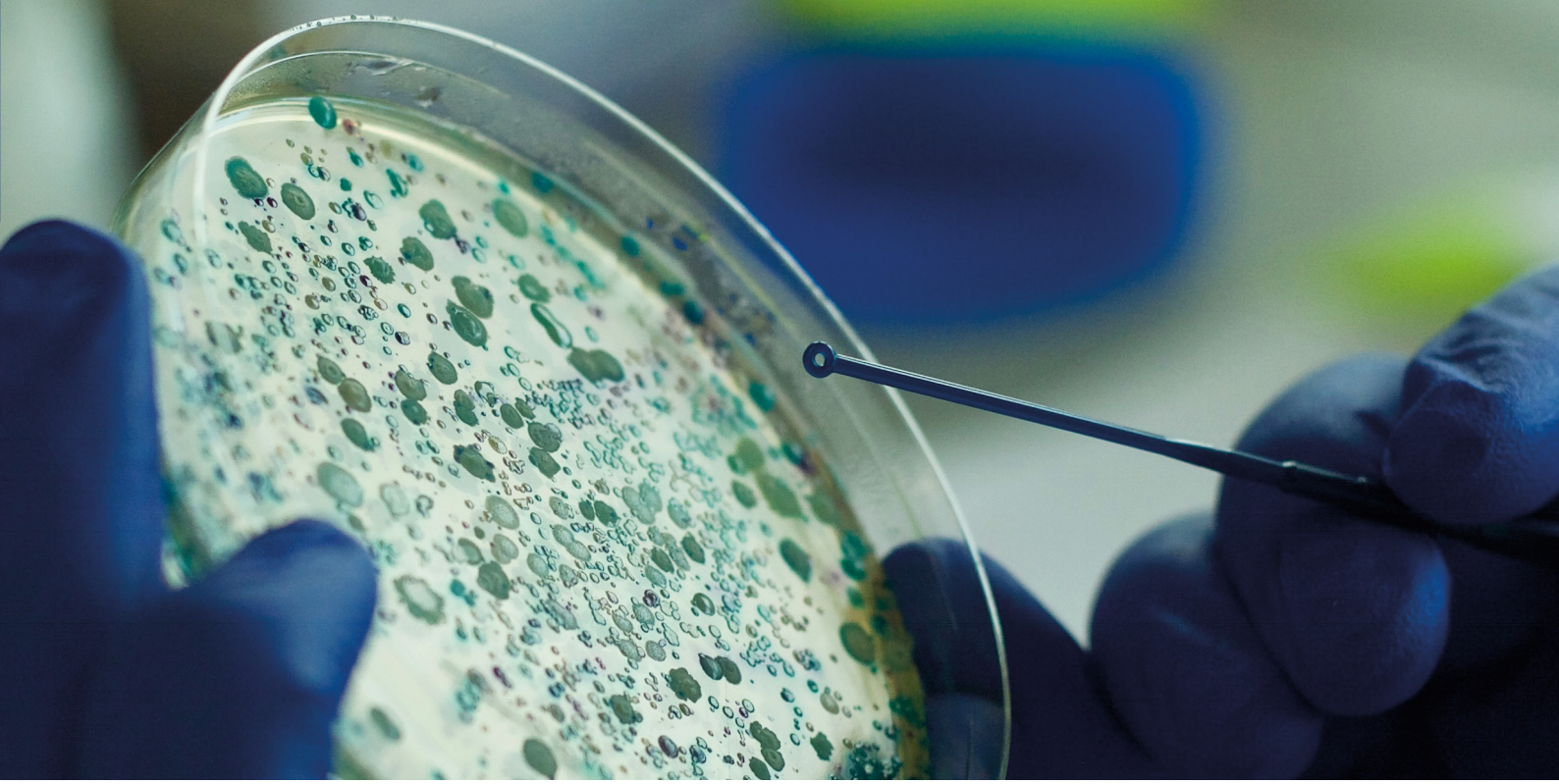

A GUIDE TO WHAT WE DO

Bringing together clinical expertise, academic excellence and industry to benefit NHS patients

NIHR | Oxford Biomedical Research Centre

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Introduction

by Oxford BRC Director Professor Helen McShane

In 2017 the Oxford Biomedical Research Centre was awarded its third round of NIHR funding – £113.7m for the five years to 2022. This increased amount was a recognition of the success and impact of the partnership between Oxford University Hospitals (OUH) NHS Foundation Trust and the University of Oxford in healthcare research over the previous 10 years. This success is founded on our outstanding researchers, working across this NHS-University partnership. The BRC has had a catalytic effect on the way we support and manage clinical research, allowing us to increase our activity, our impact and our profile – and get more value from our NIHR funding.

