RARE MUSCULOSKELETAL DISEASES IN ADULTHOOD

Priority Setting Partnership

ABOUT THE COLLABORATORS

Brittle Bone Society supports people affected by osteogenesis imperfecta throughout the UK and Ireland.

The Fibrous Dysplasia Support Society UK (FDSSUK) was formed in 2007 by a group of patients who are affected by Fibrous Dysplasia, McCune Albright Syndrome (MAS) or Cherubism, and their carers. It exists to provide information and support by sharing knowledge and experience of the condition with those who would like to know more.

XLHUK promotes X-linked hypophosphatemia (XLH) and related disorders, awareness and education for affected families, medical professionals, and the UK community at large. They support physicians, creates resources for affected individuals and their families, and foster the search for a cure.

XLH Network is a worldwide patient support organisation for people living and dealing with X-linked hypophosphatemia (XLH).

Genetic Alliance UK is the national charity working to improve the lives of patients and families affected by all types of genetic conditions. Genetic Alliance UK is an alliance of over 200 patient organisations.

The James Lind Alliance brings patients, carers and clinicians together to identify and prioritise the unanswered questions they want health research to address through Priority Setting Partnerships.

The National Institute for Health Research (NIHR) fund health and care research and translate discoveries into practical products, treatments, devices and procedures, involving patients and the public in all their work. The NIHR Oxford Biomedical Research Centre is a collaboration between the University of Oxford and Oxford University Hospitals NHS Foundation Trust to fund medical research.

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WHY SET PRIORITIES FOR RESEARCH INTO RARE MUSCULOSKELETAL DISEASES?

Fibrous dysplasia, osteogenesis imperfecta and X-linked hypophosphatemia are rare musculoskeletal diseases, which cause a number of symptoms including bone pain and skeletal deformity. There has been relatively little high quality research and a general lack of awareness among health professionals about the diagnosis and treatment of these conditions. It may therefore take years for adults with rare musculoskeletal diseases to receive a definite diagnosis or access to appropriate specialist care. This Priority Setting Partnership aimed to stimulate research on rare musculoskeletal diseases, by finding out what people with these conditions, their carers and health professionals believe to be the most important areas for future research relating to the treatment and long-term management of rare musculoskeletal diseases in adulthood.

2016 - 2017	Sep 2017- Feb 2018	Feb - Mar 2018	Apr - May 2018	Jun 2018	Nov 2018
Steering Group formed, protocol agreed, first survey developed and launched	Data analysis	Determine which questions already answered: evidence checking	Interim survey open, to reduce long list of unanswered questions	Final workshop to determine top 10 questions	Findings published and launched
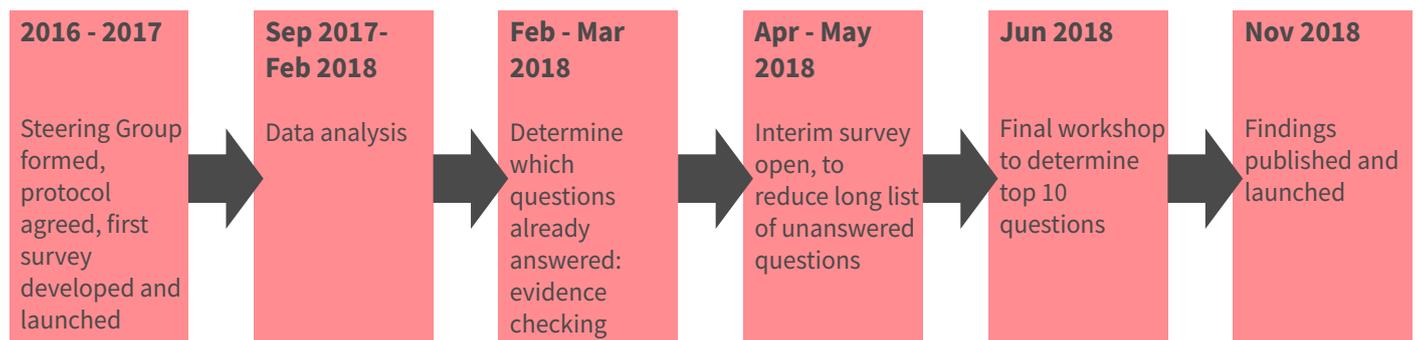
THE TOP 10 PRIORITIES FOR RESEARCH INTO RARE MUSCULOSKELETAL DISEASES

1. What is considered a good outcome of treatment in rare bone metabolic disorders? How can this be measured in studies of new treatments?

2. What is the cause of pain in people with rare metabolic bone disorders?

3. What is the psychological impact of having a rare metabolic bone disorder and how can patients and their families best be supported?

