Gaps and Opportunities for arthritis research

This reference document collates sources of insight to inform the research agenda for musculoskeletal conditions.

This is a dynamic reference document; it is refreshed by our ongoing insight gathering activities.

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| Document Version and Change Control |
| **Date** | **Version** | **Change** |
| Sept 2021 | 1.0 | Creation of version 1 |
| 16.11.21 | 2.0 | Update following request to Group Leads to review ahead of Research Strategy web page publication on Nov 24th. Adjustments made to the MSKD group content. |

Context and purpose

This reference is available to inform researchers, funding agencies (commercial, governmental and third sector), donors, policy writers and health and social care providers of areas of unmet need, where science should be working hard to advance our understanding of musculoskeletal conditions and improve treatment and care. It identifies opportunities for musculoskeletal research in the UK where targeted efforts are required.

We will continue to gather and add insight to this live reference document which presents (i) the listening activity undertaken during the development of the charity’s research strategy (ii) the research prioritisation work of Versus Arthritis’ research advisory and clinical studies groups (iii) existing priorities from other organisations that gather unmet needs and research priority areas.

This reference document is supported by a companion document, the Case for Support for Musculoskeletal Research - November 2020.

We know that Versus Arthritis cannot address all of these needs alone. We welcome collaboration and invite discussion across the UK research sector, as we lead the way in improving the lives of people with arthritis through impactful research.

Nomenclature and abbreviations

MSK – musculoskeletal

We have used the terms arthritis and MSK to represent the broad range of 150 or more MSK conditions affecting the bones, joints, muscles and spine, as well as rarer autoimmune conditions (which can affect multiple organs and systems).

Section 1

– insights from Versus Arthritis 2020/2021 listening activities

Versus Arthritis undertook a number of Listening activities between October 2020 and February 2021 to inform the development of the Versus Arthritis Research Strategy 2022-2026, Better Lives Today, Better Lives Tomorrow.

We ran 20 workshops across the four UK nations to capture the lived experience of people with arthritis, and the expertise of researchers and healthcare professionals. We gathered the insight of over 150 members of our community. Patient and volunteer groups emphasised the important need to take a whole person approach, including living with multiple diseases and both physical and mental health environments. Within Northern Ireland, Scotland and Wales we heard of the importance of engaging with regional as well as national stakeholders.

The unmet needs that were identified during these workshops are grouped below into five, somewhat overlapping, areas. Summary points of unmet need that resonated in the discussions are captured, these are supported with some quotes captured (italics) from the workshop attendees.

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| 1. **Identification and characterisation of diseases’ cause and development**

**Mechanistic understanding / Common pathways / Knowledge and understanding / Incidence / Prevalence** |
| * Greater understanding of the biology of diseases via fundamental research was a strong emerging theme.
* Although there has been progress in our understanding of how MSK diseases affect the systems of the body causing changes in function (pathophysiology), there are gaps in what we know that are holding back improvements in diagnosis and treatment in many diseases.
* Genetic and environmental factor relationships are poorly understood.
* In managing and understanding multiple conditions, there is scope to explore the common causalities of different disease (molecular, cellular).
* There is more to do in understanding what the shared characteristics and biological mechanisms of different auto-immunity and immune-mediated inflammatory disease are.
* There are gaps in the understanding of epidemiology of disease.
* Health data and intelligence is disjointed and used ineffectively.
* The cross-cutting issue of fatigue is poorly understood.
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| *“[We need] more research into genetic markers with regard to immunity. If we can understand the pre-disposition, can we be better at prevention and quicker at diagnosis?”*  |
| *“We know for a long time that some people have a pre-disposition for rheumatoid arthritis but there seems to be no advance in understanding why it is activated in some people and not others.”* |
| *“Prevention requires you to understand the early causalities.”* |
| *“Should there be more cross-working with other auto-immune groups - focus on the commonalities rather than the diseases individually?”* |
| *“Has there been specific research into the prevalence of MSK conditions within different ethnic groups? Any data around this would be helpful for GPs to have to aid swifter diagnosis.”*  |
| 1. **Awareness, Risk management, Pre disease, Prevention**