The Oxford BRC is one of the largest partnerships of its kind in the UK and comparable with any academic medical centre worldwide. We benefit from a large, integrated NHS, University and industry health science campus, where a spirit of research permeates all clinical activities, and clinical translation motivates basic science research across multiple disciplines. Many University research institutes are co-located with our hospitals, and this is complemented by one of the highest concentrations of medtech companies in the UK across our region.

The BRC's work is focused on people, patients and partnerships, underpinned by our cross-cutting Health, Wealth and Innovation Theme, which seeks to increase patient involvement, work with other aspects of NIHR infrastructure and develop partnerships with industry for growth and wealth creation.

A key aspect of our BRC is that individual research themes have been brought together in clusters, to foster cross-disciplinary activities, identify shared opportunities and so address today's biggest healthcare challenges – in a way that brings together the strengths and capabilities of the 20 individual themes.

Since its inception, the Oxford BRC has demonstrated that harnessing the expertise and infrastructure of Oxford's NHS-University partnership delivers consistent excellence in our translational research. We are committed to taking full advantage of our NIHR funding to deliver excellent research that translates into more effective treatments for patients.

About us

We bring together industry, clinical expertise and academic excellence to benefit NHS patients.

Oxford has long been at the forefront of worldwide medical research, whether it is the genetic and molecular basis of disease, the latest advances in neuroscience, or clinical studies in cancer, diabetes, heart conditions or stroke.

The NIHR Oxford Biomedical Research Centre (BRC) builds on these strengths as part of a national programme to invest in medical research, so its benefits can be quickly applied to the health service to improve diagnosis, provide better treatment and save lives.

It is a partnership between Oxford University Hospitals (OUH), one of the largest NHS acute teaching trusts in the UK, with an international reputation for specialist services and research; and the University of Oxford, consistently ranked as the world's best institution for medical teaching and research.

Established in 2007 as one of the five original BRCs, the Oxford BRC is in its third round of funding from the National Institute for Health Research (NIHR), a national body funded by the Department of Health and Social Care to accelerate NHS involvement in medical research. The BRC was awarded £113.7m for the period 2017 to 2022. This increased funding supports an expanded portfolio covering 20 research themes.

This programme of research is overseen by the NIHR Oxford BRC Steering Committee, which includes senior academic clinicians who review progress and provide guidance on scientific priorities. It reports to a Strategic Partnership Board comprising key OUH and University leaders who identify strategic goals.

This publication gives a flavour of our work and how it is transforming people's lives.

The Oxford BRC is the only NIHR BRC in the country to be certified to ISO 9001:2015 standard.

>6000
peer reviewed publications

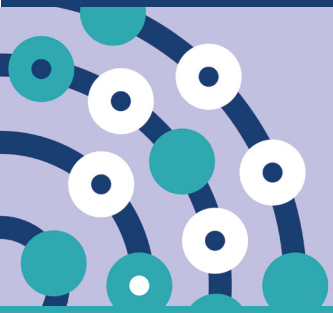
18
spin-out companies

>900
collaborations with industry (2013-2017)

£1.4 billion
external funding

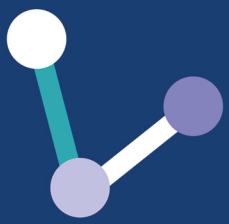
BENEFITS
for **NHS** patients

271
patents filed



>3500
NIHR academy members (student trainees)

≈4,000
research projects



>5 million
subjects recruited

Our research

Our research programmes are divided into 20 themes and take place across multiple sites, including OUH's John Radcliffe, Churchill and Horton General hospitals, and the Nuffield Orthopaedic Centre, as well as University premises throughout the city.

Oxford has one of the largest concentrations of biomedical expertise and infrastructure in the world, and the BRC benefits from a wide range of purpose-built research facilities at OUH and the University.