4. What can be done to prevent rare metabolic bone disorders in the first place, or to stop them from getting worse?

5. What are the best ways to manage fatigue linked to rare metabolic bone disorders?

6. What are the best forms of surgery to treat bones and joints in people with rare metabolic bone disorders?

7. What are the benefits and side effects of drug treatment for people with rare metabolic bone disorders in the short and long term? What is the optimal length of treatment?

8. How do rare metabolic bone disorders progress as people grow older and how is this different from normal ageing?

9. How are other parts of the body affected by rare metabolic bone disorders to cause other symptoms?

10. What are the best ways to prevent dental problems in people with rare metabolic bone disorders? Tied with

    How and why do people with rare metabolic bone disorders have different symptoms, even when they have the same genetic mutation?

SETTING THE LIMITS OF THIS PRIORITY SETTING EXERCISE

The aim of the Rare Musculoskeletal Diseases in Adulthood PSP was to identify the unanswered questions relating to the treatment and long-term management of rare musculoskeletal diseases in adulthood from patient and clinical perspectives and then prioritise those that patients and clinicians agree are the most important.

This PSP decided that treatment and long-term management should include psychosocial management, as well as diagnosis.

It was agreed to include diagnosis with the understanding that this can be challenging and the PSP has limited resources, and the steering group would therefore make the decision about how to take such questions forward depending on the responses received.

The PSP steering group agreed to focus on 3 ultra-rare conditions in this area:

— X-Linked hypophosphatemia (XLH)

— Osteogenesis Imperfecta (OI)

— Fibrous Dysplasia (FD)

The PSP steering group took a conscious decision to only focus the PSP on adults. They took the view that adult patients in this area were underrepresented in research.

It was agreed to focus on aged 16 and upwards, in order to capture the transition from paediatric to adult services.

Geography

Due to these diseases being ultra-rare, the PSP were aware that the number of healthcare professionals and patients in the UK is small. Therefore it was agreed to expand the coverage of the survey to certain other countries. These

were European countries in which steering group members had strong links and where they judged there are similar standards of care – specifically Spain, Italy, France, Netherlands, Germany, Denmark and Norway.

The PSP discussed how to elicit feedback especially if there were language barriers. To ease the burden on PSP resources it was decided to only accept responses received in English. It was also expected that a proportion of responses from non-UK partners about healthcare would be not be relevant because of differences between countries. These responses were to be excluded as well.

HOW WERE THE PRIORITIES IDENTIFIED?

Getting started

The project was driven by a steering group of patient organisations, people with one of the rare musculoskeletal conditions and clinicians. The partnership was officially launched in 2016.

The first survey

People with one of the rare musculoskeletal conditions, their friends and family members, and the health and social care professionals who support them, were asked to identify the questions they would like answered by research. They submitted their questions via an online survey between March and July 2017. A paper version of the survey was also made available via a PDF that could be printed locally for distribution.

The steering group members and other organisations supporting the project sent the survey out to their networks, via email, newsletters, social media, websites and blogs. A total of 198 people responded, with a total of 988 questions.

The people who responded were people with one of the rare musculoskeletal conditions (77%), carers, relatives or friends (11%), health or social care professionals (11%) and 1% came from other organisations.

'The process has been a very valuable bringing together of patients and healthcare professionals'
Steering Group member

Processing the survey results

Among the 988 questions submitted through the first survey were some that were not relevant to this project (364). Some people were asking for information or advice, that is, questions that do not need research to be answered (186). Others were too broad, unclear or about a completely different topic (113). Other questions were about access to services or the quality of health professionals' training (65). These might need to be addressed through changing policy and practice rather than research, and again these questions were removed.

A total of 624 questions remained. Some of these questions were asked repeatedly by many people, in slightly different ways. Similar questions were grouped together and an overarching question was written which summarised all the questions in the group. A small number of questions were only asked once. These were added to a list of overarching questions. We then checked the published evidence from research that has been carried out in the past and removed the questions that previous research had answered. At the end of this stage, we had 39 unanswered questions – this was our 'longlist' (see Appendix).

Answers to the questions that were out-of-scope or that have already been answered by research will be collated and published separately.

The second survey

The longlist of 39 questions went into a second survey, where we asked people to rank each question to indicate the degree of its importance to them. The second survey went out to everyone from the first survey who wanted to stay involved and to all the same networks to gather as much input as possible. The survey was live in April and May 2018. This time 220 people responded: 85% were patients, carers, relatives or friends, 14% were health or social care professionals and 1% came from other organisations.

There were a large number of responses from outside the UK. A larger proportion of females completed the survey compared to males. The questions in the second survey were presented in random order and were randomised each time an individual accessed the survey.

Participants were asked to consider each of the 39 questions, choose 10 and then rank them in order of priority (1 being top priority).