**Population level / Individuals at risk / Pre disease / Asymptomatic / Prevention / Screening / Biological health and wellbeing / Psychological health and wellbeing / Awareness / Recognition** |
| * We lack understanding of the determinants of pre-disease/symptoms across the life-course and in different conditions. (e.g. microbiome and diet)
* Pre-symptomatic disease biology is poorly understood, the subtypes of disease conditions defined by distinct biological mechanisms.
* We lack the array of available and accessible disease indicators, including early pre-symptomatic screening - recognising risk to enable prevention.
* Activity in arthritis screening and enabling the next generation (and the NHS) to avoid arthritis is lacking - Primary prevention.
* High levels of some diseases go unmanaged.
* Knowing and identifying risks and managing MSK health is an unmet need.
* Health data intelligence can drive population health management.
* Understanding of childhood arthritis and its genetic determinants might help in providing clues to understanding rheumatoid arthritis as juvenile idiopathic arthritis is more constant.
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| *“I want everybody who does not have a musculoskeletal condition to know what their musculoskeletal health is and how to look after it in order to prevent future conditions.”* |
| *“Want to ensure that future generations do not have the struggle we have.”* |
| *“Could there be more research into the early markers of auto-immune diseases? Is someone who has had one auto-immune disease pre-disposed to getting another? Is there research on how we get them and why and can they be avoided?”* |
| *“Focus on prevention. Prevention is better than the cure.”*  |
| *“We should be framing our thoughts as healthy life rather than healthy ageing. This can place a heavier emphasis on early prevention of many conditions.”* |
| 1. **Detection, Diagnosis, Early disease and Intervention**

**Initial symptoms / Prognosis / Early disease / Can we Cure if we catch early**  |
| * There is a lack of accessible imaging and biochemical diagnostics and prognostic disease markers, (GP vs specialised)
* Getting a diagnosis and treatment can take a long time for some MSK conditions. There is no direct line to the right diagnosis and treatments first time – companion diagnostics.
* There are challenges of arthritis conditions in young people that extend well beyond inflammatory arthritis, where earlier and more effective diagnosis is lacking.
* Support for coping with diagnosis of a chronic condition is lacking.
* While some diseases are known to be genetically linked, in most diseases use of genetic risk scores is not yet part of routine clinical management of MSK conditions.
* There is a gap in delivering good multidisciplinary services across community, primary and secondary care services.
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| *“I want the best pathways of care for people with musculoskeletal conditions that include provision of acute care quickly when necessary and support, advice and education when and how people need it.”* |
| *“Diagnosis has to be much earlier. People need the tools to be able to question doctors and push for an actual diagnosis. Has there been research into the effects of delayed diagnosis on the progression of the disease?”* |
| *“Diagnosis, even if there is no cure – being told there is a reason for the way you feel is important.”* |
| *“Monitoring needs to go beyond just squeezing joints. There has to be a better way to establish levels of degeneration in a more timely manner and ways to defer further decline to the point of surgery.”* |
| 1. **Treatment pathways to disease modification, remission, cure and management across mid, late disease, refractory disease and relapse/flare**

**Self-management / Non-medical / Personalised medicine / Multi disease / Pre and post-surgery) / Mental Health** |
| * There is a disproportionate lack of effective treatment options in osteoarthritis.
* In rarer diseases, common pathways are not being effectively connected to improve treatment options.
* We don’t know how to care for people’s arthritis and to manage the interdependencies when they have multimorbidity.
* Some diseases have a lack of treatment options, and alternatives to joint replacement are needed.
* For some diseases, treatment responses vary from person to person and several different therapies may need to be tried before symptoms are relieved. There is a need for more personalised treatment plans.
* The management of side effects and consequences of long-term medication are areas of low research activity – there is a need to find treatments with fewer side effects.
* There is a need to better phenotype people to implement a precision medicine approach.
* Biomarkers and imaging to predict disease prognosis, true (biological) disease remission and long-term side effects are lacking.
* Treatment of pain is not well managed.
* Fatigue is not well treated.
* Opportunities to halt or reverse disease progression are lacking and getting to a point of disease remission is not reliable.
* There are unmet needs in understanding the impact of diagnosis on mental health and how psychological therapies can be used to help manage MSK symptoms.
* There is scope to provide better tools for self-management.
* There is more to know about best management of gut health for arthritis.
* In health and care improvement, there are gaps in innovative implementation of new knowledge.
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| *“I want everyone who has a musculoskeletal condition to be well-informed to self-manage their condition and seek help when they need it.”*  |
| *“Not enough effort to get people off steroids.”* |
| *“Rarer forms of arthritis struggle to get visibility or funding for research.”* |
| *“Arthritis is a chronic condition, therefore people have been taking drugs for decades. How much research has been done into the effect of taking a drug for such a long time – what are the long-term side effects, is the drug still effective?”* |
| *“I want a cure for arthritis, as well as live treatment improvements and improved quality of life.”* |
| *“Pain is a concern for most patients but almost all research will help pain, do we have to have pain as a core aim?”* |
| *“Everyone needs to see the best practitioner quickly, and that doesn’t necessarily have to be a GP. It could be a physiotherapist.”* |
| *“[We need] real alternatives to joint replacement, for example cartilage replacement. Treatments where you can treat more people spending the same amount of money.”* |
| *“There should more alternatives to drugs. Again the holistic approach and alternative therapies, for example acupuncture, should be more routinely integrated into treatment.”* |
| *“Self-management has been helpful but this can be improved further. How much research has been done into the benefits of self-management?”* |
| 1. **Living with disease, symptom management and monitoring**

