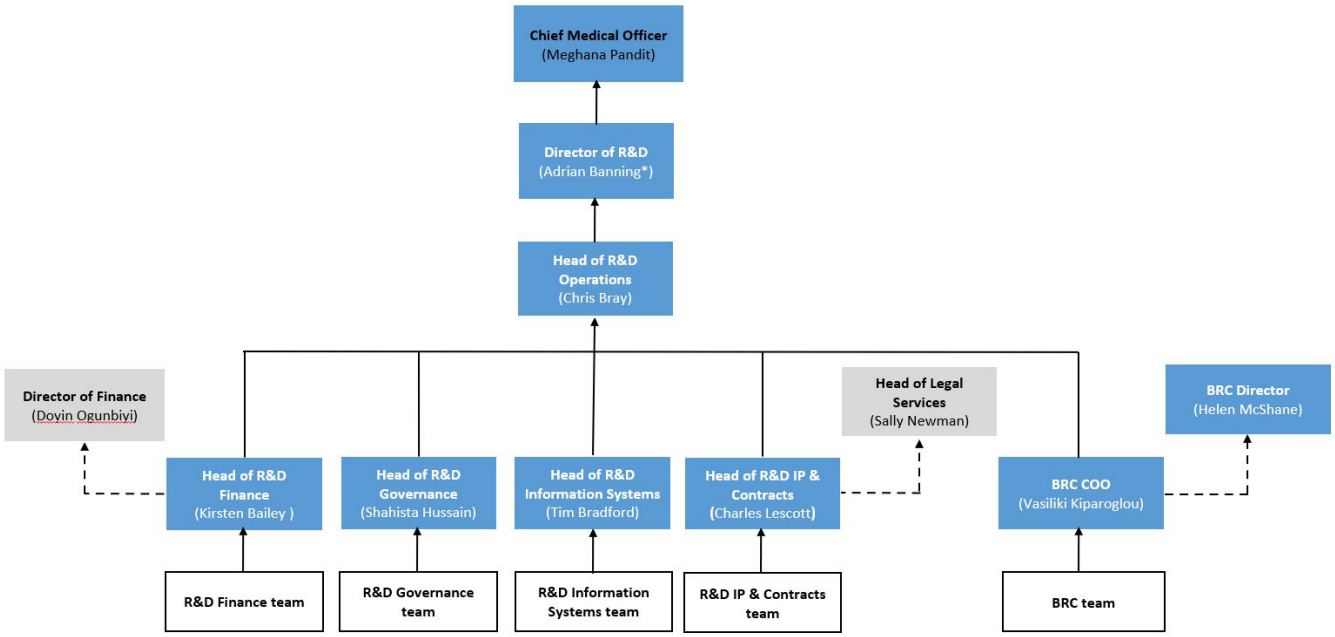
Research & Development Governance and Performance Report 2021-22

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).



*Keith Channon was Director of R&D until 31 March 2022.

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, data and other resources to further its research, meanwhile the Trust's patients and staff benefit from the contributions of world-leading clinical academics and the advances in diagnosis and treatment that stem from their research. However, the organisations' different priorities, processes and systems mean that maintaining and developing these opportunities requires careful and active management.

The Joint Research Office

1.5. 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. The JRO is overseen by the JRDC and the combined efforts of its teams have played a critical role in underpinning the continued success of the NIHR Oxford Biomedical Research Centre (see Section 5).

1.6. Further information about the activities of the JRO, including its recent expansion to become 'the Oxford JRO', by incorporating research support teams from Oxford Health NHS Foundation Trust and Oxford Brookes University, is provided in Section 10 of this report.

2. Clinical Research Activity During the COVID-19 Pandemic

2.1. After dominating clinical research activity at OUH throughout 2020-21, the impact of the COVID-19 pandemic started to ease during 2021-22. This resulted in a significant pent-up demand to set-up new (non-COVID studies) across all Trusts in England and has been a particular focus of attention at OUH.

2.2. The *Studyline* research portfolio management system, developed at OUH and shared by OUH and the University of Oxford (OU), (as well as the other five NHS Trusts in the Thames Valley and South Midlands Local Clinical Research Network (LCRN)), has continued to be 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 represented 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 maintain effective oversight, enable rapid responses as well as timely decision making and communication.

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 ~2000 active clinical research studies hosted by OUH. The design and timing of implementation of the OUH plans were aligned with parallel processes in OU'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 24 March-27 May 2020, all OUH clinical research activity was paused, except for studies directly related to COVID-19 and those where patient care is dependent on the research protocol. Since 28 May 2020 a staged resumption plan came into effect, enabling PIs to request support to resume clinical research studies that had been paused, and to set-up new studies, subject to specific conditions being met.

2.6. PIs' requests to resume paused studies, or to set-up new non-COVID-19 studies were reviewed by one of ten Local Research Oversight Groups (LROGs), each representing one or more areas of research activity at OUH. All but two of these LROGs were set-up from scratch. 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 safely during the pandemic have been met and that they consider the research to be a priority. Each LROG is also represented on the APP.

2.7. During summer 2021, OUH R&D led a comprehensive review of all the remaining paused OUH-hosted non-COVID-19 studies. At the conclusion of this review in September 2021, of the 2000 studies paused in March 2020, 1100 had been resumed. The remainder were closed – around half were found to have completed activities prior to the pandemic and the other half were closed because they were judged unlikely to be able to deliver. More than 400 new non-COVID-19 studies have also been opened to recruitment since March 2020. The net effect of these changes is that OUH currently hosts a total of ~1500 active clinical research studies (see Section 3). As a result of this review, OUH is ahead of the field with regard to adopting recent guidance from the DHSC and NHSE, and well placed to sustain and develop a diverse

portfolio of clinical research studies that is relevant to our patients and will have real impact.

2.8. In response to a surge in demand for setting up new studies at OUH during summer 2021, a range of measures taken across the R&D and clinical trials pharmacy teams has boosted set-up capacity by 60% (from ~25 to ~40/month). This has resulted in a significant and steady reduction in the total number of studies in the set-up pipeline at OUH, from a peak of 243 in August 2021, to 178 in March 2022.

2.9. The LROGs established during the pandemic are playing a key role in prioritising new studies for set-up and since February 2022 have added further value by only putting a study forward as a priority if the PI has provided assurances that it is ready for set-up activities to proceed now.

2.10. The LROGs and APP have proven to be highly effective. They have adapted as circumstances have changed since the start of the pandemic and the role they play as a link between PIs across OUH and R&D, both ways, is widely recognised and appreciated. This new structure should be of value as part of the system to help coordinate and support research across OUH as we return to more normal conditions.

COVID-19 Clinical Research

2.11. A total of 88 COVID-19 clinical research studies had been approved to take place at OUH. Four of these are sponsored by OUH and 39 by OUH. 30 were on the UK Government list of Urgent Public Health (UPH) studies. 67 were new studies, that have been set-up from scratch since March 2020. The other 21 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 Appendix A and a complete list is available online here.

2.12. More than 12,000 participants have been recruited to COVID-19 studies at OUH (with some patients being recruited into more than one study).

2.13. For two years from April 2020, 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 CRRG 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 every 1-2 weeks since the start of the pandemic, 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). Studies approved by the CRRG were, until late 2021, automatically prioritised for setup, ahead of non-COVID-19 studies.

2.14. The decision was taken (by its members) to disband CRRG in March 2022. From April 2022, proposals to set-up new COVID-19 studies will follow the same pathway as any other type of study, i.e. they will be reviewed and prioritised by the relevant LROG.

3. Clinical Research Activity

Overall activity

3.1. OUH is one of the largest research-active university hospital trusts nationally, by any measure. Clinical research expands opportunities for the development of OUH's staff, as well as empowering and engaging the patients we care for and there is increasing evidence that it should improve outcomes, even for those who do not participate directly in research.

3.2. Research features prominently in OUH's strategy for 2020-25. It is included, along with the related activities of education and innovation, in the World-Class Impact strategic theme, through which OUH can continue its global impact in improving health and care. Members of the JRO – from OU as well as OUH – were actively engaged in discussions during the development of the strategy.