Research supported by the BRC flourishes because it is fully integrated with Oxford's major hospitals, which employ more than **12,000 staff** and have one million patient contacts a year. Across the city, and in particular Oxford University, **3,000 researchers** work in **50,000 m^2 of research facilities**, many of them situated on the hospital sites.

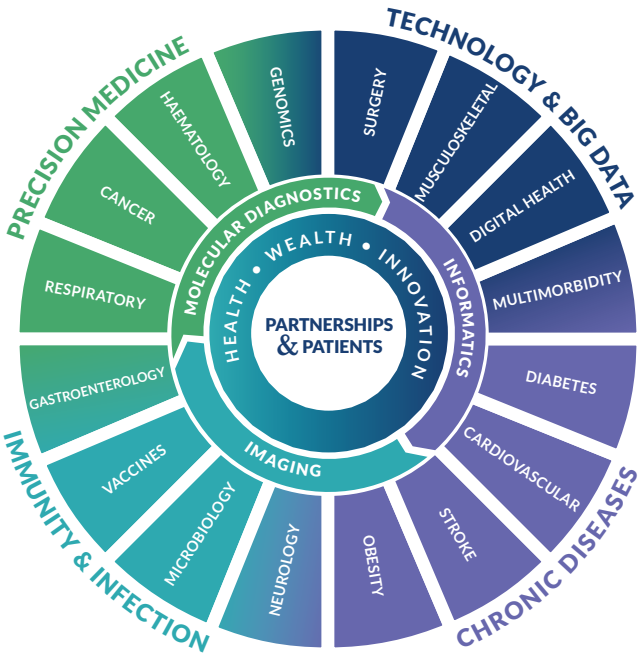
This co-location of world-class clinical and research facilities ensures that medical innovations can be quickly moved "from bench to bedside", out of laboratories, into clinical trials and on to the NHS care setting.

CHRONIC DISEASES
- Multimorbidity & Long-Term Conditions
- Diabetes & Metabolism
- Cardiovascular
- Stroke & Vascular Dementia
- Obesity, Diet & Lifestyle
- Neurological Conditions

IMMUNITY & INFECTION
- Gastroenterology & Mucosal Immunity
- Vaccines for Emerging & Endemic Diseases
- Antimicrobial Resistance & Modernising Microbiology

PRECISION MEDICINE
- Respiratory
- Multi-modal Cancer Therapies
- Haematology & Stem Cells
- Genomic Medicine

TECHNOLOGY & BIG DATA
- Surgical Innovation & Evaluation
- Musculoskeletal
- Technology & Digital Health



The University of Oxford's Medical Sciences Division is consistently ranked at the top of student satisfaction surveys and the excellence of its research is recognised by its top placing in international league tables and by ranking top for overall quality in the Research Excellence Framework, the Government's assessment of the quality of research in UK higher education institutions. OUH has the most highly-cited publications of any NHS Trust.

Many researchers share knowledge and resources across the BRC themes, so advances in genomics, for example, can be applied to other areas to provide the basis for better diagnosis and treatment.

Ensuring clinical trials are run quickly is vital to ensure successful research is swiftly adopted into the NHS and to attract outside investors, such as funding bodies and biotech companies.

> **"Oxford is an outstanding world-class biomedical and research training environment and the BRC is investing in tomorrow's new talent."**

Modernising Medical Microbiology

Making the digital hospital a reality

Research by the Oxford BRC has underpinned significant changes to how patients' vital signs are recorded. In all adult wards across Oxford University Hospitals bedside paper charts have been replaced with tablet computers through the System for Electronic Notification and Documentation (SEND) project.

Staff input vital signs, such as heart rate and blood pressure, into the tablet, which immediately provides advice on how to manage the patient's care and displays any deterioration in their condition, allowing clinical teams to prioritise those who need urgent attention. This information can be shared more quickly with clinical teams, including those working remotely, saving crucial time that was previously spent looking for and transporting paper charts.

The system, which is now being rolled out to paediatric and maternity departments, has already enhanced the clinical care of over 200,000 patients, and freed up nurses to deliver more care.

SEND is one of four products that have been licenced by Sensyne Health, as part of an agreement with the University of Oxford and Oxford University Hospitals to commercialise clinically validated digital health products arising from BRC-funded research. All should result in significant improvements in health outcomes for patients and reduce healthcare costs in the NHS.