Each question ranked 1 was given 10 points, ranked 2 was given 9 points, down to ranked 10 which was given 1 point. Points for the healthcare professionals were calculated separately to ensure equal weighting between them and patients, carers and members of the public.

This exercise resulted in the 39 questions being placed in order separately for each type of respondent; questions with the same total were ranked jointly. The scores from the separate lists were then combined, resulting in a final list of shared priorities, from 1 to 39.

The top 25 questions were taken to the next step of the process.

'I have really enjoyed being part of the Steering Group. As a patient with fibrous dysplasia, it was interesting to see what the similarities were within the three different conditions with regard to questions. There were some questions that I would never have thought about asking. On the day of the final workshop, it was interesting to hear how the views of patients and carers differed slightly from those of the medical professionals. This project has allowed us to work together and achieve some outstanding questions for future research projects.'
Steering Group member

THE PRIORITY SETTING WORKSHOP

The 25 shortlisted questions were discussed at a workshop held at Friends Meeting House in London in June 2018. Invitations to the workshop were sent out through the same networks that were used to distribute the surveys: 18 people with one of the rare musculoskeletal conditions, carers and health professionals came to the workshop, including some steering group members, some people who had taken part in the surveys and some people who were new to the project.

The participants were asked to look at the 25 shortlisted questions before they came and to think about how they would rank them in order of importance. Their priorities were obviously informed by their own experience. By coming to the workshop, and taking part in a number of small group discussions, everyone got to hear other people's views on which questions were most and least important and why. This helped the group as a whole to reach an agreement on which questions should be a priority.

The top 10 questions are listed in full on page 4 of this report. The 14 questions (from the shortlisted 25 questions taken to the workshop) that did not make the final top 10 are listed below. They are listed in order of importance as agreed by the people at the workshop:

12. Are there more effective, long-term treatments for pain (including non-opioid drugs and non-drug treatments)?

13. How does menopause impact on women with rare metabolic bone disorders?

14. How does care and support for adults need to differ from care and support for children?

15. What are the best ways to support people through that change?

16. Are people with rare metabolic bone disorders at risk of any other health conditions?

17. Could a combination of self-management approaches reduce pain and prevent bone loss (e.g. exercise, diet, life-style changes, meditation, yoga)?

18. What is the best way to link up and organise all the health professionals who care for a person with a rare metabolic bone disorder?

19. Which treatments are safer and more effective for people with OI (osteogenesis imperfecta), treatments that promote bone-building (anabolic treatments) or treatments that reduce bone loss (antiresorptive treatments)? Does combining treatments make a difference?

20. What is the best form of exercise for people with rare metabolic bone disorders?

21. How does drug treatment need to change as people with rare metabolic bone disorders get older? Is stem cell therapy an effective treatment for people with rare metabolic bone disorders?

22. Why are some health professionals unaware of rare metabolic bone disorders and how can this be improved?

23. If we have a better understanding of what causes rare metabolic bone disorders, will that help find new treatments?

24. Would specialist services result in better care for people with rare metabolic bone disorders?

25. Is life expectancy affected by rare metabolic bone disorders?

NEXT STEPS

The JLA Rare Musculoskeletal Diseases in Adulthood PSP hopes that, by identifying these priority questions for research, we will ensure that future research is focused on the issues that matter most to people with rare musculoskeletal conditions, their carers, relatives and friends and the health and social care professionals who support them.

Call to arms

Many people gave their time and effort to submit their questions and to work through the JLA process to identify the final top 10 questions for future research. We want to ensure that these efforts are respected and recognised and therefore:

— We encourage research funders to include these priorities in their research strategy and to target these topics for future research funding.

— We encourage researchers to focus their efforts on answering the highest priority questions and to mention the JLA Rare Musculoskeletal Diseases in Adulthood PSP in their applications for funding. If a researcher receives funding to address any of the listed priorities, we ask that they please inform the JLA.

