Leading the way on delivering Haemophilia studies for Industry

The NIHR Clinical Research Network deliver for Haemophilia

Haemophilia is a rare disease affecting about 6000 people in the UK. Recently, many new treatments for haemophilia have been developed resulting in the need for many competing studies to be performed in the UK simultaneously. Delivery of these studies, on time and to target, has been successfully coordinated by the NIHR Clinical Research Network.

The importance of Haemophilia research
Haemophilia is a bleeding disorder that leads to recurrent spontaneous bleeds into joints and muscles. These bleeds lead to progressive musculoskeletal disability affecting quality of life and ability to attend school and work. Treatment is with intravenous clotting factors (factor VIII and factor IX) and can mean frequent visits to hospital. In the past many patients were infected with hepatitis and HIV because they were treated with pooled blood products contaminated with these viruses.

To preserve musculoskeletal function treatment is now given prophylactically to prevent bleeds. This is effective but very expensive (cost in UK for factor VIII is about £150M per year). Since treatment has been made safe from infection by the introduction of recombinant clotting factors, new clotting factors molecules are being investigated to see whether longer acting agents can be used to reduce the number of infusions a patient needs whilst maintaining good clinical outcomes. These are the main focus of studies on the NIHR CRN National Portfolio at the moment.

Some patients develop inhibitory antibodies to their clotting factor making them resistant to conventional treatment. A number of new products are being trialed to circumvent this problem. About 25% of the Haemophilia studies on the National NIHR CRN Portfolio concern these products. These new products will inform us how to modify our management and could have a huge benefit to Haemophilia sufferers and their families as well as potentially saving millions of pounds.

Haemophilia is a rare disorder and all patients attend a small number of treatment centres coordinated by the UK Haemophilia Centre Doctors’ Organisation (UKHCDO). This means that all patients potentially eligible for studies are already known to investigators and this is a major advantage to sponsors when using the NIHR CRN (Network) to support their studies.

Challenges of delivering Haemophilia research
The main challenges to the delivery of Haemophilia research is the rarity of the disorder and resulting lack of patients available to support the research required for the large number of new products that are in the pipeline. Studies often requires patients when they are first treated with any clotting factor. These studies therefore involve young children often aged less than 2 years. These patients are very rare (about 40 a year in the UK) therefore recruiting to these studies is particularly challenging particularly as the blood sampling schedule can be demanding for small children. Also the safety and efficacy of current treatment makes involvement in clinical trials a difficult choice for many families of affected children and this is another contributing factor to the recruitment success rate for these studies.

The NIHR CRN can provide the necessary support to ensure a successful outcome for a haemophilia clinical research study and it is recommended that due to the aforementioned challenges associated with conducting clinical research on patients with this condition to utilise a specialist centre who will have the expertise and access to the population if they are available.
The UK is leading the way
The UK leads the way for Haemophilia research due to an outstanding UK-wide coordinated system for clinical care, a strong history of research delivery and the resources of the National Haemophilia Database. This clinical infrastructure has worked collaboratively with the NIHR Clinical Research Network to deliver multiple and competing studies simultaneously. The Non Malignant Haematology Specialty Group and Medicines for Children Network both part of the Clinical Research Networks work jointly to support the delivery of Haemophilia studies.

History of delivery Haemophilia studies
The UK has a strong history of involvement in new treatments in Haemophilia. Early use of cryoprecipitate and plasma derived FVIII concentrate was followed by recombinant FVIII and IX following the HIV and Hepatitis C epidemics. Many Comprehensive Care Centres in the UK have been involved in clinical trials from an early stage. The NIHR UK CRN has helped other centres to become active in research.

There is a strong ethos of continuing to improve safety and the patient experience underpinned by an enthusiastic patient support group, the Haemophilia Society and coordinated clinically by The United Kingdom Haemophilia Centre Doctors’ Organisation.

Since 2011, eleven Haemophilia studies have been completed through the network, ten of which involved children.

Robust Feasibility and helping delivery
The UK is the only country in the world that has a comprehensive National Haemophilia Database. All patients with Haemophilia in the UK are registered along with demographic details, where they are treated and what treatment is being given. Furthermore, data are collected on all patients every three months so an up to date dataset is available.

This means that the Non Malignant Haematology Specialty Group and the National Haemophilia Database can look at study inclusion/exclusion criteria and within 24-48 hours identify the approximate number of potentially eligible patients in the UK, where they are treated and whether those centres are already undertaking completing studies.

Feasibility of all Haemophilia studies coming to the networks is determined by a combination of Specialty Group and the National Haemophilia Database ensuring robust, evidence based feasibility and realistic recruitment targets. This results in the delivery to time and target of Haemophilia studies through the NIHR CRN networks.

If a study is struggling to recruit the National Haemophilia Database can help to identify new potential centres. This has allowed multiple competing studies to be successfully run in the UK simultaneously.

Collaborative working
The Non Malignant Haematology Specialty Group and the Medicine for Children Research Network have jointly worked with the National Haemophilia Database to ensure robust feasibility assessments and, with the support of MCRN and CLRN’s, study delivery. A UK wide network of clinicians through UKHCDO and the patient group The Haemophilia Society also supports trial delivery.

This collaborative approach has ensured the successful delivery of multiple, simultaneous and competing research studies.

The Non Malignant Haematology Specialty Group is committed to making a difference to industry sponsored Haemophilia studies. This has been achieved by combining existing UK-wide clinical networks and the resources of the National Haemophilia Database with the NIHR CRN and allowed multiple, potentially competing studies, to be successfully undertaken simultaneously.”

“Utilising a collaborative approach with the Specialty Group, MCRN has been successful in collating sound feasibility from experts in this field resulting in excellent study performance, bringing benefits to patients in the UK.”