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Ethics approvals

The register was submitted for ethical approval in November 2012. Approval was given by the NRES Committee North East on 30 January 2013. This approval lasts for five years. Annual updates have been provided to the Committee as per the normal conditions for approval.

Overview of the FH paediatric register

As an electronic repository of data collected by UK clinicians about their FH paediatric patients, the long-term aims of the register are to monitor the effects of current and new FH treatments, to provide comparative audit data, and to provide anonymised patient data for valid research in the paediatric FH field. The register was established and funded by the Royal College of Physicians (RCP) from January 2012 to August 2014, and has subsequently been funded by the British Heart Foundation (BHF).
Oversight of the register

Executive Committee

Members of the Executive Committee were responsible for the on-going management and governance of the register:

- Professor Steve Humphries (chair), Professor of Cardiovascular Genetics, University College London
- Dr Uma Ramaswami, Consultant Metabolic Paediatrician, Royal Free Hospital
- Rhona Buckingham, Operations Director, Clinical Effectiveness and Evaluation Unit of the Care Quality Improvement Department, Royal College of Physicians
- Dr Mary Seed, Apheresis register...Job title?
- Kevin Stewart, Manager, Clinical Effectiveness and Evaluation Unit, RCP

The Executive Committee met in person in January and June 2014, and participated in regular telephone conferences throughout the year, to address on going and forthcoming issues affecting the register.

Steering Group

The Steering Group, again chaired by Professor Steve Humphries, was made up of the Executive Committee plus other register stakeholders, including paediatric metabolic clinicians and academics, the BHF, Heart UK and a paediatric FH family representative. The Steering Group met twice in 2014, in January and September, to discuss and agree on the on-going strategic and clinical direction of the register. (See Appendix 1 for meeting minutes from the 2014 Steering Group meetings).

Project management

pH Associates, an independent research healthcare consultancy, provided the day-to-day project management of the register, including facilitation of the Executive Committee and Steering Group meetings.
Data outputs and register exposure

Manuscript

Drafting of the first manuscript based on register data commenced in 2014 and it included demographic and clinical data from the first two hundred paediatric patients registered in the system. (Note: submission made in early 2015, title ‘The UK Paediatric Familial Hypercholesterolaemia (FH) Register: Preliminary Data.’, journal ‘Archives of Disease in Childhood’ [See appendix 2 for submitted manuscript].

Presentation at conferences

During 2014, outputs from the FH register were presented at the following meetings:

- RCPCH Conference, April 2014, Birmingham – results presented (Dr Ramaswami).
- The RCPCH workshop on 10 April was well attended. There were over 50 attendees at the lunchtime symposium. Questions were mainly relating to treatment in children and follow-up. We had two on-site registrations for the register. BIMDG conference, June 2014, Stirling – results presented (Dr Ramaswami)
- Heart UK, July 2014, Warwick - workshop session (Professor Humphries)

Linking to related websites

To improve targeted online exposure, the URL of the register’s homepage, along with a description of its aims, were added to the following related websites: RCP website (www.rcplondon.ac.uk/resources/audits/FH), and Heart UK website (www.heartuk.org.uk/policy-and-public-affairs/our-campaigning-partners/fh-implementation-team-fhit/other-fh-initiatives).

Communications with registered clinicians

A register newsletter was emailed to all clinicians registered on the system in June 2014. This newsletter edition featured information on upcoming events where register results were being presented, presentation summaries from the recent RCPCH conference, and a reminder about the free genetic testing available to clinicians with registered patients on the database.

Register homepage

In 2014 the register’s homepage was updated to include an excerpt from a short FH family story and this was visible to any visitors to the website. The summary, highlighting the importance of having an information source on FH children so that UK clinicians could make sound and informed clinical decisions about patient care, was designed to increase awareness of the register and encourage clinician/patient registration.
Data capture tool

Registrations

By the end of 2014, the number of clinicians registered on the database was 77 (including four new sites in 2014). The number of paediatric patients registered was 240 (including 80 new registrations in 2014), and the number of patients with at least one annual update form completed was 130.

System improvements

Following clinician feedback and thorough internal testing of the data capture tool, a number of improvements were made to the electronic system to make it more user-friendly, which was identified as a key requirement for clinicians entering their patients’ data. These improvements included the removal of unnecessary restrictions on dates (years) and minimum/maximum data values that the system would accept, reference ranges being made clinically relevant for FH, and help text boxes being ‘cleaned up’ to ensure they were applicable and useful to the data fields.