3.3. Following the review described in Section 2.7. the number of active clinical research studies hosted by OUH has decreased for the first time and currently stands at 1493, compared with just over 2000 at the start of the COVID-19 pandemic in 2020. Of these studies, 1216 (81%) are on the NIHR portfolio, with 483 of them recruiting participants in 2021-22. The NIHR's national league table shows only one Trust in England recruited participants into more portfolio studies. OUH's recruitment to portfolio studies in 2021-22 totalled 17,499 participants, of whom 918 have been recruited to commercial contract studies – only two Trusts in England recruited more.

3.4. The high volume and variety of clinical research hosted by OUH has important benefits for our patients, and major reputational and other benefits for the Trust. OUH-UO clinical research has had major impacts on patient care in the Oxford region, the NHS nationally, and internationally, in areas as diverse as infection control, vaccines, genomics, imaging, digital health and artificial intelligence, cancer, respiratory, diabetes, surgical innovations and many others. These

advances have established new diagnostics and treatments, changed clinical guidelines for many conditions and have led to multiple spin-out companies.

3.5. These studies all have to be conducted in accordance with international and national regulations, as well as Trust frameworks (see Section 7).

Hosted and sponsored active clinical research studies

3.6. The total number of studies can be broken down into those that are **Hosted** (i.e. OUH is the NHS organisation providing the clinical environment, capabilities and patient care) or **Sponsored** (i.e. OUH takes legal responsibility for the conduct of the study, as well as hosting it) by the Trust (see Table 1).

Table 1. Breakdown of hosted and sponsored active research studies

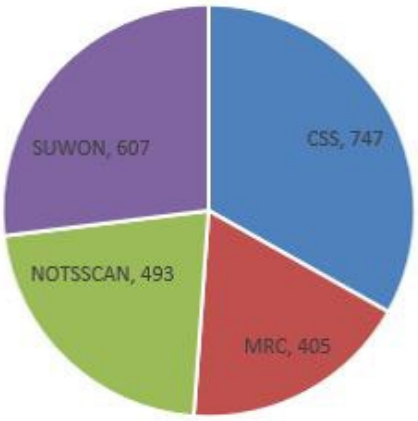
Study type		Hosted	Sponsored	Total
Interventional	Clinical trial of an investigational medicinal product	520	3	523
	Clinical investigation or other study of a medical device	67	7	74
	Other clinical trial	179	16	195
Sub-total		766	26	792
Non-interventional	Other study	639	62	701
Total		1405	88	1493

3.7. The majority of OUH active clinical research studies are hosted for external Sponsors. OU is the largest Sponsor – responsible for 390 (26% of the total). Although the number of OUH-sponsored studies is relatively small, the R&D teams have to commit a significant amount of resource to ensure the Trust's obligations as sponsor are met.

3.8. The split of interventional:non-interventional active studies at OUH is roughly 55:45.

Research activity by OUH Division

3.9. Figure 2 presents a breakdown of the 1493 studies of all types hosted by the Trust in 2021-22, according to the Clinical Divisions that are actively involved. Many studies involve more than one Division, with the Clinical Support Services Division (CSS) being involved in the largest number – usually providing pharmacy, radiology and imaging, or pathology and laboratory services to studies recruiting patients under the care of one of the other Divisions.



CSS: Clinical Support Services
MRC: Medicine, Rehabilitation and Cardiac
NOTSSCAN: Neurosciences, Orthopaedics, Trauma, Specialist Surgery, Children's and Neonates
SUWON: Surgery, Women's and Oncology

Figure 2. Active research studies by Division

Substantial and non-substantial amendments

3.10. In addition to setting-up new studies, amendments to active studies represent a significant amount of activity for the Trust's R&D teams. All amendments are reviewed by the R&D Governance team, who will reassess capacity and capability, passing them to the R&D Finance and/or Contracts teams as appropriate. This represents a significant amount of activity, with a total of 2039 substantial and non-substantial amendments reviewed during the past year (see Table 2).

Table 2. Amendment Activity

	Apr-Jun 2021	Jul-Sep 2021	Oct-Dec 2021	Jan-Mar 2022	Total 2021-22
Substantial amendments	294	296	309	338	1237
Non-substantial amendments	163	234	226	179	802
Total	457	530	535	517	2039

4. Clinical Research Performance

Background

4.1. The requirement for Trusts to measure and publish performance in initiating and delivering clinical research has been specified in the NHS standard contract since 1 October 2018. The NIHR continues to require providers of NHS services in receipt of NIHR funding to measure and publish their performance in initiating and delivering clinical research

4.2. The requirement for Trusts to submit performance metrics was suspended by the NIHR temporarily during the height of the COVID-19 pandemic, but the normal quarterly cycle of reporting has since been resumed.

Summary of performance for 2021-22 submitted to the NIHR
Data Completion

4.3. Quarterly updates of OUH performance data during 2021-22 were submitted to the NIHR on time. These data have also been published by the Trust in a readily accessible page on its website (http://www.ouh.nhs.uk/about/publications/default.aspx#research), as required by the NIHR.

Metric 1: Performance in Initiating Research
(for all interventional trials confirmed during the previous 12 months)

4.4. A total of 213 new interventional trials were confirmed at OUH during 2021-22. This is more than any other NHS Trust in England. It is also three times more than the number at OUH in 2020-21 and nearly double the number in 2019-20 ('pre-pandemic'). The number of confirmed OUH interventional trials reported every quarter during the last three years is represented by the columns in Figure 3.

4.5. The key metric used by the NIHR to monitor and to compare Trusts' performance in initiating research is the mean interval (in calendar days) between Date Site Selected (DSS) and First Participant Recruited (FPR). DSS is defined as the "*Date when the sponsor has provided the minimum defined documents to enable site to commence arrangement and/or confirmation of local capacity and capability as applicable representing that the site has been selected to take part in the study*". The mean DSS-FPR interval reported for OUH in Q4 2022, which covers the full year 2021-22, represented by the line in Figure 3, was 84 days. This placed OUH 4th in 'League 1', which consists of the 16 Trusts which confirmed at least 90 new interventional trials during this period.

4.6. The mean DSS-FPR interval of 84 days at OUH in Q4 2021-22 is only slightly higher than it was before the pandemic (79 days in Q4 2019-20).

This is despite the number of confirmed new interventional trials in 2021-22 nearly doubling in this time. This has been possible because of the new measures to streamline study set-up, outlined in Section 2.8.

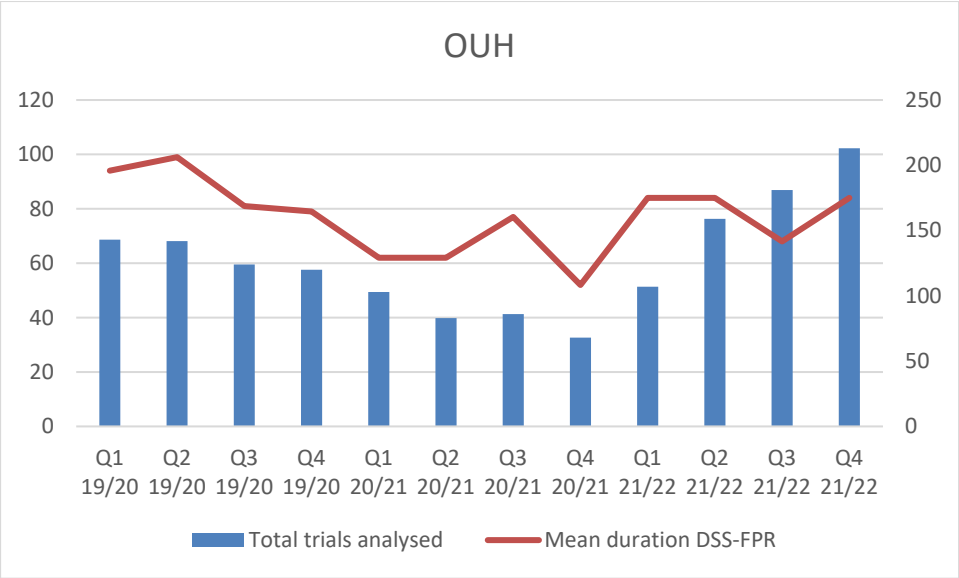


Figure 3. Quarterly interventional trial initiation metrics for OUH

4.7. Comparing the OUH data to that released by the NIHR for all Trusts in England (Figure 4), it is evident that i) OUH's mean DSS-FPR interval in 2021-22 is 11 days less than the average for all Trusts (84 compared to 95) and ii) whilst overall site initiation activity in 2021-22 has returned to pre-pandemic levels across England, at OUH it has almost doubled.

