

RESEARCH VERSUS ARTHRITIS

Reviewing the Case for Support for Musculoskeletal Research - November 2020

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Context and purpose

This review summarises evidence sources both formal and informal, technical and general, the majority of which are available in the public domain. Evidence was reviewed and collated over a six-month period from February to October 2020. The evidence review was completed to inform and underpin the development of a four year Versus Arthritis Research Strategy. It was primarily intended to equip stakeholders involved in Strategy development to test and extend the evidence base, ensuring that the Versus Arthritis Research Strategy captures the widest range of inputs and priorities. It also resources Versus Arthritis to contribute to conversations addressing the challenges and opportunities facing the wider UK medical research sector.

Definitions

Musculoskeletal¹ (MSK) disease

The term MSK disease is used to reflect a broad range of more than 150 health conditions affecting bones, joints and muscles, pain syndromes and rarer conditions of the immune system as defined by the World Health Organization (WHO) and used in the Global Burden of Disease (GBD) Study. This remit is much wider than the definition of MSK in the UK Health Research Classification System (HRCS), which separates this broad set of conditions into two main categories – MSK and Inflammatory & Immune System. The use of the term MSK throughout this document refers in all cases to the wider WHO and GBD definition except where HRCS coding data and UKCRC Health Research Analysis Forum datasets are explicitly referred to.

MSK health

Good MSK health is an important component of maintaining a person's functional abilities throughout their life course and is fundamental to healthy ageing.² The older a person is, the more likely they are to experience chronic diseases which can lead to poor MSK health, but there are steps that can be taken to reduce the risk of developing MSK conditions and better manage MSK health.³ Prevention, early detection and treatment can enable people to maintain good MSK health, remain independent and connected to their community.⁴

Research – a technical definition

Research is creative and systematic, undertaken to increase the stock of knowledge – including knowledge of humankind, culture and society – and to devise new applications of available knowledge. Research is identified by a set of common features and must satisfy five core criteria: the activity must be: novel, creative, uncertain, systematic, transferable and/or reproducible. Research encompasses three types of activity: basic research, applied research and experimental development.⁵

In its broadest sense, research includes activities from fundamental biomedical science through to quality improvement, epidemiology, clinical trials, public health and operational research.⁶ Biomedical, clinical, applied, social and biopsychosocial research activities are all within the remit of the Versus Arthritis Research Strategic Priority. Specifically, this includes health services research and implementation, qualitative research, health data and research to produce fast-paced digital interventions.

Research – an accessible definition

¹International statistical classification of diseases and related health problems. - 10th revision, edition 2010. World Health Organization.

² [Musculoskeletal health: applying All Our Health - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/consultations/musculoskeletal-health-applying-all-our-health)

³ [Productive healthy ageing and musculoskeletal \(MSK\) health - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/consultations/productive-healthy-ageing-and-musculoskeletal-msk-health)

⁴ [Musculoskeletal health: applying All Our Health - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/consultations/musculoskeletal-health-applying-all-our-health)

⁵ Frascati Manual - 2015 Edition Guidelines for Collecting and Reporting Data on Research and Experimental Development

⁶ Transforming health through innovation: Integrating the NHS and academia. Academy of Medical Sciences.

January 2020.

Research uncovers new information about a subject or finds new ways to use existing information. All research activities share some key characteristics: they explore new, original ideas formed from creative thinking, they follow an ordered, well-structured process, and they lead to outcomes that can be reliably repeated by other people even if that outcome was not expected when the activity began.

Research takes place in many different places including universities, hospitals and research institutes as well as community and business settings. Research findings are shared in a variety of ways, from traditional articles in scientific journals through to announcements on websites and via social media.

There are many types of research activity which can all make a difference for people with arthritis. These include understanding why and how disease develops in the body and the discovery and testing of new drug treatments. Research also looks at how thoughts, emotions and behaviour all contribute to a person's lived experience of their disease. Research considers the impact of a person's everyday life on their experience of disease including their work, family and wider interactions as part of society. Research looks for new ways to prevent diseases from occurring in the first place as well as improving the treatments, care and support available to people living with long-term conditions both in hospital and at home. Research explores how to capture new knowledge as it becomes available and build it into existing practice to deliver benefits through improved treatment and care.

Versus Arthritis recognises that all these different types of research activity are needed to deliver new and improved opportunities and solutions for people with arthritis.

Executive Summary – key findings from the evidence review

Musculoskeletal (MSK) conditions and MSK research:

- There are more than 150 MSK conditions affecting muscles, bones, joints, tendons and/or ligaments. Their impact for individuals is significant and their global impact is rising.
- MSK conditions are often hidden and their severity not recognised. The impact of MSK conditions, particularly within the context of chronic, multiple long-term conditions is not well addressed within the research agenda.
- The serious impact of COVID-19 on MSK health is becoming apparent.
- People with MSK conditions and MSK researchers have both highlighted the need for improved recruitment to clinical trials and greater engagement with MSK research.
- MSK research globally has traditionally focussed more on biomedical discovery/drug treatments and there is more work to do to target and mobilise research to prevent, maintain and improve MSK health through wider scope and broader representation.
- MSK research knowledge developed over many years provides a foundation to address diverse and emerging medical conditions including COVID-19.
- Priority setting for MSK research requires greater coordination and patient insight to achieve critical mass and optimise the use of limited funding.