Further system improvements planned include the facility to send auto-reminders to clinicians for completion of the annual update form once their patients have been registered on the system for more than one year.

Data entry support by BHF nurses

A total of 14 BHF-funded nursing posts in 11 sites in England were created and filled in 2014, with their key role being to perform cascade testing for known mutations, and to enter data from paediatric patients (newly diagnosed and existing patients) into the register. This additional data entry support was identified as a positive step for encouraging data entry into the register, and freeing up valuable clinician time for clinical activity. (Note: BHF funding may be extended in 2015 to include the enrolment of more nurses who could assist with data entry into the register- to be confirmed).
Quality Accounts list

The register’s inclusion on the Quality Accounts list (National clinical audit of the management of FH) was considered by the Executive Committee in 2014. While it was agreed that inclusion on the list would provide greater prominence to the register, adherence to one of the eligibility criteria (requirement of comparative reporting between registered centres), meant that due to low patient numbers and the incumbent risk to individual patient confidentiality, it was decided not to go ahead.

Future of the register

The Executive Committee is committed to ensuring the continuing success of the register so that it fulfils its aim of being a robust dataset in order to inform clinical decision-making, and drive high quality research in the field of paediatric FH. To that end, the register is planned to be transferred from its existing host, the RCP, to the National Institute for Cardiovascular Outcomes Research (NICOR) in 2015.

Transfer to NICOR

As part of the National Centre for Cardiovascular Preventions and Outcomes, and sitting within the Institute of Cardiovascular Science at UCL, NICOR is considered to be an ideal host for the register, especially given its experience with electronic databases and established IT support systems in place.

It is anticipated that with BHF-funding secured until 2016, the register is in a suitable position to be accepted into NICOR during 2015, with the hope that NICOR would then provide funding once the register was established in its new home.

Being hosted by NICOR provides the potential opportunity to modify and finesse the data capture tool further, making it even more user-friendly. For example, one potential major improvement would be the introduction of a facility to batch upload data into the register from existing data sources, such as the PASS system. This would prevent much duplication of data entry effort and save time, and would be expected to increase the quantity of patient data entered into the register overall.
Appendix 1: Steering Group meeting minutes

Minutes of FH Steering Group meeting 20 January 2014

Present
Prof Steve Humphries (Chairman)
Dr Peter Dale
Mr Slade Carter
Dr Anupam Chakrapani
Ms Judy O'Sullivan
Dr Uma Ramaswami
Dr Mary Seed
Mrs Shrooti Thakerar
Prof Andrew Neil
Mrs Amanda Pulfer (amanda@phassociates.com)
Ms Anna Bishop-Bailey (anna@phassociates.com)
Mrs Helen Cardy (helen@phassociates.com)
Dr Peter Robinson (by telephone)
Dr Nigel Capps (by telephone)

Apologies
Dr Kevin Stewart
Prof Neena Modi
Ms Rhona Buckingham
Dr Jyotsna Vohra

Publication of data
Steve and Uma have written the abstract based on the results of 100 children registered. The group discussed where a manuscript should be published.
It was agreed that it should be submitted to Archives of Disease in Childhood journal. In addition a free online journal should be considered.
The data should be available on:
• Heart UK website
• Register website so that patients can access it
• Summary article for the BHF

Family stories
Slade is in current communication with a patient who may be able to provide a story appropriate for inclusion on the website (i.e. to highlight the benefits of registering and encourage patient interest). Judy suggested that BHF nurses may also be in touch with patients who could contribute.

Other opportunities for publicity
Slade is working alongside Mary on articles on FH for a primary care audience; reference is made to paediatric FH. It was suggested that it would be appropriate to include a box containing text regarding the register and with a link to the abstract when available.
Action: Steve to contact Slade re provision of text.
**Clinical lead progress report**

Uma confirmed that it has been proposed that Homozygous FH is included within the highly specialised commissioning services. The outcome of this recommendation is pending. There are 48 cases of known Homozygous FH (adult and child). Heterozygous FH is too common to be included within the Highly Specialised commissioning services.

**BIMDG conference in Stirling – June 20 2014**

Uma and Steve have been invited to attend to discuss the register.