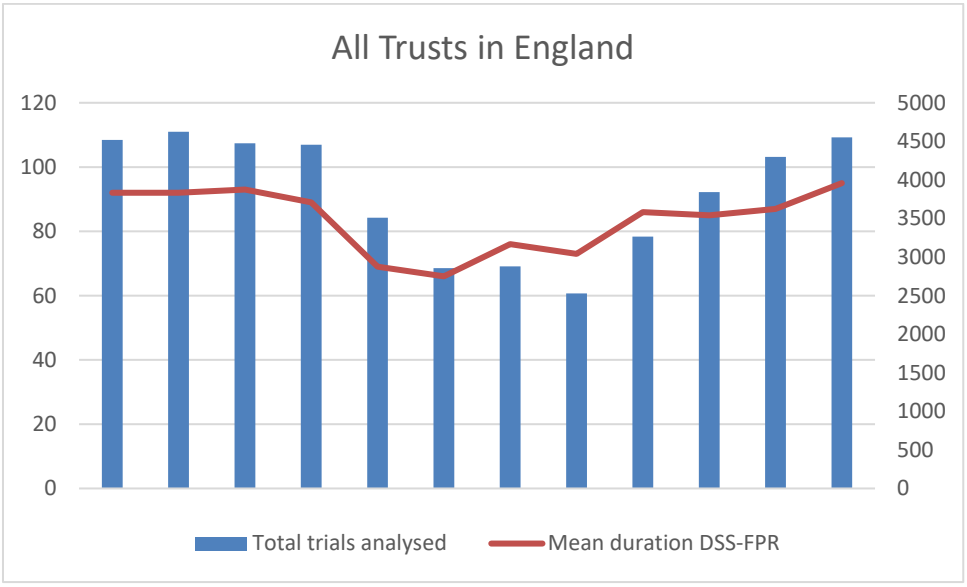


Figure 4. Quarterly interventional trial initiation metrics for all Trusts in England

4.8. Along with all other Trusts in England, OUH also has to submit to the NIHR the reason(s) why study set-up and first recruitment have been delayed – if applicable. Since Q1 2018-19 the NIHR has allowed each

Trust to set its own criteria to determine whether it considers a study to have been delayed. The approach developed by OUH R&D was to calculate study-specific target dates for first patient recruitment, based on the target total recruitment number and the time available in which to complete recruitment. If a trial does not meet its target date, then the reason(s) for this is submitted to the NIHR.

4.9. The NIHR's overall breakdown of the reasons for delay received from all Trusts for interventional trials confirmed in 2021-22 shown in Table 3, alongside the breakdown of the reasons for OUH-studies only.

Table 3. Reasons for delay for interventional trials confirmed 2021-22

Reason for delay	All Trusts (%)	OUH only (%)
A – Permissions Delayed/Denied	11	0
B – Suspended by Sponsor	1	1
C - Closed by Sponsor	1	4
D – Sponsor Delays	26	17
E – Staff Availability Issues	12	7
F – No Participants Seen	15	6
G – No Participants Consented	6	11
H – Contracting Delays	14	8
I – Rare Diseases	3	9
J – Other	12	38

4.10. Sponsor delays are the most common specific reason for delay provided by OUH and by all Trusts, However, the high percentage of 'Other' reasons recorded for OUH makes it further comparison difficult. Anecdotally, many of these 'Other' delays ay OUH relate to pharmacy greenlight for CTIMPs (drug trials), but this level of granularity is not captured in the NIHR's system for categorising delays. The lack of consistency across Trusts in terms of what actually constitutes a delay also makes it hard to make meaningful comparisons.

Metric 2: Performance in Delivering Research
(for all commercial trials closed to recruitment during the previous 12 months)

4.11. This metric only applies to trials with a commercial sponsor and relates to recruitment numbers within the time period specified in the agreed

contract with the host Trust. NIHR evaluation of this metric is limited to trials that have closed to recruitment during the previous year.

4.12. For the 12 months up to and including Q4 2021-22, 54 commercial trials were submitted, of which 61% recruited to time and target (represented by the column and line, respectively, in Figure 5). This matches OUH's performance during 2019/20 (pre-pandemic). It is also better than the overall performance of NHS Trusts in England, shown in Figure 6, 52% of whose trials recruited to time and target in 2021-22.

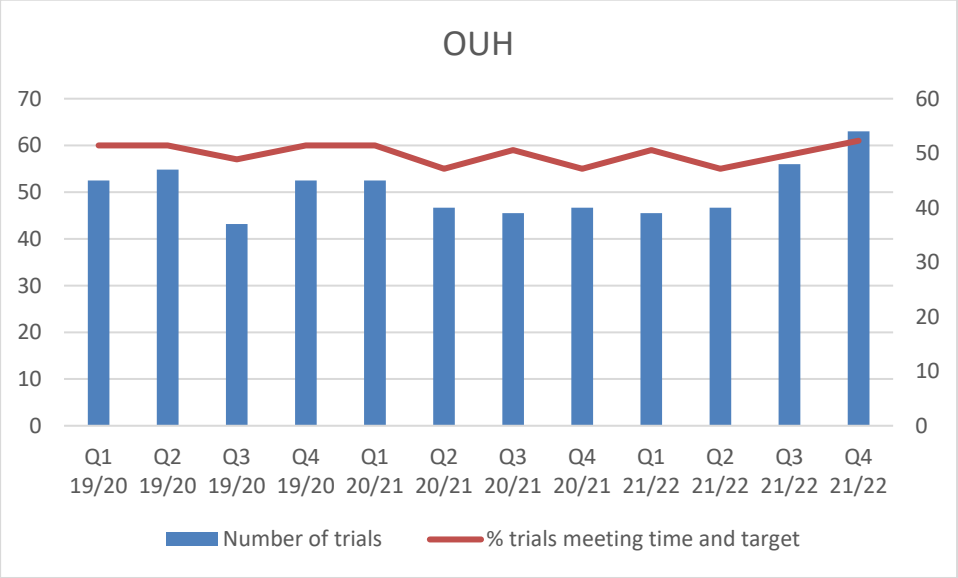


Figure 5. Quarterly commercial trial delivery metrics for OUH

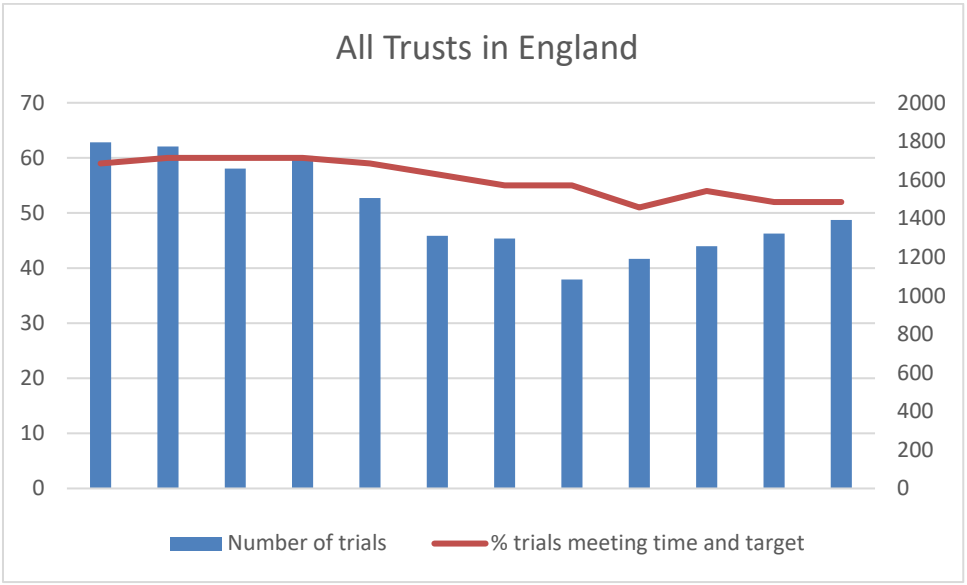


Figure 6. Quarterly commercial trial delivery metrics for all Trusts in England

4.13. The NIHR also requires NHS Trusts in England to report a reason why each commercial trial closed to recruitment. A breakdown of the

reasons why trials closed to recruitment in the year ending Q4 21-22 can be seen in Table 4.

