NIHR/Wellcome Trust Birmingham
Clinical Research Facility
Activities and Highlights, 2014
The NIHR/Wellcome Trust Birmingham Clinical Research Facility (CRF) is jointly managed by University Hospitals Birmingham NHS Foundation Trust (UHB) and the University of Birmingham (UoB) and is located in close proximity to the Institute of Biomedical Research where many Clinicians and Scientists are based.

A brief history

2002 – Birmingham CRF established at the Queen Elizabeth Hospital Birmingham with funding from a Wellcome Trust Millennial Grant, as one of five pioneering research facilities across the UK

2008 – Funding awarded by Department of Health and Wellcome Trust to establish a paediatric CRF at Birmingham Children’s Hospital

2008 – Funding awarded by the Wolfson Foundation and the Wellcome Trust to expand the CRF to incorporate a gene therapy facility and metabolic testing suite

2010 – Health Research Bus commissioned as a ‘mobile’ CRF to enable research studies to be undertaken in the community under the governance of the respective NHS Trusts

2012 – Birmingham CRF awarded £12.8 million National Institute for Health Research (NIHR) Experimental Medicine Infrastructure funding, supporting the experimental research programme through to 2017

2013 – Opening of the Ground floor of the CRF at UHB, greatly increasing the capacity to deliver experimental research with an addition of six clinic rooms, four day-case beds and cardiac testing rooms.

2014 – Commissioning of the Advanced Therapies Facility (ATF)

2014 – Official opening of the Inflammation Research Facility, a satellite facility based in the new Queen Elizabeth Hospital Birmingham

September 2014
Summary of achievements 2014

This has been an exciting and challenging year for the Birmingham CRF - the research portfolio has increased, mirroring the expanded facility which now includes a functional Inflammation Research Facility (IRF) in the Centre for Translational Inflammation Research (CTIR) and the newly commissioned Advanced Therapy Facility (ATF), adjacent to the CRF and directly above the Tissue Biorepository (HBRC), which will deliver cell therapy and a clinical trials pharmacy.

The IRF will be officially opened on 19 November by Michael Atherton O.B.E. (ex England cricket captain), maintaining our tradition of a sporting theme for official openings as Gary Lineker opened the main CRF in 2002. The IRF has recorded over 1000 patient visits and new developments this year include the embedding of research clinics into the facility.

All these structures now come under the overarching governance of Birmingham Health Partners (BHP) - a partnership between University Hospitals Birmingham NHS Foundation Trust (UHB), Birmingham Children's Hospital NHS Foundation Trust (BCH) and the University of Birmingham (UoB) to provide strategic and scientific oversight of research across all three partner organisations. The CRF will play a complementary role to the Institute of Translational Medicine (ITM) which is due to open in 2015. The CRF will continue to deliver early phase and experimental studies while the ITM will focus on stratified medicine and cohort studies.

The CRF has also been instrumental in attracting additional research funding to Birmingham, for example £1.2 million funding from the NIHR Translational Research Collaboration for Rare Diseases (RD-TRC) paediatric cross-cutting theme (April 2013 to March 2017). The strong research infrastructure within BHP and the central location of the CRF and IRF facilitates complex research visits, research training and strong scientific and clinical oversight of research projects.

A key focus for the CRF is developing and supporting a strong programme of patient and public involvement (PPI) and patient and public engagement (PPE). Birmingham CRF is represented on the national UKCRF Network workstream whose aim is to develop a CRF PPI/PPE programme. Locally, the CRF links with specialty–based patient groups, for example within liver, diabetes, paediatrics and rheumatology to develop research protocols, patient information sheets and to review patient satisfaction. As part of our evolving public
Research is a core business of the NHS and integral to the improvement of patient outcomes. Non-medical clinicians need to be better equipped to undertake health care research and be inspired to be the research leaders of the future. Access to a placement in a clinical research facility gives interns the opportunity to see world-class research in action.

Prof Lorraine Harper, Head of Education, Birmingham Health Partners
Prof Fiona Irvine, Head of Nursing UoB

engagement strategy, we have designed an innovative programme of workshops for Sixth Form students that will provide the young people with an insight into clinical research and protocol development.