**Scotland**

Dr Peter Robinson has agreed to be part of the Steering group on behalf of Scotland. He explained the current situation in Scotland to the group.

Peter is a metabolic paediatrician in Glasgow. There are currently three metabolic paediatricians in Scotland although one is to move to work in Manchester imminently. He works with Dr Alison Cozens who is based in Edinburgh. They are around 40 paediatric FH patients in Glasgow. Peter raised some concerns regarding recruiting patients into the paediatric FH register since there are already two databases which require similar information to be recorded for these patients in Scotland. He feels that entering data into a third database may be too much of a duplication of work for colleagues. He also raised the challenges associated with governance approval at local Health Boards.

pH confirmed that the ethical approval given covers Scotland so there would not be a need to resubmit. In addition the register is exempt from local board approval. Peter would need the ‘buy-in’ from local colleagues however.

Peter would like to read all documentation regarding the register including the approvals.

**Project progress report**

It is recognised that improvements to the database are necessary. Preparatory work has started and there will be a meeting on 20 Feb 2014 to discuss improvement to the paediatric FH register database with Paul Cripps. Peter Dale has documented some problems with data entry into the site.

**RCPCH conference**

There is a need to publicise the fact that there will be a workshop on paediatric FH at the RCPCH conference.

It was felt that there may be considerable interest among delegates and the team should check on the capacity of the room for the workshop.

The session will be promoted through the next edition of the register newsletter and it is hoped via flyers in delegate bags.

**Hope video and leaflets**

Steve has secured funding to convert the US Hope film into a British version. This is ongoing.

Uma is working on the production of leaflets aimed at children alongside Heart UK. They will be aligned to the Hope film. Two leaflets are being produced, one for children aged eight and under and another for those older than eight years.
**Quality Accounts list – National clinical audit of the management of FH**

Steve explained to the group that inclusion in this list is something that would give the register more prominence. Three of the four requirements for inclusion are met, however in order to be eligible there will need to be some comparative reporting. It was agreed in principle that it would be a positive thing for the register to be included but that we need to ensure that patient confidentiality is maintained during reporting due to the small numbers of patients. Various mechanisms for maintaining confidentiality were discussed.

**Budget**

Currently the register is funded until February 2015. The BHF has been approached for funding support for an additional period. A formal proposal will be required by the BHF for register funding. It will be submitted to Catherine Kelly. In the first instance a short document including a summary of the project, the reason the funding is required and an exit strategy should be submitted to Judy in advance of meeting on February 28 2014.

**AOB**

**Database issues**

It was agreed that retrospective patients should be added to the register but a few changes may need to be made on the database to allow this (e.g. date of diagnosis). Once these changes have been made then the opportunity to add these patients will be communicated to the registrants.

Peter Dale questioned whether there was a need to record birth weight in the database since it is often not in the notes and difficult data to obtain. It was agreed that birth weight was important and should be included.

It was suggested that the database proforma could be printed out and given to patients to complete in the waiting room whilst they wait for their appointment. They may be able to answer some of the questions needed for the database that are difficult to obtain by other means e.g. birth weight, gestational age.

Parents’ lipid levels – it was agreed that a ‘n/a’ box could be added to this field.

Peter also noted various other queries relating to help messages and reference ranges – these have been noted and will be taken to the meeting with the database manager in February 2014.

**BHF funding FH nurses**

Judy confirmed that 11 FH nurses have been funded around the country. These nurses will be based in Bristol, Southampton, Royal Free, Guys and St Thomas’, The Brompton, Manchester, Sheffield and Sunderland. Recruitment should be completed by April/May.

This should lead to an increase in paediatric FH patients being identified.

Further nurses may be funded in the future.
Minutes of FH Steering Group meeting 30 Sept 2014

Changes to Steering group members
Jules Payne (Chief Executive HEART UK) will replace Slade Carter
Jo Whitmore (FH nurse lead at BHF) will replace Judy O’Sullivan (BHF)
Anne Greenough (VP RCPCH) will replace Neena Modi
Shrooti Thakerar, patient representative, has left the Steering Group as she is now too busy. She will need to be replaced. Ideally the person will have FH themselves and have at least one child with FH.

Apheresis register
There are approximately 90 patients on the apheresis register currently. The group agreed that this register is not very well known and considered ways to increase its presence with clinicians. Options discussed included; presenting a paper at a paediatric symposium, and/or engaging with the British Paediatric Surveillance Unit (BPSU).