Table 4. Reason for closure of commercial studies 2021-22

Reason for study closure	Number of studies closed	
	OUH (n=54)	All Trusts (n=1392)
Recruitment finished	41 (76%)	1145 (82%)
Withdrawn by host	7 (13%)	209 (15%)
Withdrawn by sponsor	6 (11%)	38 (3%)

4.14. The vast majority of studies (76%) that closed to recruitment at OUH in the 2021-22 did so because study recruitment had finished. However, because there is often competitive recruitment between sites in multicentre studies in some cases OUH may not have reached its target.

4.15. Comparing the reasons for study closure at OUH with the reasons reported by all Trusts in England, the main difference is in the proportion withdrawn by the sponsor. The absolute numbers are relatively low, so this may be due to chance, but it will be monitored closely in future metrics submissions.

5. NIHR Oxford Biomedical Research Centre (Oxford BRC)

5.1. The 20 NIHR BRCs in England, including the Oxford BRC hosted by OUH, have all been awarded an eight-month costed extension, to 30 November 2022.

5.2. The outcome of the competition for the next round of BRC designation and funding, for five years from December 2022, is due to be announced in June 2022. The Oxford BRC's Stage 1 bid, involving 15 research themes, was approved to proceed in full, meaning that the partnership was eligible to apply for the maximum award of £100m. The Stage 2 bid was submitted in October 2021 and representatives of the Oxford BRC, from OUH and the University of Oxford, attended interviews with an international panel of experts on 7 April 2022. The Oxford BRC has worked closely with the Oxford Health BRC to ensure their renewal bids are complementary but distinct.

5.3. An analysis of the Oxford BRC's publications between 2012 and 2017 - the BRC's second five-year period of NIHR funding - revealed not

only the large number of research publications by its researchers, but also the huge network of collaborations in which they were involved. The 2,377 translational research papers published during this period were cited more than 155,000 times, with a citation rate seven times higher than equivalent publications.

COVID-19 Research

5.4. 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.

5.5. Oxford BRC researchers have highlighted how the BRC's infrastructure gave it the agility and capacity to respond rapidly with research projects to tackle COVID-19. In a commentary published in the open access BMC Health Research Policy and Systems journal, the BRC team said the development of the Oxford AstraZeneca vaccine and the RECOVERY Trial were examples that "illustrate capability and capacity at an organisational and individual level in a dynamic environment" to respond to this public health challenge. They noted that this response was "underpinned by swift adaptation and repurposing of existing research resources and expertise" by the BRC. The BRC has supported more than 100 COVID-19 projects, 34 of which were Urgent Public Health studies nationally prioritised by the NIHR.

5.6. COVID-19 studies supported by the Oxford BRC that have had 'World-Class Impact' (one of OUH's five Strategic Themes) include the ongoing RECOVERY trial, the Oxford Vaccine trials and related studies, surveillance surveys, and an increasing number of Long-COVID studies. Summary descriptions of these, along with illustrative examples of the wide variety of other COVID-19 research carried out at OUH, are provided in Appendix A.

Other research (non-COVID-19)

5.7. As COVID-19 restrictions have eased during 2021-22, many other research studies have been able to resume activity, leading to a large number of other diverse advances which have been led or enabled by the Oxford BRC; many new studies have started to recruit participants and other studies have announced important results that should lead to improved patient care in the future.

5.8. A selection of illustrative examples of non-COVID-19 research studies is provided in Appendix B.

People, Leaders and Awards

5.9. A number of Oxford BRC-supported researchers who played prominent roles in the global response to the COVID-19 pandemic were honoured as part of the Queen's 2021 Birthday Honours list. They include:

- Professor Sir Adrian Hill
- Professor Dame Sarah Gilbert
- Professor Sir Martin Landray
- Professor Sir Andrew Pollard
- Professor Teresa Lambe OBE
- Professor Derrick Crook OBE

Other notable Oxford researchers honoured include: Professor Sir Peter Horby and Professor Catherine Green OBE. Another Oxford BRC-supported researcher honoured by the Queen was Professor Sir Keith Willett, National Director for Emergency Planning and Incident Response to NHS England and NHS Improvement.

5.10. In March 2022, Seven Oxford academics, six of them supported by the Oxford BRC, were named NIHR Senior Investigators in recognition of their outstanding leadership in research. Three were named Senior Investigators for the first time: David Beard, Professor of Musculoskeletal and Surgical Science; Julia Hippisley-Cox, Professor of Clinical Epidemiology and General Practice; Najib Rahman, Professor of Respiratory Medicine. Three more were reappointed as Senior Investigators: Eleanor Barnes, Professor of Hepatology and Experimental Medicine; Graham Ogg, Professor of Dermatology; and Paul Aveyard, Professor of Behavioural Medicine.

5.11. Professors Gilbert, Landray and Horby were among 50 prominent biomedical and health scientists elected to the Academy of Medical Sciences' Fellowship. Other Oxford BRC researchers elected to the Fellowship were: Professor Graham Ogg, and Professor Heidi Johansen-Berg.

5.12. Professor Susan Jebb, the Oxford BRC's Theme Lead for Obesity, Diet and Lifestyle, was appointed as the new Chair of the Food Standards Agency.

5.13. Oxford BRC Senior Fellow Dr David Eyre, who played a leading role in OUH's COVID-19 staff testing programme, was named as the recipient of the Healthcare Infection Society's (HIS) 2021 Early Career Award.

Training

5.1. In July 2021 the Oxford BRC announced the appointment of its latest group of Senior Research Fellows – the third cohort of emerging research leaders to receive the accolade. As in 2020, the selection process was a coordinated effort with the NIHR Oxford Health BRC and the NIHR Applied Research Collaboration (ARC) for Oxford and the Thames Valley.

5.2. The second edition of the Oxford BRC's Next Generation Leaders Programme came to a successful close on 6 September 2021, with the 25 course participants presenting the healthcare research quality improvement projects that had been working on. The programme was commissioned and designed by the BRC to enable early to mid-career researchers and health professionals to develop key skills in leadership and management capability.

5.3. The Oxford BRC launched its first dedicated senior leadership training programme on 28 February 2022. Fourteen senior leaders affiliated to the BRC and from a diverse range of fields across the University of Oxford and OUH attended the first workshop on the topic of Senior Leadership Practices.

Patient and Public Involvement and Engagement in Research

5.4. The Oxford BRC published its new patient and public involvement and engagement (PPIE) strategy in October 2021. The new strategy was produced following extensive consultations with PPIE contributors and researchers and other key stakeholders. New PPIE contributors from communities not usually involved - such minority ethnic and LGBT+ communities, and young adults - contributed a total of 200 hours to develop the strategy.

5.5. The Oxford and Oxford Health BRCs held a networking and learning event focused on the importance of diversity in research. The event, held on 22 March 2022 at Oxford's Blavatnik School of Government, was attended by around 60 research-focused professionals from across the city. The purpose of the event was to offer support and practical advice to those working in research on how to involve people from diverse communities in their work.

