Rare Inherited Anaemias Priority Setting Partnership

PROTOCOL March 30th 2016

Purpose

The purpose of this protocol is to set out the aims, objectives and commitments of the Rare Inherited Anaemias Priority Setting Partnership (PSP) and the basic roles and responsibilities of the partners therein.

Steering Group

The Rare Inherited Anaemias PSP will be led and managed by the following:

Patient representatives:

- Nick Meade/ Amy Hunter, Genetic Alliance UK
- Dominic Messenger, Diamond Blackfan Anaemia UK
- Elizabeth Blackmore, Congenital Anaemia Network
- Caroline Clifford
- Heather Paul
- Rachel Wearmouth

Clinical representatives:

- Dr Noemi Roy, Academic Clinical Lecturer & Haematologist, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, Oxford
- Professor Irene Roberts, Professor of Paediatric Haematology, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, Oxford
- Dr Jenny Welch, Consultant Paediatric Haematologist, Sheffield Childrens Hospital
- Dr Subarna Chakravorty, Consultant Paediatric Haematologist, Kings College London
- Dr Anu Rao, Consultant Haematologist, Great Ormond Street
- Carol Anderson, Anaemia Nurse Specialist, East Kent Hospitals NHS Trust

The Partnership and the priority setting process will be supported and guided by:

- The James Lind Alliance (JLA)
    - Sheela Upadhyaya, JLA Adviser
- NIHR Oxford Biomedical Research Centre (BRC)
    - Sandra Regan, Patient Involvement and James Lind Alliance Project Manager

The Steering Group includes representation of patient/carer groups and clinicians[1].

The Steering Group will agree the resources, including time and expertise that they will be able to contribute to each stage of the process. The JLA will advise on this.

Background to the Rare Inherited Anaemias PSP

The JLA is a project which is overseen by the National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC). Its aim is to provide an infrastructure and process to help patients and clinicians work together to agree which are the most important treatment uncertainties affecting their particular interest, in order to influence the prioritisation of future research in that area. The JLA defines an uncertainty as a "known unknown" – in this case relating to the effects of treatment.

Patients suffering from rare inherited anaemias may take years to arrive at a precise diagnosis, if at all. Lack of specialist knowledge, or poor access to the few centres of specialist expertise in these conditions, means that not all patients with these disorders will have access to the same standard of care. Often, lack of research into these rare disorders means that few treatments are available if at all, and even when there are treatments, there is inconsistent access to these for all patients across the UK and incomplete knowledge of when each treatment should be instituted. A PSP into rare inherited anaemias will provide an opportunity for uncertainties in the diagnosis and management of these conditions to be identified with a view to focusing research into these disorders.

Aims and objectives of the Rare Inherited Anaemias PSP

The aim of the Rare Inherited Anaemias PSP is to identify current uncertainties in the diagnosis, treatment, management and care delivery of people of all ages with rare inherited anaemias, and the impact on their families, from patient and clinical perspectives, and then prioritise those that patients and clinicians agree are the most important.

By Rare Inherited Anaemias, we mean:

- Diamond-Blackfan Anaemia
- Congenital Dyserythropoietic Anaemia
- Congenital sideroblastic Anaemia
- Red cell Membrane disorders
- Red Cell Enzyme disorders
- transfusion-dependent unexplained inherited anaemias

By people of all ages, we mean:

- children and adults, bearing in mind the possible implications of gathering data from young people;
- people who live in the United Kingdom, or whose questions are submitted in English and have UK relevance.

The extreme rarity of these conditions and the lack of equitable access to either diagnostic or treatment modalities for patients across the UK highlight the need to focus on what patients, carers and clinicians feel are the most pressing uncertainties regarding the care of these patients. One particular difficulty is the lack of adequate patient organisations representing these patients.

[1] In some cases, it has been suggested that researchers are represented at this level, to advise on the shaping of research questions. However, researchers cannot participate in the prioritisation exercise. This is to ensure that the final prioritised research questions are those agreed by patients, carers and clinicians only, in line with the JLA's mission.

Other inherited anaemias (such as Sickle Cell Anaemia, Thalassaemia and aplastic anaemias, including Fanconi Anaemia) are rare when considered in the context of the entire UK, and there is no doubt that there remain numerous treatment uncertainties for patients with these conditions. Nevertheless, patients with Sickle Cell Anaemia or Thalassaemia do not suffer the same delay in diagnosis as patients suffering from the other inherited anaemias and for those with Aplastic Anaemia the main clinical issues are part of a global bone marrow failure of which anaemia is a very small part. Patients with such anaemias would certainly benefit from a JLA PSP being carried out in their conditions, which might focus on the treatment uncertainties in each condition separately. Therefore, these are not included in the scope for the Rare Inherited Anaemias PSP, and the Steering Group has contacted the relevant organisations to inform them.