**Work / Leisure / Ease of living / Mobility** |
| * The experiences of living with arthritis vary considerably, improve understanding the relationship between MSK disease (including access to care) and socio-economic inequality
* Options for enabling people to manage their condition are limited.
* Need to understand how to fully support people in work and those returning to work.
* Better evidence-based tools to support patients in self-management, shared decision-making, and activity. How to help people self-manage pain.
* There need to be better outcomes for people with long-term disease.
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| *“Chronic diseases need chronic monitoring.”* |
| *“More research on the social and societal difficulties of living with arthritis, [for example] product development, building access.”* |

Section 2

– insights from Versus Arthritis research advisory groups / clinical study group

The Versus Arthritis research advisory groups unite specialist researchers, people with lived experience of arthritis and healthcare professionals with one common goal - to highlight the research that is needed to push back against arthritis.

They work across the research spectrum – from discovery and translational science, treatment development and evaluation to disease management and health service research.

They have an integral role in continuously identifying unmet needs in arthritis research and informing prioritisation of research areas.

Our advisory groups help inform our activities, dynamically updating this 'Gaps and Opportunities for arthritis research' reference document and finding ways to keep listening to diverse groups of people.



Including lupus, antiphospholipid syndrome, scleroderma (systemic sclerosis), Sjogren’s syndrome, myositis, vasculitis, Behcet’s syndrome and overlap / undifferentiated connective tissue disease.

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Hundreds of thousands of people in the UK are affected by autoimmune conditionsand many of these have musculoskeletal impacts. These conditions occur when the immune system attacks and damages tissues, instead of just targeting foreign microorganisms such as viruses and bacteria which make us ill. As rare, complex, multisystem, disparate diseases, autoimmune rheumatic diseases are challenging to research and treat. The areas that are damaged varies between conditions but can involve vital tissues and organs including the skin, lungs, heart, kidneys, and gut, as well as the joints. Autoimmune rheumatic diseases are potentially reversible diseases, with commonalities of pathogenesis and drug targets. Despite recent advances there is still unmet need in treatment options, although emerging clinical esearch and greater understanding of disease biology together with new available therapies may herald a new biologic era for rare diseases that could revolutionise treatment approaches.

**Gaps and Opportunities:**

* The UK has vibrant, collaborative expertise in translational clinical science and international leaders in this area.
* There is need to inspire the next generation of rare disease clinician scientists.
* There are research avenue opportunities because COVID19 has highlighted the importance of immune response and tissue damage that is also central in to autoimmune rheumatic diseases.
* There is a lack of profile for rare diseases within government and even within MSK research, lower priority diseases and lack of evidence of disease impact. Putting immune mediated inflammatory diseases together can give greater collective impact to raise profile: political grouping but investigative splitting​.
* In the NHS rare diseases are uniquely supported via a single service commissioning system through NHS England - Specialised Rheumatology has many service commissioning policies which reflects both the lack of approved therapies but also the availability of multiple candidate therapies that patients and expert clinicians want access to.
* Many services all see rare and autoimmune diseases but there is need to use commissioning levers to drive up research, Rheumatology is in the vanguard of national rare disease registration with Public Health England.
* There are Health service research needs regarding navigation of health and care services for rare diseases - including access to specialist diagnostic & management services and transition from paediatric to adult care.
* Disease management is often delayed due to a lack of clinical management quality standards, despite evidence of delayed diagnosis in rare and autoimmune disorders. Post COVID the biggest limit on management is service capacity and the focus on recovery and management of waiting list as well as the limitations of new practice approaches such as remote clinics.
* Disease assessment tools are not optimal – there are limitations of medically-focused outputs, and a lack of patient reported outcome measures (quality of life measures are absent).
* Despite progress in the understanding of these diseases, there is still unmet need in treatment options with a need to move away from steroids (not always the appropriate treatment and can be used too readily), access to other better drugs (re-purposing) is needed.
* It is a challenge to access the correct biological samples and allied data in these diseases
* Rare disease clinical trials are harder to design and recruit to, often requiring recruitment across countries and BREXIT represents a specific challenge in terms of trials and regulation for rare diseases.
* There is need and opportunity to work across EU boundaries with organisations to help offset the negative impact of BREXIT.
* There Is opportunity to innovate in clinical and translational research in clinical research design and build on the COVID experiences.
* The UK has well-functioning established research infrastructures providing opportunity to engage in integration of rare disease research in these structures (UK Genomics, UK Biobank).
* The UK Strategy for Rare Diseases is building momentum (themes = Empowerment, Prevention, Diagnosis, Care co-ordination, Research).
* There are opportunities to collaborate more with Pharma, with repurposing drugs and with multiple disease specific charities.