5.6. The BRC was one of 13 organisations taking part in a three-month assessment of their delivery of race equality in health research. The initiative, led by the NIHR, involves organisations delivering health research in higher education, local government, the NHS, the private sector and voluntary sector. It informed the NIHR Race Equality Framework, which was launched in April 2022.

5.7. To mark Black History Month, the Oxford BRC sponsored an online talk on October 2021 by health activist, social commentator and cultural historian Patrick Vernon OBE, who discussed Inequalities in Healthcare and Research, seen through the lens of Black British history.

5.8. A study by Oxford BRC researchers concluded that the markers of achievement for monitoring gender equity in BRCs should take into account contextual factors specific to BRCs and women's career progression and professional advancement.

5.9. A travelling NIHR photography exhibition launched in early 2020 has continued to visit locations around the Thames Valley. 'The Body Unlocked: How Research is Changing Lives' aims to engage with members of the public to encourage greater participation in research. Having started the year in the John Radcliffe Hospital's West Wing, it has visited Maidenhead, Slough, Newbury, Aylesbury and Windsor, before returning to Oxford's Central Library. It will shortly travel to Milton Keynes.

5.10. An innovative new treatment for children with type 1 diabetes that is offered at the Oxford Children's Hospital has been featured on BBC's The One Show. The report featured OUH's paediatric diabetes team, who are supported by the BRC, and a six-year-old patient, who has been fitted with a hybrid closed-loop system, also known as an artificial pancreas.

5.11. The local health research comms network has delivered regular media and social media training to researchers from partner organisations. The Oxford BRC communications manager and his LCRN counterpart have delivered the online training to around 170 people.

5.12. The Oxford BRC took part in the NIHR's Your Path in Research campaign, which aims to encourage healthcare professionals to become more engaged in research. This included positive profiles of OUH NMAHPs (Nursing, Midwifery an Allied Health Professionals) who have got involved in research as a way of improving patient care.

5.13. The Oxford BRC supported the production of a new video aimed at patients and the public by the Centre for Personalised Medicine on polygenic risk scores and how they can be used in healthcare.

5.14. Preparations are underway for a stakeholder event in May 2022 celebrating the 15th anniversary of the Oxford BRC. The Oxford and Oxford Health BRCs are also holding a joint Open Day at Oxford Town Hall on 5 July, the first since 2019.

6. NIHR Oxford Clinical Research Facility (Oxford CRF)

6.1. A CRF Group, chaired by Dr Andrew Brent, OUH Deputy CMO, was established in the summer of 2021 at the request of Dr Bruno Holthof (OUH CEO). The group's immediate priority was to support Prof Duncan Richards (who is also a member of this group) to prepare and OUH's bid (£5m) for the competition for NIHR Clinical Research Facility designation and funding (2022-27). This bid was submitted in September 2021. It featured a federated model, bringing together the existing NOC CRF, the CRU at OCDEM and the new Experimental Medicine CRF set-up by OU on the Churchill site in summer 2021, as well as new proposed paediatric and outpatient CRFs. The CRF was one of three joint projects with OU part-funded by a grant from OUH announced in June 2021.

6.2. It was announced on 28 February that the Oxford CRF has been awarded NIHR designation and funding, as one of five new CRFs nationally. The separate Oxford Health CRF's bid for re-designation and funding was also successful. The new NIHR Oxford CRF was awarded £1m funding over five years from September 2022 (compared to the £5m requested), which is understood to be the same as the other new NIHR CRFs.

6.3. The original bid is now being prepared for resubmission to the NIHR, with a reduced number of posts, aligned with the confirmed funding awarded by NIHR. Some of the OU posts included in the original bid will now be supported from other sources of funding available to OU.

6.4. The CRF Group's main focus is to develop a Collaboration Agreement to set out how OUH and OU will run the federated Oxford CRF in partnership.

7. Research Governance

Background

7.1. Research governance refers to the framework 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:

7.2. 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.

7.3. 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.

7.4. 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 become an EU Regulation on 31 January 2022), into domestic legislation. This is still the case, although the UK government has recently carried out a consultation for legislative changes for clinical trials, the outcome of which is awaited.

7.5. 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).

7.6. 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.

7.7. 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).

7.8. 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.

7.9. 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).

7.10. OUH Frameworks for R&D Governance, Training and Monitoring – Locally, clinical research is governed by a number of OUH 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

7.11. 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 OUH R&D Governance team conducts a wide variety of activities, which are summarised below. As indicated, many of these involve working in close collaboration with their JRO colleagues in OU's Research Governance, Ethics and Assurance (RGEA) team.

Oversight of Compliance and Safety

7.12. 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 for each OUH-sponsored trial.

7.13. 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.

7.14. Compliance checks. The governance team also 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.

7.15. 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.

7.16. Consent. As part of the actions identified by the HTA's inspection of the OU's HTA Licence 12217 in 2018, the Trust recognised the need for improved consent processes 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 their wishes. R&D contributed to a review of OUH's consent policy and processes, which has led to appropriate consent for clinical samples and clinical data to be used in future research studies being integrated with consent for clinical procedures.

Training

7.17. In collaboration with the OU Research Governance, Ethics and Assurance (RGEA) team, the OUH R&D Governance team prepares and delivers training to both Trust and University staff. This covers all research related legislation and GCP, with separate courses designed for staff new to trials and to provide an update/refresh for experienced researchers.

7.18. For CTIMPs (drug trials) 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.

7.19. 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.

7.20. It has not been possible to provide face-to-face CTIMP training or non-CTIMP training during the period covered by this report, due to the COVID-19 pandemic. However, 187 people attended training on Obtaining HRA and Ethics Approval which was delivered online and a further 826 applicants have been accepted onto the online GCP training course, which they work through in their own time.

7.21. Good Research Practice (GRP) training, which used to be delivered in-person, was suspended in March 2020 due to the of the COVID-19 pandemic. It has since resumed via MS-Teams and 41 people have attended since January 2022.

Research Passports

7.22. The Governance team processed and authorised 72 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

7.23. 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 RGEA 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 120 projects during 2021-22.

8. Research and Development Finance

8.1. The R&D Finance team provides management accounting, costing, and pre and post award financial support to researchers undertaking or seeking to undertake research activity within OUH. The team's major responsibilities include managing the finances for the Oxford BRC and the Thames Valley & South Midlands Local Clinical Research Network (LCRN), which are both hosted by OUH; costing commercial and non-

commercial studies, and providing and paying invoices for studies once they are active.

8.2. 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 Current Activities to 31 March 2022

8.3. For the 2021-22 financial year, the annual income and expenditure budget for R&D was set at £55 million. As shown in Table 5, This included income and expenditure of £43 million from major NIHR grants for hosting the 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.

Table 5. High level breakdown of 2021-22 R&D budget

Research Funding by area	**2021-22 Expenditure (£m)**
NIHR Biomedical Research Centre (BRC)	23
NIHR Local Clinical Research Networks (LCRN)	17
NIHR Research Capability Funding (RCF)	2
Other NIHR grants	1
Other income (commercial & non-commercial)	12
	55

8.4. Overall research income and expenditure for the year returned to pre-covid levels for commercial and non-NIHR non-commercial studies.

8.5. Grant applications to various funding bodies remained active during the year at a similar level to the previous year.

8.6. At the end of the financial year (31 March 2022) all the major NIHR programme and smaller grants achieved a breakeven position as planned, and income slightly exceeded expenditure, by £200k (<1.7%), for the individual study accounts for all the commercial and other non-commercial trials and other research activities.

Research Capability Funding

8.7. The NIHR sets out that the purpose of RCF 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 people and patient-based research, and 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. As a result of this flexibility, RCF has been a very important funding stream for research at the Trust.

8.8. The RCF award received by OUH in 2021-22 was £2.3 million. This was used to contribute towards research overhead costs, the costs of managing NIHR grants, and the RCF panel made over 50 individual awards in support of research, including awards to cover maternity costs to enable grant funded research to continue while key research staff have been on maternity leave.