The objectives of the Rare Inherited Anaemias PSP are to:

- work with patients and clinicians to identify uncertainties in the diagnosis, treatment, management and care delivery of people of all ages with rare inherited anaemias, and the impact on their families;
- to agree by consensus a prioritised list of those uncertainties, for research;
- to publicise the results of the PSP and process;
- to take the results to funding bodies to be considered for funding.

NB. this PSP is being run alongside that on Musculoskeletal Rare Diseases in Adulthood, with shared data management, and there may be possible synergies on uncertainties that apply to all rare diseases.

Partners

Organisations and individuals in the United Kingdom will be invited to take part in the PSP, which represent the following groups:

- adults and children who have Congenital Dyserythropoietic Anaemia; Congenital sideroblastic Anaemia; Diamond Blackfan Anaemia; Red cell Membrane disorders; Red Cell Enzyme disorders; transfusion-dependent unexplained inherited anaemias

- carers of people who have Congenital Dyserythropoietic Anaemia; Congenital sideroblastic Anaemia; Diamond Blackfan Anaemia Red cell Membrane disorders; Red Cell Enzyme disorders; transfusion-dependent unexplained inherited anaemias

- medical doctors, nurses and professionals allied to medicine with clinical experience of Congenital Dyserythropoietic Anaemia); Congenital sideroblastic Anaemia; Diamond Blackfan Anaemia Red cell Membrane disorders; Red Cell Enzyme disorders; transfusion-dependent unexplained inherited anaemias

It is important that all organisations which can reach and advocate for these groups should be invited to become involved in the PSP. The JLA will take responsibility for ensuring the various stakeholder groups are able to contribute equally to the process.

Exclusion criteria

Some organisations may be judged by the JLA or the Steering Group to have conflicts of interest. These may be perceived to adversely affect those organisations' views, causing unacceptable bias. As this is likely to affect the ultimate findings of the PSP, those organisations will not be invited to participate. It is possible, however, that interested parties may participate in a purely observational capacity when the Steering Group considers it may be helpful.

As noted above in Aims and Objectives, by Rare Inherited Anaemias, we mean:

- Diamond-Blackfan Anaemia
- Congenital Dyserythropoietic Anaemia
- Congenital sideroblastic Anaemia
- Red cell Membrane disorders
- Red Cell Enzyme disorders
- transfusion-dependent unexplained inherited anaemias

Other conditions (such as Sickle Cell Anaemia, Fanconi Anaemia, Thalassaemia and aplastic anaemias) have not been included.

METHODS

This section describes a schedule of proposed stages through which the PSP aims to fulfil its objectives. The process is iterative and dependent on the active participation and contribution of different groups. The methods adopted in any stage will be agreed through consultation between the partners, guided by the PSP's aims and objectives. More details and examples can be found at www.JLAguidebook.org.

1. Identification and invitation of potential partners

Potential partner organisations will be identified through a process of peer knowledge and consultation, through the Steering Group members' networks and through the JLA's existing register of affiliates. Potential partners will be contacted and informed of the establishment and aims of the Rare Inherited Anaemias PSP

The Steering Group should draft the invitation, and an agreement should be reached as to the best organisation to distribute it.

2. Stakeholder awareness raising [2]

Stakeholder awareness raising will have these key objectives:

- to introduce the Rare Inherited Anaemias PSP;
- to identify potential partner organisations which will commit to the PSP and identify individuals who will be those organisations' representatives and the PSP's principal contacts.

3. Identifying treatment uncertainties

Each partner will identify a method for soliciting from its members questions and uncertainties of practical clinical importance relating to the treatment and management of Rare Inherited Anaemias A period of around 3 months, depending on response will be given to complete this exercise.

The methods may be designed according to the nature and membership of each organisation, but must be as transparent, inclusive and representative as practicable. Methods may include membership meetings, email consultation, postal or web-based questionnaires, internet message boards and focus group work.

Existing sources of information about treatment uncertainties for patients and clinicians will be searched. These might include DCSH and other national guidelines, and can include question-answering services for patients and carers and for clinicians; research recommendations in

[2] PSPs will need to raise awareness of their proposed activity among their patient and clinician communities, in order to secure support and participation. Depending on budget this may be done by way of a face to face meeting, or there may be other mechanisms by which the process can be launched.

systematic reviews and clinical guidelines; protocols for systematic reviews being prepared and registers of ongoing research.

The starting point for identifying sources of uncertainties and research recommendations is NHS Evidence: www.evidence.nhs.uk.

In addition to treatment uncertainties, this PSP also aims to address uncertainties in diagnosis, management and care delivery of people of all ages with rare inherited anaemias, and the impact on their families. Relevant literature will therefore be searched to derive any uncertainties in these areas also.

4. Refining questions and uncertainties

The Steering Group will need to have agreed exactly who will be responsible for this stage – the JLA can advise on the amount of time likely to be required for its execution. The JLA will participate in this process as an observer, to ensure accountability and transparency.