Other Sensyne licensed products use new technology to support and monitor patients outside hospital, reducing the number of clinics they need to attend. These include GDm-Health, a smartphone application that allows women with gestational diabetes to collect their own blood glucose measurements, which can be read in real time by clinical teams.

Similarly, the SUPPORT-HF project provided a tablet computer for heart failure patients to monitor and send data to clinicians about their blood pressure, heart rate and weight. This simple software, which allows patients to take control of their treatment from their own homes, is now being developed so it can be deployed more widely across the NHS.

The ordering of blood has improved considerably across OUH thanks to the BRC-supported Real-Time Blood Transfusion Data and Decision Support project. This provides the most recent blood results to clinicians when orders are made, and alerts them to inappropriate orders. It has been combined with an existing electronic transfusion process incorporating barcode patient identification and handheld computers at the bedside to verify the correct blood is transfused. This means the entire hospital transfusion process – integrated with OUH's electronic patient record system – is paperless, a first in the UK, and saves it £500,000 a year.

Scanning to predict heart disease

A new imaging technique that provides an early warning of coronary artery disease – and the risk of heart attacks – has been developed with Oxford BRC support.

Computed tomography angiography (CTA) is already a routine procedure, but half of all heart attacks happen in people who do not have the severe coronary disease the procedure detects. The new technique, which can be applied as a new feature in CTAs, identifies those patients who are at risk of heart attacks, allowing early preventative measures and improving the treatment of thousands of people living with the disease.

Coronary artery disease occurs when atherosclerotic plaques build up in the arteries that serve the heart, causing the vessels to narrow. When they block without warning they lead to a heart attack. Current diagnostic methods rely on detecting damage that has already been caused by these plaques, when the damage is irreversible and treatment options are limited.

The BRC-supported team has discovered a bidirectional communication between the heart arteries and the fat surrounding them. The fat surrounding these arteries 'senses' inflammation coming from the adjacent artery, resulting in altered fat composition.

The new imaging technology, called 'perivascular fat attenuation indexing' (FAI), tracks the changes in the fat surrounding inflamed arteries, even if plaques or narrowings are not visible.

Patient and public involvement

Working with patients and members of the public is a vital part of how the BRC functions and has a major role to play in its future.

Patient and public involvement (PPI) helps keep research relevant and accountable. The Oxford BRC is publicly funded, so it is important that the public has a say about how research is conducted and how the results are used. Some of the best research ideas come from patients telling us what matters to them.

The BRC invests significant resources in training the researchers it funds to work with patients and tapping in to the huge benefits public involvement can bring to their work. Our PPI team offers guidance, policies and resources, as well as discussing with researchers how patient involvement can improve individual projects.

We also work with our partner organisations, including other parts of the NIHR infrastructure, to offer advice and training to patients and members of the public who want to get involved and contribute to research projects. We provide training on topics as varied as understanding research jargon and statistics, or setting research priorities.

Our research themes often have a dedicated panel of patients to provide first-hand input on policies or the design of projects.

How genome sequencing is tackling disease

The University of Oxford, with considerable support from the BRC, has become an important centre in the fight against drug-resistant disease, in particular for its work using whole genome sequencing (WGS) to identify different strains of tuberculosis. Using WGS, diagnosis can be achieved in a day, whereas current methods can take a month.

In 2017, working with Oxford BRC, Public Health England (PHE) launched the first national microbiology service in the world to use WGS routinely. Together, as part of a worldwide collaboration called CRyPTIC, they demonstrated how our understanding of TB's genetic code is now so detailed we can predict which commonly used anti-TB drugs are best for treating a patient's infection and which are not.

The study revealed an unparalleled accuracy in predicting the susceptibility of the bacterium to anti-TB drugs, raising the prospect of quicker, cheaper and more accurate diagnoses for a disease that claims 1.5 million lives each year.

Such is Oxford's pre-eminence in the field of antimicrobial resistance (AMR) that the BRC was awarded £1.8m in capital funding by Department of Health and Social Care to purchase state-of-the-art equipment to boost its work in this area. This included long-read sequencers and powerful computers to analyse the results, and flow cytometers and robots for extracting DNA and RNA, which allow researchers to accelerate the development of vaccines and monoclonal antibodies to combat AMR.