Financial Planning 2022-23

8.9. The following budget has been set for 2022-23:

Research Funding by area	2022-23 Expenditure budget (£m)
NIHR Biomedical Research Centre (BRC)	22
NIHR Local Clinical Research Networks (LCRN)	18
NIHR Research Capability Funding (RCF)	1
Other NIHR grants	1
Other income (commercial & non-commercial)	11
	53

8.10. 2021-22 represents the fifth and final year of the current designation for all BRCs. Funding from the NIHR for the current BRC had been due to end in March 2022. However due to the impact of the COVID-19 pandemic an eight month costed extension has been awarded to the end of November 2022.

8.11. The outcome of the Oxford BRC's application for re-designation and funding for the next 5 years is expected by the end of June 2022. The new BRC award will begin in December 2022. Once the details of the award are known, the core budgets for each of the individual research Themes, as well as the management team, will be confirmed.

8.12. Under the current agreement with the NIHR, OUH will continue to host the LCRN for the Thames Valley and South Midlands until 31 March 2024. Funding levels for 2022-23 have been confirmed, including the allocations to each of the six Trusts covered by the LCRN.

8.13. The LCRN budget to support research at OUH for 2022-23 is £7.25 million. Although this is an uplift of 3%, it actually represents flat funding once the national pay awards and increased employment costs have been factored in. Final budgets to support research in each clinical area at OUH have been considered and awarded as the funding allocation allowed. The budget setting process was communicated in the usual way, with the network management team and the R&D finance team working closely with stakeholders to agree budgets before the start of the financial year.

8.14. As in previous years the BRC and LCRN budgets forecast a break-even position for 2022-23.

8.15. The Research Capability Funding (RCF) award to OUH for 2022-23 is £1.2 million. This is a very significant 50% drop compared to the funds received last year (£2.3 million). DHSC have been reducing the total national annual allocation to this funding stream since 2019-20. Weightings for qualifying income received by NHS organisations hosting BRCs and other NIHR infrastructure contracts have been reduced significantly since last year, and RCF payments associated with Senior Investigators are being phased out (those appointed after April 2019 no longer attract an RCF weighting). OUH R&D is working with senior Trust finance colleagues to agree how best to allocate this reduced RCF income in 2022-23 to support research activities in line with the NIHR guidance for this funding.

8.16. The expectation is that the NIHR will continue to reduce the amount of RCF awarded to NHS Trusts over the coming 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.

8.17. The budget for income (and expenditure) from commercial and other non-commercial studies has been set conservatively at £11.5 million, to match pre-COVID budgets.

8.18. The National Contract Value Review Process for the costing of commercial studies is expected to be implemented during 2022-23, following a delay of more than two years due to the COVID-19 pandemic. The aim of this new process is to standardise and streamline the costing of multi-site commercial contract research, in particular to minimise duplication of effort at each site, so these trials can be set-up more quickly in the UK. OUH R&D has been actively engaged in discussions with the national group responsible for piloting and rolling-out this new process.

9. Research Contracts and IP

9.1. During the year to 31 March 2022, 1,233 research and IP related cases were finalised on behalf of OUH. This is a 38% increase on the previous year, reflecting the growing demand for research in 2021-22, as the impact of the COVID-19 pandemic has started to wane. A full breakdown of the Research Contracts and IP team's main activities in 2021-22 is provided in Figure 7.

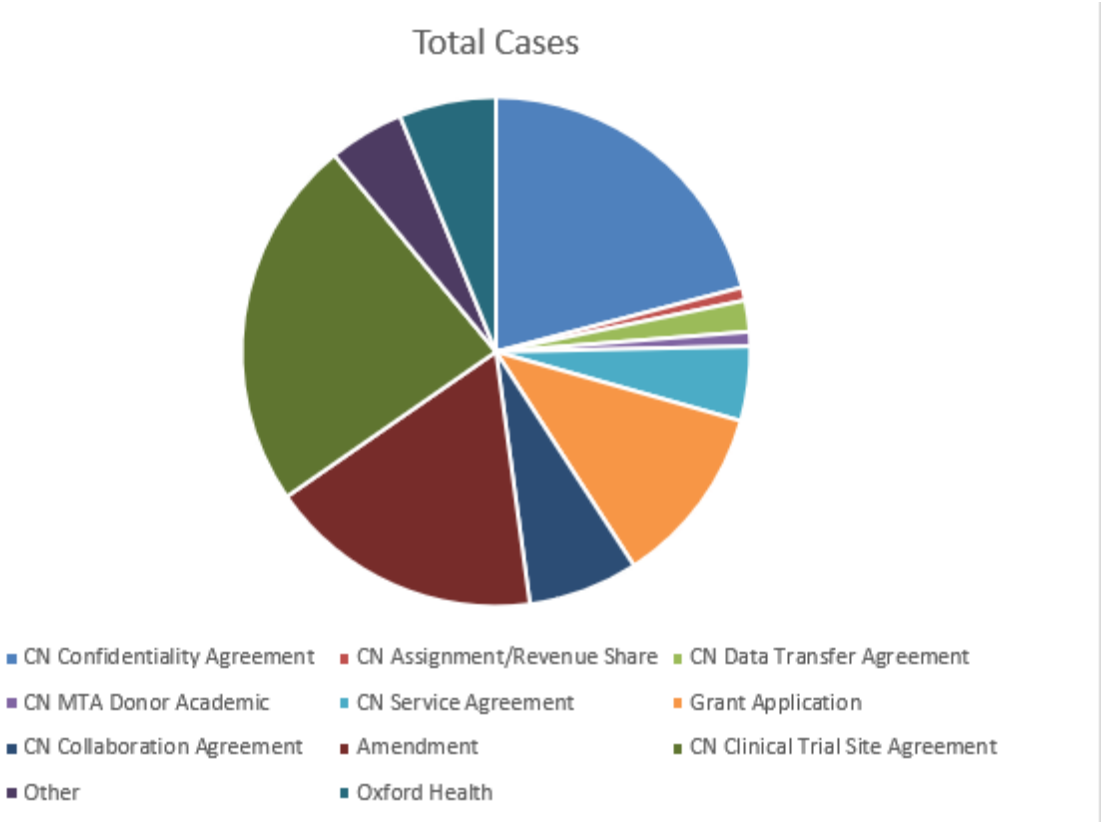


Figure 7. Breakdown of Research Contract and IP activities completed 2021-22

9.2. The largest category was Clinical Trial Site Agreements (311) for new studies, followed by Confidentiality Disclosure Agreements (275) and then study Amendments (230). Together these account for two thirds of the Research Contracts and IP team's activities in 2021-22.

9.3. The team also continued its contracting service to Oxford Health NHS Foundation Trust, closing 81 cases (an increase of 15% compared to the previous year).

9.4. The remaining categories, which include Material Transfer Agreements, Service Agreements, Collaborations, Data Transfer Agreements and IP related agreements, account for 337 (27%) of the cases completed in 2021-22.

9.5. The Head of IP and Research Contracts and senior members of his team are directly engaged in discussions to agree new data sharing arrangements with the University of Oxford and will implement processes to manage these in relation to research studies.

10. The Oxford Joint Research Office

10.1. The JRO has played a key role in enabling Oxford's world-leading response to the COVID-19 pandemic, 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.

10.2. With the encouragement and support of the Oxford Academic Health Partners (OAHP), the JRO Co-leads for OUH and OU have been working with colleagues from Oxford Brookes University (OBU) and Oxford Health NHS FT (OH) to expand the JRO partnership to enable closer working and coordination of research support activities across the NHS/academia interface. This led to the JRO Terms of Reference (ToR) being updated to include all four organisations and approved by the Joint R&D Committee (JRDC). An agreed announcement about the expansion of the JRO, to include OBU and OH, was made simultaneously on the websites of all four partner organisations, as well as OAHP, on 8 April 2022.