**Unifying areas which cut across autoimmune MSK diseases:**

* Diagnostic pathways (delays), early intervention, prevention
* Glucocorticoid usage - burden/benefit of treatment
* Shared features of autoimmune rheumatic diseases - molecular mechanisms and genetics, 🡨🡪 inform undefined diseases
* Fatigue
* Common system outcome (renal and cardiovascular) and organ failure
* Drug repurposing
* Social care



Including osteoarthritis, crystal disease, regional and widespread pain (back pain, shoulder pain, tendinopathy, other regional pain syndromes, fibromyalgia), metabolic bone disorders (e.g. osteoporosis and rare diseases), musculoskeletal injuries caused by acute traumatic events.

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| Sept 2021 | 1.0 | Creation of version 1 [Group perspectives captured 2019, Heatmap exercise 2020, Group prioritisation exercise 2020-2021] |
| Nov 2021 | 2.0 | Following request to Group to review, adjustments made to order, inclusion of areas to reflect the research avenues identified by the group, the issue of early diagnosis and coding.  |

Musculoskeletal disorders are conditions which involve the joints, ligaments, muscles, nerves, and tendons which together make up the MSK system. Many of these conditions can result in pain and limited mobility which can reduce quality of life. Some of these conditions are very rare, but many are very common such as [osteoarthritis](https://www.versusarthritis.org/about-arthritis/conditions/osteoarthritis/) and tendonitis. There is enormous but inadequately defined distress caused by these diseases, which are being ‘normalised’ and deprioritised amid a ‘climate of tolerance’. Issues around early, accurate diagnosis and consistent coding of these disorders in healthcare records mean that we may not be able to count the full prevalence and impact of these conditions. There is relative neglect of research into common musculoskeletal disorders from grouping with all rheumatic and musculoskeletal diseases and arthritis.

**Gaps and Opportunities:**

* There is poor understanding of the mechanisms of many of these disorders but lots of opportunities through strong laboratory models of disease in many areas.
* In discovery research, there have been recent important findings but there's a downward researcher capacity (losing people and/or not attracting new researchers) in this area.
* In experimental medicine the trajectory is upward but the capacity in this area is still incredibly low.
* Many discoveries do not reach trials or the clinic, or do so very slowly, a so-called ‘Valley of death’ for translation.
* Bioinformatics and data are an underutilised resource: there is opportunity to harness use of ‘big data’ in these common disorders to answer research questions.
* There is opportunity for innovative, interdisciplinary research (e.g., around shared mechanisms) and linkage of NHS data (for observational studies and clinical studies) with UK Biobank and Joint registries, but poor coding of many common MSK disorders is a blocker to good quality, larger scale research.
* Medical technology (such as joint replacements) research is strong and innovatively world leading.
* There is more to do in health intelligence research and applied health – ensuring knowledge from research actually reaches patients with arthritis.
* There is perceived low viability/high difficulty of clinical trials in this area.
* There is a need for cost-effectiveness research for any new interventions.

**Research prioritisation 2020-2021:**

The Group is gathering broader insight on what are considered the most important areas of research to better understand and manage musculoskeletal conditions.