To sleep, perchance to … improve mental wellbeing

Alongside air, water and food, sleep is one of the essentials of life. Yet 10 to 12 per cent of the population don't get enough of it due to insomnia, and disturbed sleep is known to be an important factor in many neurological and mental health conditions.

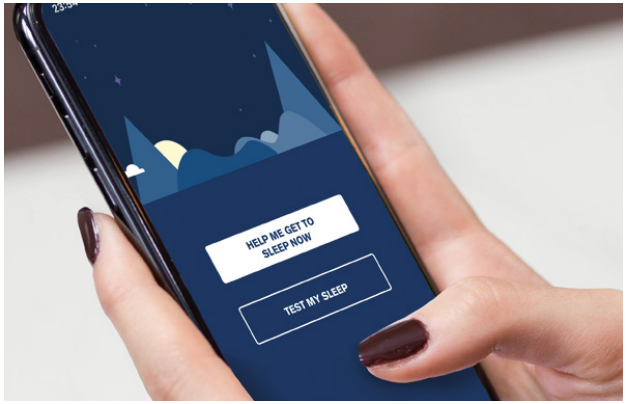
While cognitive behavioural therapy (CBT) has been shown to be an effective way of breaking the vicious cycle between negative thoughts and emotions and poor sleep, there are not enough trained practitioners to meet the demand from people who would benefit.

Oxford BRC-funded researchers from the University of Oxford's Nuffield Department of Clinical Neurosciences carried out the largest research trial into whether digital CBT – accessed via smartphone or tablet – could help tackle insomnia.

During the 12-month trial, this dCBT approach was shown to help more than 75% of insomnia sufferers achieve normal sleep, leading to an overall improvement in wellbeing, mental health and quality of life.

In October 2018, the Sleepio app became the first NHS roll-out of direct-access digital medicine. Initially it was made available in Berkshire, Buckinghamshire and Oxfordshire, before being rolled out across other parts of the South East in 2019.

The app, which aims to reduce an over-reliance on medication, works by helping people to discover their ideal personal sleep pattern and overcome the 'racing mind' that so often prevents people from sleeping.



Vaccines

Oxford is the only BRC with a vaccine-manufacturing capability, a position that was further enhanced in December 2018 when the UK government announced a £66m investment in the UK's first-ever dedicated Vaccines Manufacturing Innovation Centre, to be based in Oxfordshire not far from the University of Oxford's Jenner Institute. The new centre will lead efforts to tackle diseases such as Ebola and Lassa fever, as well as boosting the growth of the UK's life sciences industry.

Global attempts to combat influenza took a step forward when Oxford BRC researchers launched the world's first widespread human testing of a universal flu vaccine among NHS patients.

Flu kills up to 500,000 people a year, many of them elderly or vulnerable, and the team from the Jenner Institute are recruiting 500 people aged over 65 in the Thames Valley to test the vaccine.

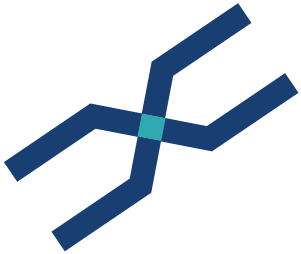
It is believed the vaccine will offer a stronger protection against Influenza A because it uses a different mechanism to get the body to protect against the virus. Where the current vaccines use surface proteins – which, like the virus itself, change every year – to stimulate the body's immune system to produce disease-fighting antibodies, the new vaccine uses the core proteins, which remain virtually unchanged in different strains, allowing researchers to create vaccines that will work against all of them.

Crucially, the new vaccine stimulates the immune system to boost influenza-specific T-cells, instead of antibodies, that kill the virus as it tries to spread through the body.

A new typhoid vaccine that is safe and effective for adults and children has been evaluated in Oxford. The trial was carried out by Prof Andrew Pollard, the Oxford BRC Co-Theme Lead for Vaccines. The BRC funded the initial work on the human challenge model in 2011.

Children are particularly susceptible to the disease, but current vaccines do not confer lasting immunity in children, or come in inappropriate formats. Now, for the first time, children under the age of two will be protected, prompting the hope that the disease can be held back in the countries where it claims the most lives.

Researchers tested the Vi-TT vaccine in a controlled human infection model, which involved 112 participants consuming a drink containing the bacteria. The vaccine's effects have now been assessed in 100,000 children in African and Asia.