10.3. The ToR for the JRDC have also been updated, to include formal representation from OBU and OH, to help fulfil the Committee's remit to provide oversight, direction and support to the JRO; the Director of OxINMAHR from OBU (Prof Paul Carding) and the Director of R&D from OH (Dr Vanessa Raymont) are now members of the JRDC

10.4. These developments should help enable members of the expanded JRO to identify and to implement many improvements organically, without having to wait for a proposed new four-party (OUH, OU, OBU and OH) Joint Working Agreement.

10.5. An off-site away day, for members of the expanded JRO from all four of the partner organisations, is planned for June 2022. The last in-person JRO away day was held in October 2018 and did not involve either OH or OBU. The Schedule includes two talks by researchers about their studies which depend upon support from two or more of the JRO partners, and a panel discussion chaired by Prof Helen McShane with senior executives representing all four partners. There will also be a breakout group session in which mixed groups will work together to help

define and refine some of the major common objectives which will be the focus of the expanded JRO's activities in the short-medium term.

10.6. Members of the JRO from OUH and OU have been involved directly in ongoing discussions with senior colleagues regarding the arrangements for:

- a Memorandum of Understanding to facilitate joint working between both organisations, in support of the federated model of Clinical Research Facilities (CRFs) as part of the new NIHR Oxford CRF, whose designation and funding commences in September 2022.

- updating the basis for joint research work involving OUH clinical data, including governance, intellectual property (IP) and infrastructure aspects.

- setting up and operating a Trusted Research Environment (TRE), in partnership with OU and other NHS Trusts across the region and nationally.

11. Recommendation

11.1. The Trust Board is asked to receive this report for information.

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

RECOVERY trial

The RECOVERY Trial, the world's largest randomised trial of potential COVID-19 treatments, has now found four drugs that reduces the risk of death when given to hospitalised patients with severe COVID-19. The trial showed that baricitinib, an anti-inflammatory drug normally used to treat rheumatoid arthritis, was effective when given to hospitalised patients in addition to dexamethasone and tocilizumab, two other anti-inflammatory treatments which have previously been shown to reduce the risk of death in these patients. The trial also found that Ronapreve, an antiviral drug 'cocktail' developed by the US company Regeneron reduced deaths in hospitalised COVID-19 patients who have not mounted their own immune response. The treatment uses a combination of two monoclonal antibodies that bind to two different sites on the coronavirus spike protein, neutralising the virus's ability to infect cells.

The trial, which is supported by the Oxford BRC, found that a number of potential treatments – including aspirin, colchicine, azithromycin, hydroxychloroquine, lopinavir and convalescent plasma – were not effective in hospitalised patients. These discoveries have changed clinical practice worldwide and been credited with saving hundreds of thousands, if not millions, of lives. The trial, which has recruited over 47,000 participants across 198 sites in six countries, continues to study a number of potential treatments.

The RECOVERY Trial's paper on the effectiveness of the dexamethasone in hospitalised COVID-19 patients, published in the New England Journal of Medicine in June 2020, was named the BMJ's UK Research Paper of the Year in October 2021.

Oxford vaccine trials and related studies

Some 2.6 billion doses of the Oxford/AstraZeneca coronavirus vaccine have been manufactured and released to more than 180 countries worldwide. The vaccine, developed in trials supported by the Oxford BRC, has been found to be highly effective against all known variants. It is estimated to have helped prevent 50 million COVID-19 cases and five million hospitalisations and saved more than one million lives.

In June 2021, the Oxford vaccine team found that a longer delay of up to 45 weeks between the first and second dose of the vaccine leads to enhanced immune response after the second dose. They also found that a third dose given more than six months after the second dose leads to a substantial increase in antibodies and induces a strong boost to immune response against SARS-CoV-2, including variants.

An Oxford BRC-supported study by University of Oxford's Health Economics Research Centre found that there is much greater consistency in public attitudes

across a range of countries about who should be prioritised for COVID-19 vaccination, which could have potentially informed national roll-out strategies.

More people in England at high risk from COVID-19 got priority access to vaccines thanks to new technology developed by a University of Oxford-led team of researchers that can identify those who may be most vulnerable to the virus. Research by a cross-organisational team led by Professor Julia Hippisley-Cox with support from the Oxford BRC, led to the development of a risk prediction model called QCOVID, which has been independently validated by the Office for National Statistics. The platform looks at a number of health and personal factors to assess whether someone is at a higher risk from COVID-19. NHS Digital used this model to develop a population risk assessment, enabling the government to prioritise groups with higher risk for vaccination, and provide appropriate advice and support. In July 2021, QCOVID won the Florence Nightingale Award for Excellence in Healthcare Data Analytics, and in early 2022, the NIHR published a case study on QCOVID.

The results of the largest ever study to compare the risks of cardiovascular events – such as myocarditis, pericarditis, and cardiac arrhythmia – between different vaccines and COVID-19 infection were reported. The study, led by Oxford BRC-supported researchers, was the first to investigate the association between cardiac events and the Oxford-AstraZeneca vaccine. The main findings were that, while there are some increased risks of rare heart-related complications associated with vaccines, these are much lower than the risk associated with getting COVID-19.

Researchers from the University of Oxford's Molecular Haematology Unit found that antibody responses to the first doses of COVID-19 vaccine in people with chronic myeloid blood cancers were not as strong as those among the general population, a finding useful for influencing the design of vaccination strategies. The study, which included 60 patients with chronic myeloid blood cancers at the Churchill Hospital, was supported by the Oxford BRC.

COVID surveillance

The ONS COVID-19 Infection survey produces regular updates on how the virus is progressing through the UK population, providing vital information to scientists and the government to influence how the pandemic should be managed. The survey, led by senior Oxford BRC researcher Professor Sarah Walker and one of the NIHR's COVID-19 urgent public health studies, is a major community surveillance survey led by the University of Oxford, the Office of National Statistics (ONS) and the DHSC. Among its important findings were that there had been significant reductions in COVID-19 infections after a single dose of the Oxford-AstraZeneca or Pfizer-BioNTech vaccines, and that vaccination was effective in individuals aged over 75 or with underlying health conditions. The survey also produced evidence that these vaccines offered good protection against new infections of the Delta variant of concern, albeit less than against the Alpha variant. By April 2022, some 535,000

people from more than 250,000 households across all four nations of the UK had taken part in the study.

Oxford University and the multinational computer technology corporation Oracle have joined forces to create a Global Pathogen Analysis System (GPAS) to help governments and medical communities identify and act on variants of the COVID-19 virus faster. The platform combines Oxford's Scalable Pathogen Pipeline Platform (SP3), developed with support from the Oxford BRC, with Oracle's Cloud Infrastructure (OCI).

Long-COVID studies

Researchers from Oxford and Sheffield have identified abnormalities in the lungs of long COVID patients who are experiencing breathlessness that cannot be detected with routine tests. A pilot of the EXPLAIN study, which is supported by the Oxford BRC, is using hyperpolarised xenon MRI scans to investigate possible lung damage in long COVID patients who have not been hospitalised with COVID-19 but who continue to experience breathlessness. These initial results, which garnered considerable national media coverage, show that there is "significantly impaired gas transfer" from the lungs to the bloodstream. A previous study had used the same cutting-edge method of imaging to establish that there was persistent lung abnormalities in patients who had been hospitalised with COVID-19 several months after they were discharged.

EXPLAIN was one of two BRC-supported studies to benefit from NIHR funding to help better understand long COVID, improve diagnosis of the condition and find new treatments. This research feeds into the national PHOSP-COVID platform, looking at long-term effects of COVID-19.

Results from the PHOSP-COVID study showed that people who were hospitalised with COVID-19 and continued to experience symptoms five months later show limited further recovery one year after hospital discharge. They also confirmed earlier research that people who were less likely to make a full recovery were female, obese and required invasive mechanical ventilation during their hospital stay. Oxford investigators supported by both the Oxford BRC and Oxford Health BRC, have been prominent in PHOSP-COVID, providing expertise in multi-organ imaging, mental health and lung disease.

A new national study involving researchers from Oxford 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, which was 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.