The Group has recently carried out part two of an online research prioritisation exercise (the survey closed at start of October 2021), which asked respondents to score/rate a list of research themes or research avenues (on their Importance and Impact), using a CHNRI-like prioritisation process. The stakeholders responding to the survey included people who have a musculoskeletal condition, care for a person living with a musculoskeletal condition, researchers, healthcare professionals, industry representatives, research funders, healthcare providers, government policy makers.

Part one of the exercise had sought opinions on the top priorities for musculoskeletal disorders research, to gather a ‘long’ list of research areas for musculoskeletal diseases, from a survey run between November 2020 – January 2021. The group had then worked with patients with arthritis within and without the group to refine into 68 research avenues.

The methodology applied in this process has been shared publicly: https://medrxiv.org/cgi/content/short/2021.10.04.21264485v1

It is also the intent to make the ranked list of priorities in MSK disorders research publicly available here and by publication in a peer-reviewed journal by 2022.

Early activity in this process was grouped into four priority areas identified by the Group : 1. Mechanisms 2. Diagnosis & Impact 3. Managing & Living Well with musculoskeletal disorders 4. Successful Translation.

Examples of themes or uncertainties which could be answered by research from the first survey (which contributed to research avenues in the second survey):

* Shared mechanisms across many diseases e.g., pain
* Pathogenesis of disorders
* Predictive factors and models; methods for defining meaningful subgroups
* Need for prevention - earlier in life course
* Understanding links between disease and pain/flare
* Desire/impact of earlier, accurate diagnosis
* Use of screening programmes
* Use of artificial intelligence and technology, remote monitoring
* Risk stratification; pharmacogenomics and genetic risk scores
* Agreed meaningful outcome measures, used routinely
* Self-management - Who responds best, what is best package
* Use of standardised, national information
* Use of apps for self-triage and monitoring
* Activity and exercise – staying active safely
* Integration of care - through each service from diagnosis to management at home
* Workplace interventions, sports/community interventions
* Striving for new treatments which are cures/disease modifiers
* Knowledge mobilisation: “Ensuring that research-proven tests, treatments and approaches are routinely available in clinical practice”
* Funding to maximise translation - being pioneering, follow on funding for such discoveries is important
* Tissue repair/stem cells/tissue engineering
* Looking at causes and not just symptoms
* Understanding why some people develop chronic pain and not others
* Understanding the relationships between MSK disorders and other long term conditions
* Objective markers and measures of [msk disorders] - to allow measurement of the impact on individuals and society



Including adult inflammatory arthritis, peripheral and axial spondyloarthritis (SpA), psoriatic arthritis (PsA), enteropathic-associated arthritis, seronegative arthritis and related conditions

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| Sept 2021 | 1.0 | Creation of version 1 [Group perspectives captured 2019] |
| Nov 2021 | 2.0 | Following Opportunity for review by whole Group – order of some content, clarifications and additions to represent the groups research avenues, highlighting issues around diagnosis and data coding. |

Inflammatory arthritis is an umbrella term used for a group of arthritic conditions which cause pain, stiffness and damage to joints including [rheumatoid arthritis](https://www.versusarthritis.org/about-arthritis/conditions/rheumatoid-arthritis/), [psoriatic arthritis](https://www.versusarthritis.org/about-arthritis/conditions/psoriatic-arthritis/) and [axial](https://www.versusarthritis.org/about-arthritis/conditions/ankylosing-spondylitis/) spondyloarthritis. These conditions are caused when our immune system mistakenly attacks our joints, leaving them inflamed and painful. Other body systems and organs can also be attacked, which is what makes these conditions complex and harder to understand. Treatment responses and long-term management of these conditions vary from person to person. Sometimes several therapies need to be tried before symptoms are relieved. Different types of inflammatory arthritis have different needs. We seek a future where people with inflammatory arthritis have access to more personalised and effective treatments at all stages of their condition.

