



## **Musculoskeletal Rare Diseases in Adulthood Priority Setting Partnership**

**PROTOCOL May 5th 2016**

### **Purpose**

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

### **Steering Group**

The Musculoskeletal Rare Diseases in Adulthood PSP will be led and managed by the following:

- Patient representatives:
  - Heather Delaney, Fibrous Dysplasia Support Society UK
  - Oliver Gardiner, XLH Network
  - Lorraine Lockhart
  - Maria Newman
  - Elaine Rush, Brittle Bone Society
  - Paul White
  
- Clinical representatives:
  - M Kassim Javaid, Consultant Rheumatologist and Associate Professor in Metabolic Bone Disease, Oxford University Hospitals Foundation Trust & University of Oxford
  - Richard Keen, Director, Metabolic Bone Disease Unit, Royal National Orthopaedic Hospital
  - Stuart Ralston, Honorary Consultant Rheumatologist & Professor of Rheumatology, University of Edinburgh
  - Laura Watts, Academic Clinical Fellow Core Medical Training/Rheumatology, University of Oxford
  - Jennifer Walsh, Endocrinologist & Senior Clinical Lecturer, Metabolic Bone Centre, Northern General Hospital

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/carers groups and clinicians.

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 Musculoskeletal Rare Diseases in Adulthood 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.

The National Institute of Health Research (NIHR) Rare Diseases (RD) Translational Research Collaboration (TRC) launched a programme to improve phenotyping<sup>1</sup> of rare diseases and in October 2013, the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Science (NDORMS) at the University of Oxford was selected to host the Musculoskeletal RD TRC. This led to a growing research infrastructure focused on the epidemiology<sup>2</sup> and mechanisms of rare diseases<sup>3</sup> - the initiation of this PSP is a logical next step in this body of work.

### **Aims and objectives of the Musculoskeletal Rare Diseases in Adulthood PSP**

The aim of the Musculoskeletal Rare Diseases in Adulthood PSP is to identify the unanswered questions relating to the treatment and long-term management of Musculoskeletal Rare Diseases in Adulthood from patient and clinical perspectives and then prioritise those that patients and clinicians agree are the most important. Diagnosis is also included (with the caveat that whilst we recognise that diagnosis can be challenging, the PSP has limited resources and will therefore make the decision about how to take such questions forward depending on the responses that are received).

The objectives of the Musculoskeletal Rare Diseases in Adulthood PSP are to:

- work with patients and clinicians to identify uncertainties relating to the treatment and long-term management of Musculoskeletal Rare Diseases in Adulthood
- agree by consensus a prioritised list of those uncertainties, for research
- publicise the results of the PSP and process
- take the results to research commissioning bodies to be considered for funding

By Musculoskeletal Rare Diseases we specifically mean the 3 conditions of X-Linked Hypophosphataemia – XLH; Osteogenesis Imperfecta – OI; and Fibrous Dysplasia – FD.

By adult, we mean 16 years and upwards, in order to capture the transition from child to adult and inform the paediatric debate.

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<sup>1</sup> Detailed description of the characteristics of patients and their disorders

<sup>2</sup> The study of the patterns, causes, and effects of health and disease conditions in defined populations

<sup>3</sup> The faults in molecular and cellular processes that cause specific diseases

For the purposes of this PSP, treatment and long-term management includes psycho-social management, as well as diagnosis (see above).

The geographical area for this PSP will be the UK plus specified European countries where Steering Group members have strong network links and there are similar standards of care – specifically Spain, Italy, France, Netherlands, Germany, Denmark and Norway. Survey responses will be requested in English in order to reduce burden on PSP resources. Any questions received that are not relevant to the UK healthcare delivery context will be provided to the PSP European partners.

## **Partners**

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

- people aged 16 or over who have XLH; OI; or FD
- carers of people aged 16 or over who have XLH; OI; or FD
- medical doctors, nurses and professionals allied to medicine with clinical experience of XLH; OI; or FD

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.

## **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 at 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](http://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 Musculoskeletal Rare Diseases in Adulthood PSP and invited to attend and participate in an initial stakeholder meeting.

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

## **2. Awareness-raising**

Awareness-raising will be via a dedicated website hosted by the Oxford University Hospitals Foundation Trust under their agreement with the NIHR Oxford Biomedical Research Centre James Lind Alliance “hub”. This will be linked to partner websites and can provide links to partner sites in return.

## **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 Musculoskeletal Rare Diseases in Adulthood. A period of approximately 12 to 18 months will be agreed by the Steering Group 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 can include question-answering services for patients and carers and for clinicians; research recommendations in systematic reviews and clinical guidelines; protocols for systematic reviews being prepared and registers of ongoing research. The Steering Group will need to decide which sources to search.

The starting point for identifying sources of uncertainties and research recommendations is NHS Evidence: [www.evidence.nhs.uk](http://www.evidence.nhs.uk).

## **4. Refining questions and uncertainties**

The Steering Group will need to agree 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 and the effects of treatments. These raw questions will be assembled and categorised and refined by a Data Manager who will be employed for this purpose, and who will also manage the data for the PSP in Rare Inherited Anaemias in order to share resources and recognise where there is overlap between the two PSPs, which might result in a set of priorities applicable across rare diseases more widely. The questions will be prepared as “collated indicative questions” which are clear, addressable by research and understandable to all. Similar or duplicate questions will be combined where appropriate.

Systematic reviews and guidelines will be identified and checked by representatives from the steering group 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 – i.e. 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.

Uncertainties which are not adequately addressed by previous research will be collated and recorded on a template in line with the endorsed JLA process. The process will be used to record how questions submitted have been checked to confirm they are unanswered. The data should be submitted to the JLA for publication on its website on completion of the priority setting exercise, taking into account any changes made at a final workshop, in order to ensure that PSP results are publicly available.

## **5. Prioritisation – interim and final stages**

The aim of the final stage of the process is to prioritise through consensus the identified uncertainties relating to the treatment and long-term management of Musculoskeletal Rare Diseases in Adulthood. 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 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. More information is available in the JLA Guidebook at <http://www.jla.nihr.ac.uk/guidebook>.

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 Musculoskeletal Rare Diseases in Adulthood 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 such as Wellcome Trust, Horizon 2020, and Arthritis Research UK. 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.

## **Publicity**

As well as alerting funders, partners and Steering Group members are encouraged to publish the findings of the Musculoskeletal Rare Diseases in Adulthood 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 Musculoskeletal Rare Diseases in Adulthood Priority Setting Protocol.

Heather Delaney, Patient Representative, Fibrous Dysplasia Support Society UK

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Date: .....

Oliver Gardiner, Patient Representative, XLH Network

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