Other COVID studies

University of Oxford researchers, led by NIHR Oxford BRC Director Professor Helen McShane, launched a coronavirus human challenge trial to look at what kind of immune response to COVID-19 can stop people from becoming re-infected. The team also want to find out how the immune system reacts to a second infection.

Artificial intelligence (AI) technology to scan for heightened blood vessel inflammation can calculate a person's risk of death from COVID-19 and COVID-19 variants. Using routine chest CT scans and machine learning, a team led by Oxford BRC researcher Prof Charalambos Antoniades have developed a COVID-19 'signature' that detects biological red flags in the fat surrounding the blood vessels in the chest to measure the level of cytokine-driven vascular inflammation in people infected with the virus.

A proof-of-concept trial found that the rheumatoid arthritis treatment namilumab is a potential therapeutic to treat patients who are hospitalised with COVID-19 pneumonia and who have high levels in their blood of a protein called CRP, which are associated with inflammation and are a potential early marker to predict risk of severe COVID-19. The CATALYST Trial is a collaboration between the Universities of Birmingham and Oxford and is supported by the Oxford BRC. A second arm of the trial, led by Oxford, found that the drug infliximab, was not more effective than usual care.

Researchers from Oxford, supported by the BRC, have identified the gene responsible for doubling the risk of respiratory failure from COVID-19. Sixty percent of people with South Asian ancestry carry the high-risk genetic signal, which could partly explain the excess deaths seen in some UK communities.

The largest study of people with type 1 diabetes admitted to hospital with COVID-19 found that those with higher body mass index, poorer kidney function and the presence of microvascular complications were at greater risk of death and/or admission to intensive care. However, the study, supported by the Oxford BRC, also found that risk of severe COVID-19 was very low in people with type 1 diabetes who are under 55 years of age without microvascular or macrovascular disease. This national audit brought together clinical researchers from 40 NHS centres with data scientists and informaticians at OUH and the University of Oxford.

A study by Oxford University researchers found that liver problems were common among patients with COVID-19. Patient data revealed that baseline hypoalbuminemia (a possible indication that the liver is producing low levels of albumin) and rising alkaline phosphatase (ALP), which can be a sign of liver damage, could be prognostic markers for death. The research was carried out under the auspices of the NIHR Health Informatics Collaborative (HIC), which make routinely collected clinical data available for translational research in selected therapeutic areas. The NIHR HIC viral hepatitis theme is led by OUH and the University of Oxford, through the Oxford BRC.

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

SYMPLIFY study

Volunteers in Oxfordshire are taking part in a study that will trial a revolutionary new blood test that can detect more than 50 types of cancer before symptoms appear. The aim of the SYMPLIFY study, which is led by the University of Oxford and supported by the Oxford BRC, is to demonstrate how the Galleri test, which uses sequencing technology to check for the earliest signs of cancer in the blood, could be used to increase cancer detection rates and improve diagnostic pathways. In addition to SIMPLIFY, the NHS is piloting the test in primary care settings in a trial called the NHS Galleri trial, which will screen 140,000 people for cancer using the test.

Malaria Vaccine

Researchers from the University of Oxford's Jenner Institute, supported by the Oxford BRC, reported that a malaria vaccine they are developing was the first to meet the World Health Organization's goal of a malaria vaccine with at least 75% efficacy. The findings of the Phase IIb randomised, controlled, double-blind trial showed 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 then started for a Phase III licensure trial to assess large-scale safety and efficacy in 4,800 children across four African countries.

The CRyPTIC research project

Using cutting-edge genomic sequencing techniques, researchers at the University of Oxford have identified almost all the genomic variation that gives people resistance to 13 of the most common tuberculosis (TB) drug treatments. The CRyPTIC research project collected the largest ever global dataset of clinical TB samples, consisting of over 15,000 samples from 27 countries. The findings from the team, who are supported by the Oxford BRC, were published in nine pre-print papers.

Phase I PanDox study

University of Oxford researchers began recruitment to a study looking at whether chemotherapy medication can reach pancreatic tumours more effectively if encapsulated within a heat-sensitive shell and triggered with focused ultrasound. The Phase I PanDox study, which is supported by the Oxford BRC, is similar in design to the earlier TARDOX study, which found that this approach increased drug uptake in patients with liver tumours.

Other (non-COVID-19) research

The first patient has been dosed using a new drug, PORT-2, aimed at improving treatment options for melanoma and non-small cell lung cancer (NSCLC) and re-sensitising patients with checkpoint therapy-resistant tumours. The Oxford-led study,

supported by the BRC, is investigating the tolerability and efficacy the drug, developed to target invariant natural killer T (iNKT) cells and trigger a cancer-specific B and T cell response to tumours.

University of Oxford researchers have launched a pilot study to conduct routine testing of newborn babies for spinal muscular atrophy (SMA) for the first time. If treatments are delivered at birth, newborns have the best chance of living long and healthy lives. If treated later, when the condition is identified because of the symptoms, they may survive, but with a severe disability. Now, a population-based newborn screening study, supported by the Oxford BRC, has been launched across the Thames Valley. It aims to make it possible to detect SMA within days of birth, before symptoms develop, so that any affected newborn can receive diagnosis and treatment at the earliest possible opportunity.

A team at the Oxford Centre for Clinical Magnetic Resonance Research has developed a new cardiac magnetic resonance (CMR) scan for detecting heart muscle disease. The current 'gold standard' for imaging heart muscle disease is CMR, using a method called late gadolinium enhancement, which requires injection of a contrast agent into the patient. This prolongs the scan, increases the cost and is riskier in some patients. The researchers, supported by the Oxford BRC, have developed a solution called 'virtual native enhancement', which combines MR images and AI to produce images that are similar to traditional contrast-enhanced images, but without the need to inject the contrast dye.

A multidisciplinary team comprising University of Oxford academics and OUH pathologists has developed an algorithm that automates requests for further investigation of diagnostically uncertain prostate biopsies. The team, supported by the Oxford BRC, used biopsies annotated by the pathologists to train an AI tool to detect tissue regions with ambiguous morphology and decide which cases needed the additional process of immunohistochemistry. It is anticipated this tool will save a considerable amount pathologists' time.

OUH clinicians and University of Oxford engineers have begun using artificial intelligence alongside endoscopy to get more accurate readings of the pre-cancerous condition Barrett's oesophagus and so determine patients most at risk of developing cancer. The BRC-supported researchers say the new AI-driven 3D reconstruction of Barrett's oesophagus achieved 97.2% accuracy in measuring the extent of this condition in real time, enabling clinicians to assess the risk, the best surveillance interval and the response to treatment more quickly and confidently.

A world-first scientific study has shown that whole genome sequencing (WGS) can uncover new diagnoses for people across a wide range of rare diseases and could deliver huge benefits for the NHS. The study was based on analysis of the genes of 4,660 people who took part in the 100,000 Genomes Project. University of Oxford genomics researchers, supported by the Oxford BRC, were among the study's authors.

A study has identified potential new therapeutic targets for the treatment of inflammatory bowel disease (IBD), giving hope to millions of patients with ulcerative colitis or Crohn's disease. The research team from the University of Oxford's Kennedy Institute of Rheumatology and Translational Gastroenterology Unit (TGU) were supported by the Oxford BRC. The study defined a subset of patients with IBD who do not respond to current therapies such as anti-TNF therapy, paving the way for more precisely targeted treatments in future.

A study by Oxford orthopaedic researchers has found that hip replacements using cement improved the quality of life of patients, compared to uncemented implants. The White 5 trial, which is supported by the Oxford BRC, found that patients having the cemented treatment showed a statistically significant improvement in quality of life at one month and four months after the procedure, although there was less difference after 12 months.

A clinical trial was launched to offer a novel treatment option for patients with the blood cancer myelofibrosis (MF). The PROMise trial, launched by the Cure Leukaemia-funded Trials Acceleration Programme, will involve patients at 15 NHS centres, including Oxford's Churchill Hospital. Its Chief Investigator is Prof Adam Mead, the Oxford BRC's Co-theme Lead for Haematology.