**Gaps and Opportunities:**

* UK Inflammatory arthritis research is cutting edge, high quality, innovation, internationally leading.
* There is strength in the clinical & research networks (Research into Inflammatory Arthritis Centre, The British Society for Spondyloarthritis, British Psoriatic Arthritis Consortium, European alliance of associations for rheumatology) also local and national patient networks, and opportunity to expand and embed stronger links across academics and within the NHS.
* There is a lack of support for next generation researchers (dedicated sustainable funding). Researchers are leaving inflammatory arthritis / musculoskeletal areas for research in other areas with better funding.
* There are some established research cohorts and disease registers, though a lack of sufficient well-phenotyped cohorts required for big data, biomarker, and epidemiology studies.
* There is need and opportunity to support routine collection of high-quality data around adult inflammatory arthritis to support UK informatics research.
* There are good connections and collaborations with industry for drug development / biomarker discovery and development / discovery science and repurposing of drugs.
* There are gaps in addressing comorbidities in adult inflammatory arthritis research.
* There are gaps in lifestyle & early diagnosis research.
* There is bias in clinical trials (populations often not representative of clinical practice).
* There are unmet needs around measuring and managing pain (subjective outcomes, high placebo effects).
* There are research gaps in a number of areas
	+ research into the biological mechanisms of these diseases
	+ prevention of adult inflammatory arthritis
	+ holistic care and management of comorbidities
	+ stratified medicine, grouping patients based on risk or treatment response
	+ evidence for multidisciplinary care / clinics
* There are opportunities to support translational development and commercialisation of biomarkers.

**Priority research areas:**

* Fatigue understanding and management is a cross cutting theme across these disease
* Pain understanding and management is a cross cutting theme across these disease
* Influence of diet and lifestyle factors on disease development and progression
* Various aspects around periods of increased disease activity (flares)
* Various questions around risk and management of other health conditions (Comorbidities)



Active across all disease areas of the adult advisory groups, **topic specific groups** operate in sub groupings of diseases.

Works in partnership with the [National Institute of Health Research’s](https://www.nihr.ac.uk/explore-nihr/support/clinical-research-network.htm) clinical research network.

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| Sept 2021 | 1.0 | Creation of version 1 [group perspectives and 2020 prioritisation exercise] |
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Paediatric rheumatology refers to the study of rheumatic diseases in children and young people. Rheumatic diseases include conditions that cause pain and swelling in joints, such as arthritis. In children and young people, the most common form of arthritis is known as [Juvenile Idiopathic Arthritis](https://www.versusarthritis.org/about-arthritis/conditions/juvenile-idiopathic-arthritis/). 1 in every 1,000 young people in the UK has arthritis. Arthritis and rheumatic conditions in children and young people can be complex. Severity and impact vary from one person to another, and symptoms can alter greatly from day to day. The experience of growing up with arthritis can have a negative impact on all aspects of a young person’s development.

**Gaps and Opportunities:**

The Royal College of Paediatrics and Child Health calls for a continued focus and coordinated effort to promote child health research. [Turning the tide - five years on (2018) | RCPCH](https://www.rcpch.ac.uk/resources/turning-tide-five-years)

* The UK has a highly collaborative, though small, community and has established itself as a pivotal country in trial design and delivery of investigator-initiated studies with input from industry.
* Attracting new paediatric researchers within an intense clinical care environment is a threat to the area and paediatric academics are dwindling in number.

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* There are specific issues around transition from paediatric to adult services and difficulties accessing research which spans this divide
* By prioritising research which facilitates early diagnosis and age-appropriate treatments, there is the opportunity to limit the damage and impact of disease for both the child and the adult they become.
* Study of rare diseases in children might lead to breakthrough in management of adult rheumatic diseases.

**Research prioritisation 2020:**

The Group conducted a research prioritisation exercise in 2020; Group members reached out through their various network links to patients and parents, clinicians, trainees, allied healthcare professionals and researchers. Almost 300 research priority questions were gathered. Once the list was reviewed for duplicates and questions already answered, in progress or beyond the scope of the Group, 88 areas of unmet need were identified. Some of these were framed as specific questions and some as broader areas. The group identified a top 10 from the specific questions and a top 10 from the broader questions.

Healthcare care research Priorities (November 2020)

A narrower list was generated focussed on key questions in healthcare research to link to the activities of the National Institute for Health Research. The 10 top ranked topics for future paediatric rheumatology clinical research are presented in a random order in the table below. The italics show which area of activity within the Clinical Studies Group each topic arose from.

Further to this, a *Top 3 Research Priorities* were agreed by the Group, these are highlighted in green.