The consultation process will produce “raw” unanswered questions about diagnosis, treatment, management and care delivery of people of all ages with rare inherited anaemias, and the impact on their families. These raw questions will be assembled and categorised and refined by a Data Manager - who will need to be recruited and who will also support the data work for the PSP in Musculoskeletal Rare Diseases in Adulthood - into “collated indicative questions” which are clear, addressable by research and understandable to all. Similar or duplicate questions will be combined where appropriate.

The existing literature will be researched by relevant steering group members qualified to complete a literature search to see to what extent these refined questions have, or have not, been answered by previous research.

Sometimes, uncertainties are expressed that can in fact be resolved with reference to existing research evidence - ie they are "unrecognised knowns" and not uncertainties. If a question about treatment effects can be answered with existing information but this is not known, it suggests that information is not being communicated effectively to those who need it. Accordingly, the JLA recommends strongly that PSPs keep a record of these 'answerable questions' and deal with them separately from the 'true uncertainties' considered during the research priority setting process.[3] This PSP will aim to signpost such answerable questions via partners’ websites, and to indicate in the final report who might be best placed to take which questions forward.

Uncertainties which are not adequately addressed by previous research will be collated and prepared for entry into a relevant section within the UK Database of Uncertainties about the Effects of Treatments (UK DUETs - www.library.nhs.uk/duets) This will ensure that the uncertainties have been actually checked to be uncertainties. This is the responsibility of the Steering Group, which will need to have agreed personnel and resources to carry this accountability. The data should be entered into UK DUETs on completion of the priority setting exercise, in order to ensure any updates or changes to the data have been incorporated beforehand.

5. Prioritisation – interim and final stages

The aim of the final stage of the priority setting process is to prioritise through consensus the identified uncertainties relating to the diagnosis, treatment, management and care delivery of people of all ages with rare inherited anaemias, and the impact on their families of Rare Inherited Anaemias

[3] Steering Group members should insert information on how they intend to do this.

This will be carried out by members of the Steering Group and the wider partnership that represents patients and clinicians.

The interim stage, to proceed from a long list of uncertainties to a shorter list (e.g. up to 20), may be carried out over email, whereby organisations consult their membership and choose and rank their top 10 most important uncertainties.

The final stage, to reach, for example, 10 prioritised uncertainties, is likely to be conducted in a face-to-face meeting, using group discussions and plenary sessions.

The methods used for this prioritisation process will be determined by consultation with the partner organisations and with the advice of the JLA. Methods which have been identified as potentially useful in this process include: adapted Delphi techniques; expert panels or nominal group techniques; consensus development conference; electronic nominal group and online voting; interactive research agenda setting and focus groups.

The JLA will facilitate this process and ensure transparency, accountability and fairness. Participants will be expected to declare their interests in advance of this meeting.

Findings and research

It is anticipated that the findings of the Rare Inherited Anaemias PSP will be reported to funding and research agenda setting organisations such as the NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC), which includes the HTA Programme, and the MRC, as well as the major research funding charities. In addition, findings will be reported at relevant disease specific meetings/ conferences to be mapped by the Steering Group. Steering Group members and partners are encouraged to develop the prioritised uncertainties into research questions, and to work to establish the research needs of those unanswered questions to use when approaching potential funders, or when allocating funding for research themselves, if applicable.[4]

Publicity

As well as alerting funders, partners and Steering Group members are encouraged to publish the findings of the Rare Inherited Anaemias PSP using both internal and external communication mechanisms. The JLA may also capture and publicise the results, through descriptive reports of the process itself. This exercise will be distinct from the production of an academic paper, which the partners are also encouraged to do. However, production of an academic paper should not take precedence over publicising of the final results.

Signed by the Steering Group

The undersigned agree to follow the Rare Inherited Anaemias Priority Setting Protocol.

Carol Anderson, Anaemia Nurse Specialist, East Kent Hospitals NHS Trust

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Date: ……..

Elizabeth Blackmore, Congenital Anaemia Network

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[4] Add further detail here about how and where the priorities will be developed and researched.

Date: ……..

Subarna Chakravorty, Consultant Paediatric Haematologist, Imperial College London
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Date: ……..

Caroline Clifford, Patient Representative
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Date: ……..

Nick Meade/ Amy Hunter, Genetic Alliance UK
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Date: ……..

Dominic Messenger, Diamond Blackfan Anaemia UK
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Heather Paul, Patient Representative
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Date: ……..

Anu Rao, Consultant Haematologist, Great Ormond Street Hospital
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Date: ……..

Irene Roberts, Professor of Paediatric Haematology, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, Oxford
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Noemi Roy, Academic Clinical Lecturer & Haematologist, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, Oxford
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Date: ……..

Rachel Wearmouth, Patient Representative
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Date: ……..

Jenny Welch, Consultant Paediatric Haematologist, Sheffield Childrens Hospital

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Date: ……..

Sheela Upadhyaya, The James Lind Alliance

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Date: ……..