Educating the next generation of researchers continues to be a priority for the Birmingham CRF. The successful Academic FY2 programme which provides a unique Academic Medicine training opportunity for trainee doctors across the West Midlands Deanery has now run through the CRF for nine years. An exciting new programme to educate researchers from disciplines other than medicine is the West Midlands Clinical Academic Internship Programme, being run as a pilot with funding awarded by Health Education West Midlands (www.birminghamhealthpartners.co.uk/caip). Eighteen interns have been appointed to start in October 2014.
Research highlights

There are many exciting research developments taking place in the CRF, particular highlights in 2014 include:

**Early phase gene and immunotherapy research:** A key achievement this year has been the recruitment in October 2013 of the first patient to the gene therapy AdUP trial, a Phase I single site study which has taken ten years of intense pre-clinical work-up prior to the opening of the clinical stage. This complex study involved collaborating internally with several UHB departments (operating theatres, pharmacy, imaging and the Genetically Modified Safety Committee) and externally with the Cancer Research Clinical Trials Unit based at the University of Birmingham.

**Cardiovascular research:** The cardiovascular suite in the CRF now houses a variety of studies with funding from the Wellcome Trust, a British Heart Foundation programme grant and Industry. These studies are already providing comprehensive clinical data which will inform future research programmes.

**Metabolic studies:** A new experimental medicine project funded by the Academy of Medical Sciences is studying whether brown adipose tissue (BAT) can offer a protective effect against the onset of diabetes. This project, supported by Professor Mike Symond’s group from the University of Nottingham will be carried out in the CRF using new state of art thermo-imaging techniques to assess BAT activity. Potentially, this research could be very significant in understanding the processes by which the body breaks down sugars.

**Rare disease research:** The paediatric CRF has a strong track record of delivering complex clinical trials for rare inherited metabolic diseases. A current example of this is an early-phase industry sponsored clinical trial of a drug with potential use in severe forms of Long-Chain Fatty Acid Oxidation Disorders (local investigator - Dr Saikat Santra). Children and young people affected by the condition have defects in the metabolic pathway that converts fatty acids into energy, which result in deficiencies in energy metabolism. Many of the clinical complications are not controlled by current standard care. Alongside day-case visits supported by the CRF nursing team, the study also utilises the specialist exercise testing equipment in the CRF’s Metabolic Laboratory.

**Research clinics:** These are a key part of the CRF service and increase the number of patients being recruited to research studies. One example is the CANVAS study a three year PhD research project, funded by a Wellcome Trust Research Training Fellowship with the cost of the trial drug funded by Vasculitis UK. The study incorporates a small open-label randomised controlled clinical trial being run...
through the renal research clinic in the CRF. It aims to further investigate ways in which chronic cytomegalovirus (CMV) infection adversely affects the immune system and cardiovascular system in people with ANCA associated vasculitis. It also aims to provide proof of principle that treatment of chronic CMV infection with an anti-viral agent can ameliorate the negative effects of CMV on the immune system, with the potential to reduce the risk of heart disease and stroke for patients.

**Inflammation research:** In 2013/14 a bespoke room was equipped to carry out minimally invasive ultrasound-guided knee biopsy procedures on patients with inflammatory arthritis. This procedure, currently being carried out at only four UK centres, provides tissue samples of equivalent high quality to formal arthroscopy. The advantage to the patients is that it is a brief minor procedure with no requirement for rest or time off work and adverse events are extremely rare. The procedure has to be carried out in a high specification procedure room available in the CRF, which meets minimum requirements for numbers of air changes per minute. The ability of the CRF to perform this procedure has attracted two main research streams from the Medical Research Council and from industry partners interested in conducting high intensity early phase trials of new therapeutics in arthritis.
Vaccination studies: The CRF has collaborated with the Jenner Institute in Oxford on a series of studies to trial potential vaccinations against TB as alternatives for the BCG immunisation which now has limited efficacy. The vaccination is a genetically modified product currently injected in Oxford, but is planned to be delivered through the Advanced Therapies Facility (ATF) once it is fully operational, so the vaccinations can be given in Birmingham. The Birmingham CRF has been very successful in recruiting patients from the diverse local population.