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| Ref | Topic |
| **A** | Bone: Clinical trials of biological and other agents (e.g., bisphosphonates) in chronic recurrent multifocal osteomyelitis - *Clinical Studies Group research priority* |
| **B** | Juvenile idiopathic arthritis: In patients with juvenile idiopathic arthritis, does implementation of a treat to target management strategy compared to the current standard care lead to improvements in disease activity and damage, steroid sparing and quality of life? *Trainee research priority* |
| **C** | Lupus: In children and young people with lupus, does implementation of a treat to target management strategy, as opposed to standard care lead to improvements in disease activity and damage, steroid sparing and improving quality of life and fatigue*? – Juvenile Systemic Lupus Erythematosus topic specific group and trainee research priority* |
| **D** | Juvenile dermatomyositis: Establish clinical trials in juvenile dermatomyositis to evaluate the effect of novel treatments (e.g., JAK inhibitors), biologics (e.g., TNF blockers) and other treatments currently used to improve disease control and steroid sparing - *Juvenile dermatomyositis* *topic specific group research priority* |
| **E** | Juvenile idiopathic arthritis: Trial of anti-TNF vs JAK inhibitors treatment in juvenile idiopathic arthritis - *Clinical Studies Group and Juvenile idiopathic arthritis topic specific group research priority* |
| **F** | Scleroderma: Trial of mycophenolate versus methotrexate in localised scleroderma - *Trainee and scleroderma topic specific group research priority* |
| **G** | Juvenile idiopathic arthritis: How do we optimally manage childhood onset juvenile idiopathic arthritis in adulthood? - *Clinical Studies Group research priority* |
| **H** | Non-inflammatory: How can we best recognise children at risk from persistent pain problems to ensure early intervention? - *Allied health professional research priority* |
| **I** | Juvenile idiopathic arthritis: Trial of early biologics with methotrexate vs methotrexate on its own in newly diagnosed juvenile idiopathic arthritis - *Clinical Studies Group research priority* |
| **J** | Juvenile idiopathic arthritis: A trial comparing intra-articular steroid injections and escalation e.g., systemic measures in juvenile idiopathic arthritis - *Trainee and consumer research priority* |

Section 3

– insights from other stakeholder organisations

We collate here other sources that highlight priorities for musculoskeletal research based on unmet needs, we recognise the richness and value in capturing and referencing these collectively.

## European Alliance of Associations for Rheumatology

## The ‘European alliance of associations for rheumatology’ represents people with arthritis, health professionals in rheumatology and scientific societies of rheumatology in all the European nations. The document ‘RheumaMap 2019: Making the case for unmet needs in rheumatology’ [EULAR | EULAR - RheumaMap](https://www.eular.org/public_affairs_rheumamap.cfm) identifies unmet needs and main challenges in research and innovation and proposes key areas where long-term strategic efforts can help reduce the enormous burden of these conditions in Europe.

## James Lind alliance priority setting partnerships

[Priority Setting Partnerships](https://www.jla.nihr.ac.uk/priority-setting-partnerships/) (facilitated by the [James Lind Alliance](https://www.jla.nihr.ac.uk/about-the-james-lind-alliance/)) generate Top 10 lists of highlight areas for research - clinicians, patients and carers identify and prioritise evidence uncertainties in areas of health and care that could be answered by research, the musculoskeletal relevant lists are:

## [Early Hip and Knee Osteoarthritis | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/early-hip-and-knee-osteoarthritis/)

[Broken Bones in Older people - Musculoskeletal Injury: fragility fracture of the lower limb and pelvis | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/broken-bones-in-older-people/)

[Broken Bones of the Upper Limb in People over 50 (Fractures of the Shoulder, Arm or Wrist) | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/broken-bones-of-the-upper-limb/)

[Common Conditions Affecting the Hand and Wrist | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/common-conditons-affecting-the-hand-and-wrist/)

[Elbow Conditions | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/elbow-conditions/)

[Foot and Ankle Surgery | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/foot-and-ankle-surgery/)

[Fibromyalgia (Canada) | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/fibromyalgia-canada/)

[Foot Health | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/foot-health/)

[Hip and Knee Replacement for Osteoarthritis | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/hip-and-knee-replacement-for-osteoarthritis/)

[Juvenile Idiopathic Arthritis (Netherlands) | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/Juvenile-idiopathic-arthritis/)

[Psoriatic Arthritis | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/psoriatic-arthritis/)

[Rare Musculoskeletal Diseases in Adulthood | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/rare-musculoskeletal-diseases-in-adulthood/)

[Revision Knee Replacement | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/Revision-knee-replacement/)

[Surgery for Common Shoulder Problems | James Lind Alliance (nihr.ac.uk)](https://www.jla.nihr.ac.uk/priority-setting-partnerships/surgery-for-common-shoulder-problems/)