Database
Paediatric birth weight is a mandatory field in the database and many clinicians find it difficult to locate this information, particularly at the time of data entry. Group to reconsider whether these data are worth collecting. The group decided that we should analyse the data of the current 200 registered patients to find out whether birth weight indicates anything of interest.

Clinical lead progress report
Manuscript should be submitted to a journal with a broad circulation. Uma suggested that the BMJ be considered.
BIMDG meeting – the BIMDG would like to capture dietary data however this is not included in the FH database currently. Discussion to continue as to whether dietary data is something to include in the register in the future.
Management of FH guidelines – Uma to write these with the emphasis on how to treat FH. Once written they need to reach a wider audience.

2015 publicity/promotion
RCPCH conference – April 2015
The group agreed that we should re-run the same lunchtime workshop at the RCPCH conference next year. Also to look into whether we could get a stand and/or put our leaflets in the delegate packs. Possibility of having the HOPE video on a loop?
HEART UK conference – September 16-18 2015 at Royal College of Surgeons.
Nigel mentioned that the conference will be entitled ‘Lipids in the Community’.
Society for the Study of Inborn Areas of Metabolism
Anupam suggested that an abstract could be put to the SSIEM meeting 2015.
Increasing recruitment
An extra 24 patients have been registered since January 2014. Steve said that this was disappointing and the group considered how we can increase patient recruitment. Steve will write to all non-registering clinicians to remind them about the register and encourage participation.
It is hoped that the appointment of the BHF FH nurses will have a significant impact on recruitment if the technology permits.
Future of project

Quality Accounts list – national clinical audit of the management of FH

The Executive Group will discuss whether to pursue the QA list for 2015/16 at the next Executive group meeting and make a recommendation to the Steering group.

Budget

BHF funding started on 1 August 2014 for two years. Rhona is currently discussing the transfer of the project to NICOR and will update the group as this progresses.

The future

Group agreed that the register should be represented at the 2015 RCPCH and HEART UK conferences.

Consider submitting abstract to SSIEM.

BHF FH nurse training will take place on 8/9 December 2014. It may be possible that there is space for other nurses to attend. Jo to confirm how many BHF nurses will attend.

AOB

Covance research study – Steve has been approached by Covance to take part in a paediatric FH research study. Group agreed that Steve should request the protocol to share with the group.

The general feeling from the group was that we would not release clinicians names to Covance but could tell the registered clinicians to contact Covance should they wish to find out more about the study themselves.

Peter would like to find out how we can encourage parents/grandparents to put their children forward for testing. He has written a short article which we will put in the next register newsletter.

BHF NewsBeat magazine – Steve features in an article in the magazine.
Appendix 2: Submission of primary manuscript

Abstract

Background: The NICE 2008 Guidelines on the treatment and management of Familial Hypercholesterolaemia (FH) recommend that children with FH should be considered for statin treatment by the age of 10 years. The Paediatric FH Register was established in 2012 to collect baseline and long term follow-up data on all children with FH in the UK.

Methods: Paediatricians and adult lipidologists have been invited to enter baseline data on any child with a clinical diagnosis of FH using an electronic capture record. They are prompted annually to update records with regard to lipid levels, growth trajectory and any side effects of statin use if prescribed.

Results: Baseline data is on 232 children (50% boys, 80% Caucasian), with a mean age at diagnosis of 10.1 years (range 0-16 years), an untreated mean (+SD) total cholesterol of 7.61(+1.48)mmol/L and LDL-Cholesterol (LDL-C) of 5.67(+1.46)mmol/L. 63% had a family mutation recorded and 48% (111/232) of the children are currently treated with statin; these children were older, (mean age 13.7 v 11.6 years) and had stronger evidence of a family history of early coronary heart disease (CHD) in parent or first degree relative (28.4% v 19.0% p = 0.09). The diagnostic LDL-C in those subsequently treated was higher than in those not currently on statins (6.01(+1.46)mmol/L v 5.31(+1.37)mmol/L (p = 0.00007). In statin-treated children mean LDL-C level was reduced by 35% (2.07(+1.38)mmol/L) compared to a reduction of 5.5% (0.29(+0.87)mmol/L), p = 0.0001 in those not on statins.

Conclusions: The data indicates that treatment decisions on children are appropriately based on a stronger family history of CHD and higher LDL-C.
Contact details

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