Industry Sponsored Research: The CRF has supported the UK delivery of a complex Phase II industry sponsored clinical trial evaluating the safety, efficacy, and pharmacokinetics of enzyme replacement therapy in children under five years of age with Hypophosphatasia (HPP) a rare, inborn error of bone metabolism. HPP in infants is characterized by severe, refractory rickets, non-traumatic fractures, pulmonary compromise, and failure to thrive. This complex protocol has required significant support, including nursing outreach from the CRF. Building on this success, future studies in other disease areas. The CRF will deliver the Phase 1 (first in man) study of this project which is being run by Professor Ann Logan with funding from the Wellcome Trust Health Innovation Challenge.

The CRF provides a high quality, research orientated and highly patient focused environment for undertaking minimally invasive procedures in consenting patients and is vital to the continued success of this research programme. In particular the ability to book patients into a pre-existing session without having to compete with frequently overloaded NHS facilities is important.

Dr Andrew Filer - Principal Investigator
Research improving patient outcomes

Studies being carried out in the CRF have significant potential to improve patient outcomes in the future. Some examples are outlined below:

- A study being conducted by Dr Liz Sapey to identify the impact of administering statins to patients with pneumonia has the potential to transform the way in which patients with pneumonia are treated in the future and may improve outcomes for these patients. The role of the CRF is to provide governance, excellent research nurse support and the facility where patients can be seen.

- The large number of trials into new therapies for hepatitis C has resulted in a number of patient successes. In the ‘Turquoise’ trial 11 patients were randomised and cured of their disease whilst the ‘Sapphire’ trial also cured six patients. This could potentially have a very significant impact for patients with this previously incurable illness.

- The highly publicised anti-cancer treatment for malignant melanoma has received media attention and there are two related studies running in the CRF. Patients have benefited markedly from the treatment, with disease burden reducing dramatically during their first nine weeks of treatment. These trials have also shown benefit for patients with non small cell lung cancer.

- The development of a synthetic bioactivated membrane dressing has potential to significantly reduce scarring and improve outcomes for burns patients. The CRF will deliver the Phase 1 (first in man) study of this project which is being run by Professor Ann Logan with funding from the Department of Health and Wellcome Trust through the Health Innovation Challenge Fund.
None of the research carried out in the CRF could take place without patients being willing to participate in research studies; sometimes fully aware that the research is not going to benefit them directly but that it will make a difference to patients in the future. Therefore it is fundamentally important that patients have a good experience of their care in the CRF, that they feel well-looked after and that their participation in research is valued.

It is also important that patients are involved in how research studies are designed and the CRF is very active in working with investigators to encourage patient involvement at the early stages of protocol development. The newly formed Birmingham Rheumatology Research Patient Partnership (R2P2) is an exciting development actively involving patients in rheumatology research. Patient representatives of this group work with the project leads on specific projects and are engaged in the design, delivery and dissemination of research. http://www.birmingham.ac.uk/r2p2

The CRF is committed to collecting feedback from patients and their families on their experience of the CRF and taking part in research. Further plans are in place to ensure we build upon ways in which we gather feedback, using new technology to ensure we listen and respond quickly to the views of our patients.

“From the first day we arrived you have looked after my child and me, informed us, been a shoulder to cry on and supported us to give their injections safely……..We want to thank you for not only providing this outstanding treatment but for all the support you have given our family throughout our stay here in Birmingham” (Parent of Trial Participant)

I have been attending the clinical research unit at the Queen Elizabeth Hospital every three weeks since June 2013. On every occasion I have always found everyone working on the unit and associated with it friendly, courteous and professional. I have always been made to feel welcome and I have always felt that staff had a genuine concern for my health and general welfare. In particular the two nurses managing my treatment plan,….. have been particularly sensitive and sympathetic are consistently good tempered and have a ready sense of humour. I have spent a good many hours on the research unit and I have observed staff to treat all patients consistently, in the same professional, kind, courteous and well-tempered manner.

In summary, I am so grateful to have been referred to this research unit and so grateful to have been cared for by all the medical and nursing staff involved in my care. I would find it difficult to believe that I could have had better care anywhere other than the Queen Elizabeth. I can only describe my ‘patient experience’ in this research unit as first class. P.T.