Collaborating with industry

Commercialising innovation to bring it to more patients

An important priority for of the Oxford BRC is to work with the life sciences industry, which is well-established in Oxford, to develop and commercialise the medical breakthroughs we fund to ensure they benefit as many NHS patients as possible.

BRC staff work closely with the University of Oxford's Business Development and Research Services offices and the Oxford Academic Health Science Network (AHSN) to foster that engagement with industry.

As well as its fruitful relationship with Oxford University Innovation (OUI), the BRC's partnerships with industry range from programmes with small and medium-sized enterprises to large strategic collaborations with pharmaceutical companies in drug discovery research and clinical development. The BRC has worked with more than 50 companies to get products or services at a stage where they can be offered to the NHS and international health systems.

The BRC has helped to fund major collaborations with large blue chip companies, including McLaren Applied Technologies in surgical simulations, training and outcomes; Illumina and Oracle in whole genome sequencing and analysis for rare inherited diseases and cancers; and Complete Genomics in chemotherapy resistance monitoring.

The BRC builds and maintains a dialogue with industry through promotional activities at industry conferences, as well as organising Technology Showcases with our colleagues at OUI and the AHSN, which attract leading scientists, entrepreneurs and healthcare professionals to network and explore opportunities to commercialise innovations in fields such as precision medicine, digital health or therapeutics.

Our Academic Industry Meeting (AIM) days, on topics such as biomedical imaging or anti-microbial resistance, bring academic researchers, industrial representatives and clinicians together to identify areas of common interest and potential collaboration.

A crucial element in the Oxford BRC's engagement with the life sciences industry is Oxford University Innovation (OUI), a wholly-owned subsidiary of the University of Oxford that oversees the University's technology transfer and consulting activities.

Innovations OUI has commercialised include medical devices, drugs and vaccines, diagnostic equipment, patient monitoring tools and digital applications across clinical themes as varied as dementia, cancer, diabetes, and infectious disease.

OUI helps BRC-funded researchers to apply their expertise and research for wider social and economic benefit, by forging links with partners who can commercialise their innovation for the benefit of wider society, and especially for NHS patients.

With its commercial know-how, for example in the field of protecting intellectual property, OUI has helped to set up at least 12 spin-out companies that originated with BRC-funded research. Much of the income generated goes back into supporting research at the University.

Among the spin outs are:

Ultromics – uses artificial intelligence alongside a large imaging database to improve diagnosis of coronary artery disease.

Oxehealth – the first joint spin-out company from the University and OUH, on a project to monitor and analyse patients' vital signs remotely using conventional digital cameras.

Vaccitech – a spin-out from the University of Oxford's Jenner Institute, developing T cell-inducing vaccine products; its trials include a universal influenza vaccine and a vaccine for prostate cancer.

OrganOx – has developed new technologies to preserve organs for transplant at room temperature, reducing tissue deterioration and so increasing the number of organs suitable for transplantation.

Gene therapy to halt sight loss

Oxford BRC has been at the forefront of attempts to treat sight-loss conditions using gene therapy.

A trial, led by Prof Robert MacLaren, to tackle choroideremia, a rare genetic cause of blindness, has shown positive results in terms of visual acuity gains across patients taking part.

The trial, which began in 2011, involved 14 patients at the Oxford Eye Hospital receiving a single injection into the back of the eye of a virus containing the missing gene.

By the end of the study, published in 2018, there was a sustained gain in vision across the group of patients as a whole. A similar trial is being carried out with patients who have a more common form of blindness, retinitis pigmentosa.

Now gene therapy is being deployed against the UK's most common cause of sight loss, age-related macular degeneration. Prof MacLaren carried out the first procedure designed to correct the underlying gene defect in a new Phase 1 trial in January 2019.

Rather than 'curing' the condition, it is hoped the gene therapy will halt the progress of the disease, meaning that in future, early intervention might stop the disease before an affected patient experiences significant vision loss.

Oxford's research in retinal gene therapy has led to the creation of a spin-out company, Nightstar Therapeutics, which was floated as a publicly traded company on the NASDAQ stock exchange in September 2017 with a market capitalisation of around $600m.

Over 50,000m² of research facilities

The Botnar Research Centre

The Wellcome Centre for Human Genetics

Old Road Campus

John Radcliffe Hospital

The Big Data Institute

Partnership working

Oxford is one of the most research-active communities in the world and home to a significant knowledge base, comprising the universities, health services and life sciences industry.