— We encourage funders, researchers and all interested parties to share this report with others and to raise awareness of the need for more research on rare musculoskeletal conditions in the UK.
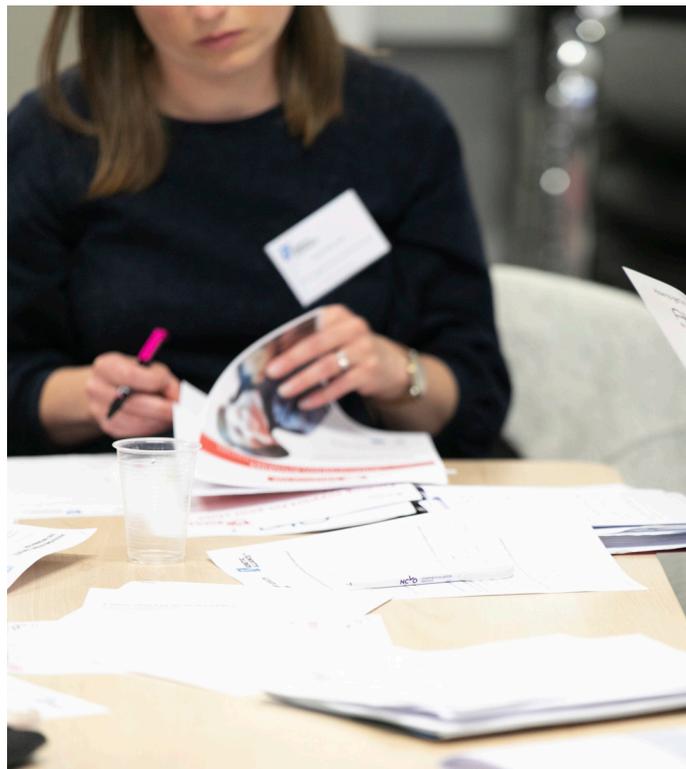
If you have any queries or comments about this work, please contact Amy Hunter amy.hunter@geneticalliance.org.uk.

Further information about the project can be found at: www.jla.nihr.ac.uk/priority-setting-partnerships/rare-musculoskeletal/

If you would like more information and advice about rare musculoskeletal conditions, please contact FDSSUK, XLHUK, XLH Network or Brittle Bone Society.

ACKNOWLEDGEMENTS

Members of the Steering Group were:

Heather Delaney, Patient Representative, Fibrous Dysplaysia Support Society UK

Roger Francis, Emeritus Professor, Institute of Cellular Medicine, University of Newcastle upon Tyne.

Oliver Gardiner, Patient Representative, XLH Network & RUDY

Amy Hunter, Genetic Alliance UK

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Sheela Upadhyaya, JLA Adviser

Laura Watts, Rheumatology Registrar, Oxford Deanery

Jennifer Welsh, Endocrinologist & Senior Clinical Lecturer, Metabolic Bone Centre, Northern General Hospital

Paul White, Patient Representative

'It is a privilege to be involved with a study that could change my children's and their children's future. The thought of them having to endure the physical pain that I do all day and all night is unthinkable and heart breaking so any research into our complicated rare diseases can only be for a better future.'
Steering Group member.

APPENDIX: THE FULL LIST OF RESEARCH QUESTIONS

— What is considered a good outcome of treatment in rare bone metabolic disorders? How can this be measured in studies of new treatments?

— What is the cause of pain in people with rare metabolic bone disorders?

— What is the psychological impact of having a rare metabolic bone disorder and how can patients and their families best be supported?

— What can be done to prevent rare metabolic bone disorders in the first place, or to stop them from getting worse?

— What are the best ways to manage fatigue linked to rare metabolic bone disorders?

— What are the best forms of surgery to treat bones and joints in people with rare metabolic bone disorders?

— What are the benefits and side effects of drug treatment for people with rare metabolic bone disorders in the short and long term? What is the optimal length of treatment?

— How do rare metabolic bone disorders progress as people grow older and how is this different from normal ageing?

— How are other parts of the body affected by rare metabolic bone disorders to cause other symptoms?

— What are the best ways to prevent dental problems in people with rare metabolic bone disorders?

— How and why do people with rare metabolic bone disorders have different symptoms, even when they have the same genetic mutation?

— Are there more effective, long-term treatments for pain (including non-opioid drugs and non-drug treatments)?

— How does menopause impact on women with rare metabolic bone disorders?

— How does care and support for adults need to differ from care and support for children? What are the best ways to support people through that change?

— Are people with rare metabolic bone disorders at risk of any other health conditions?

— Could a combination of self-management approaches reduce pain and prevent bone loss (e.g., exercise, diet, life-style changes, meditation, yoga)?

— What is the best way to link up and organise all the health professionals who care for a person with a rare metabolic bone disorder?

— Which treatments are safer and more effective for people with OI (osteogenesis imperfecta),

treatments that promote bone-building (anabolic treatments) or treatments that reduce bone loss (antiresorptive treatments)? Does combining treatments make a difference?

— What is the best form of exercise for people with rare metabolic bone disorders?

— How does drug treatment need to change as people with rare metabolic bone disorders get older?

— Is stem cell therapy an effective treatment for people with rare metabolic bone disorders?

— Why are some health professionals unaware of rare metabolic bone disorders and how can this be improved?

— If we have a better understanding of what causes rare metabolic bone disorders, will that help find new treatments?

— Would specialist services result in better care for people with rare metabolic bone disorders?

— Is life expectancy affected by rare metabolic bone disorders?