“ I have been an outpatient at the [Birmingham] Clinical Research Facility for the last two and a half years and I have found all the nursing staff to be very accommodating and professional and willing to do all they can to make my visits as comfortable as possible. They are very caring and I have always felt able to trust them with any concerns I have as well as in delivering my treatment. There have been times when I have had other health queries and issues not related to the trial and the nursing staff have helped me with those, too. I would definitely recommend the CRF to anyone else taking part in a clinical trial or who is interested in clinical research. F.L.

The CRF is committed to collecting feedback from patients and their families on their experience of the CRF and taking part in research. Further plans are in place to ensure we build upon ways in which we gather feedback, using new technology to ensure we listen and respond quickly to the views of our patients.

Patient experience of the Birmingham CRF
Activity: April 2013 to March 2014

The activity of the CRF is measured in different ways and is reported annually to the NIHR. There are **quantitative** reports which include numbers of patients seen, length of visits, type and phase of research studies; **qualitative** reports which include data on publications arising from studies and the impact that the research is having on patient care and **financial** reports detailing how the NIHR grant is being used.

**Patient visits**
The numbers of patient visits are shown in Table 1. Telephone visits are recorded only where they take place as part of the research study protocol and as such, are used more as a source of data collection in adult rather than paediatric research.

Table 1
**Number of patient visits to the CRF, across both sites**

<table>
<thead>
<tr>
<th></th>
<th>Outpatient (&lt;4hours)</th>
<th>Day patient (4-8 hrs)</th>
<th>Inpatient / overnight (8+ hours)</th>
<th>Telephone</th>
<th>Laboratory</th>
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<tbody>
<tr>
<td>UHB</td>
<td>8097</td>
<td>1196</td>
<td>267</td>
<td>397</td>
<td>39</td>
</tr>
<tr>
<td>BCH</td>
<td>1899</td>
<td>543</td>
<td>103</td>
<td>28</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Occupancy**
For 2013/14, the average percentage occupancy figures are 39 percent for UHB (an increase of 5 percent compared with 2012/13) and 29 percent for BCH, reflecting that some high intensity paediatric studies have recently transitioned back into standard care. These figures are comparable with other research facilities nationally.

**Health category of studies**
Figure 1 below shows the percentage of studies carried out in each speciality and across both sites, as identified by the UK Clinical Research Collaboration health category definitions. Figure 2 shows the breakdown of studies by phase or type of research.

![Fig.1 Health Category of Studies](image)

![Fig.2 Study Type](image)
Types of research
The CRF is multi-specialty and receives funding from NIHR specifically to carry out Experimental Medicine research. However, funded later phase studies which have an experimental element or complex visits which cannot be accommodated elsewhere in the Trust will also be considered. The CRF staff work closely with UHB Research and Development teams to ensure research projects are carried out in the most appropriate setting. Please note that the CRF space is dedicated research space, so it is not appropriate for any NHS service work to be undertaken in the facility.

Facilities
The CRF has multi-purpose generic rooms which include clinic rooms, inpatient beds, outpatient rooms, day-case facilities and meeting rooms. Specialist rooms include a metabolic studies area, endoscopy suite and high specification isolation rooms.

Specialist equipment includes:
- iDexa bone density and body composition scanner
- endoscopy equipment
- iE33 ultrasound scanner
- moxus (UHB) + Oxycon Pro(BCH) indirect calorimeters
- exercise bikes and treadmill
- procedure rooms for biopsies and invasive procedures
- sample processing laboratory
- tissue culture laboratory
- pQCT scanner and jump force plate
- sphygmocor (non-invasive cardiovascular testing)

The Health Research Bus is a mobile clinical research facility which enables research in the community. It is equipped with a bone density scanner, clinic rooms, and sample processing laboratory.

Application process to use the CRF
All research projects running through the CRF must be approved by the Scientific Advisory Committee (SAC) which reviews the study for scientific merit. This approval is required to make use of CRF facilities, staff, equipment or laboratories. It is advisable for investigators to contact the Clinical managers to discuss the feasibility of a study prior to an application being made to the SAC.

SAC application forms are available on the website, www.research.uhb.nhs.uk/crf along with meeting dates, deadlines and a list of the relevant supporting documentation that is required.
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