Working with partners, the BRC is able to harness this expertise to drive forward innovation in healthcare research. Itself a collaboration between a major acute NHS trust and a world-leading centre for healthcare research, the BRC benefits from being at the centre of a major hub for healthcare innovation.

It works, through the Oxford Academic Health Science Centre (AHSC), with Oxford Health NHS Foundation Trust, which provides mental health and community services, and with Oxford Brookes University. The AHSC coordinates clinical and academic excellence within and between the partners, and with other key stakeholders in the Thames Valley region, to tackle today's major health challenges.

Our collaboration with Oxford Health NHS Foundation Trust will continue to grow after the Trust was awarded a BRC in adult mental health, older adults and dementia, and precision psychological treatments in 2017.

The BRC is part of a network of other NIHR organisations, collaborating on projects and sharing resources and expertise. These include NIHR CLAHRC Oxford, which carries out ground-breaking applied health research in the Thames Valley region, and the NIHR Medtech and In vitro diagnostics Co-operative (MIC) Oxford, which works to identify emerging in vitro diagnostic technologies to improve the way disease is diagnosed in NHS primary care settings.

The BRC also works closely with the NIHR Clinical Research Network: Thames Valley and South Midlands, which provides the practical support – such as offering training and support to NHS professionals – to allow high-quality clinical research to take place in the local NHS.

The Oxford Academic Health Science Network (AHSN) plays a key role in ensuring that BRC-funded research is put into clinical practice by bringing together universities, industry and the NHS. The AHSN, which aims to improve health and prosperity in the Thames Valley, has helped to roll out BRC-supported research such as a hospital electronic blood transfusion management system and a smartphone app for pregnant women with diabetes to monitor their blood sugar level.

Working with healthcare partners around the country is vital and includes collaborations with four other BRCs to provide an experimental medicine approach to new HIV strategies and a multi-centre clinical trial for gene therapy to halt or reverse rare sight-loss conditions.

Sharing healthcare data to underpin the highest quality research is an increasingly vital component in future innovations, and Oxford is one of five BRCs to contribute data as part of the NIHR Health Informatics Collaborative to support studies into viral hepatology, acute coronary syndromes, ovarian cancer, renal transplantation and critical care across the BRCs.

The BRC also works with UK and European funding bodies to source extra investment for development and has brought in more than £1bn in external funding since its inception in 2007, significantly boosting the effectiveness of the investment from the NHS.

Is shoulder decompression surgery really necessary?

How effective is shoulder decompression surgery, a common treatment for impingement? BRC-funded research found that the clinical benefits of this procedure were no more effective than having no treatment at all.

The surgery is carried out on 21,000 people each year in the UK, but the research, led by Prof Andy Carr, head of the BRC's Musculoskeletal Theme, found that a placebo was just as effective at relieving pain.

The findings suggest that for some types of elective surgery, the benefits can be explained to some extent by patients' expectations that their symptoms will improve after treatment.

It also opens a debate as to whether some expensive or risky procedures should undergo the same kind of rigorous testing that drugs are required to pass.

Improving our understanding and treatment of long-term conditions

One of the UK's biggest healthcare challenges is people living with a number of chronic conditions. Those who experience cardiovascular problems are also likely to suffer from obesity, hypertension, respiratory conditions or depression.

There is, therefore, huge value in conducting long-term, large-scale studies which can track how healthcare needs are changing for individuals and for the population as a whole.

The Oxford Vascular Study (OxVasc) is one such study. Started in 2002, it is the first and only population-based study in the world looking at all acute vascular events, such as strokes and heart attacks, simultaneously in the same population. More than 10,000 people living in Oxfordshire have taken part in the study.

Working with a number of local GP practices, OxVasc has improved our understanding of these conditions, and how we can improve treatment for patients. Among other things, researchers have explored the incidence of vascular events, the role of hypertension in vascular conditions, the links between stroke and dementia, and whether certain genetic biomarkers make some people more susceptible to stroke.

Already the findings of OxVasc have resulted in a number of important changes to clinical practice, for example to guidelines around the world on how patients with TIAs (mini-strokes) are treated, reducing the risk of major stroke soon afterwards.

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Cover picture: Modernising Modern Microbiology

Further information visit:
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