Wider research sector considerations:

- Awareness of and support for medical research is high among the UK general public, but engagement is required to inspire appreciation of opportunities beyond drug treatments.
- UK R&D depends and thrives on a highly networked research system. The route to successful translation of research outputs frequently depends on partnership and collaboration to de-risk innovative science and bridge the 'Valley of Death', where promising scientific discoveries may fail to be translated into new treatments and innovative solutions which could benefit the public.⁷
- There is growing recognition of the importance of co-development of research which addresses common platforms and mechanisms of disease.
- There is more to be done to empower the health system to systematically promote research and effectively mobilise new innovations.
- A positive culture is essential to improve diversity across research and innovation, increase patient involvement and create a thriving research ecosystem.
- Researchers have responded flexibly and creatively to COVID-19 but research activity has been profoundly affected. Medical research charity investment in high-quality cutting-edge research, careers and infrastructure has a significant and direct benefit to the UK economy, but the dual challenges of Brexit and COVID-19 present significant economic challenges and uncertainties.

⁷[Lost in translation: the valley of death across preclinical and clinical divide – identification of problems and overcoming obstacles | Translational Medicine Communications | Full Text \(biomedcentral.com\)](#)

Versus Arthritis rationale statement

With a commitment to research, we are not working on building a rationale for *why* the charity invests in research. We can however see that our current approach is not enough and there are changes to make:

1. Versus Arthritis (and legacy charity Arthritis Research UK) has shaped, funded, commissioned and championed research into MSK conditions for many years.
2. There are numerous examples of where this research activity and MSK research more generally, has had a positive and life-changing impact on the wellbeing of people with arthritis and related MSK conditions.
3. But the balance of research and scale of funding isn't optimally aligned with or proportionate to the scale of the problem and MSK research isn't prioritised.
4. Use of research findings is inconsistent and is subject to extensive delays.
5. Research and the landscape isn't sophisticated enough to meet the complex health care needs of people with arthritis and other MSK conditions.
6. A better balance of different types of research, with different providers and partners is necessary to deliver more impact.

1. Versus Arthritis – a funder, commissioner and champion of MSK research

1.1 Versus Arthritis research funding

The top response given by respondents to a Versus Arthritis survey in 2013 to the question “*What is the most important thing for an arthritis charity to do?*”, was ‘*Fund research*’.⁸ Medical research remains in the top three priorities for charitable giving by the public.⁹ Versus Arthritis was the fourth largest charitable funder of medical research in the UK in 2018 and the largest public funder of research into MSK conditions.¹⁰ Versus Arthritis has £132.4 million currently invested in cutting-edge research across the UK, from lab-based projects to clinical trials, to projects impacting on health services. Versus Arthritis was listed in the top five most influential UK research charities in 2019.¹¹ Figures demonstrate that for each £1 of funding received from Versus Arthritis, an additional 72 pence has been secured from other funding organisations by researchers, approximating to £85 million of follow-on funding.¹² The MRC/ESRC/BBSRC-Versus Arthritis Advanced Pain Discovery Platform¹³ is Europe’s largest ever single investment in pain research and will support large-scale and ambitious multidisciplinary consortia to pursue innovative, ambitious research questions in a ‘condition agnostic’ manner. Through this ambitious and innovative platform, Versus Arthritis will take the lead in tackling the pain of MSK disease. The Versus Arthritis Action Plan (2018) includes a commitment to 1) continue investing in exceptional, innovative research that addresses issues that matter most to people with arthritis and 2) continue to grow the UK’s capacity in musculoskeletal research and foster collaboration across the growing community of researchers at all stages of their career.¹⁴

1.2 Versus Arthritis Centres

Versus Arthritis recognises the importance of funding excellent science regardless of geographical location, building on regional strengths and national collaborations. Over a 10-year period, Versus Arthritis established 13 Centres of Excellence, each focussing on discrete MSK research challenges ranging from genetics and epidemiology to biomechanics and primary care; from sport and exercise to health and work; from adolescence to ageing.¹⁵ Versus Arthritis Centres of Excellence include institutions from across England, Scotland and Wales. Seven Centres comprise multiple partners; three include NHS Hospital Trusts. Three Versus Arthritis Centres are funded in partnership to maximise their reach and impact; two with MRC and extra support from the host institutions and one with Great Ormond Street Hospital Children’s Charity. The Centre for Sport, Exercise and Osteoarthritis Versus Arthritis is strengthened by several international collaborators, utilising expertise from Sweden, the Netherlands, Australia and USA.

1.3 Versus Arthritis as a commissioner and leader of research

In addition to funding external research activities, Versus Arthritis has undertaken and commissioned policy-based research to explore wide-ranging issues affecting people with arthritis including why and

⁸ Arthritis as a Compelling Cause. Research report on qualitative and quantitative work conducted by Ipsos MORI on behalf of Arthritis Research UK. 2013.

⁹ CAF UK Giving 2019: An overview of charitable giving in the UK. Charities Aid Foundation. May 2019.

¹⁰ UK Health Research Analysis 2018 (UK Clinical Research Collaboration, 2020) ISBN 978-0-903730-29-7

¹¹ The five most influential medical research charities in the UK. Pharma Boardroom. January 2019. Accessed online 16th November 2020 at <https://pharmaboardroom.com/articles/the-5-most-influential-medical-research-charities-in-the-uk/>

¹² Annual Report. Versus Arthritis. 2016.

¹³ <https://mrc.ukri.org/research/initiatives/advanced-pain-discovery-platform-apdp/>

¹⁴ Defying Arthritis at Every Age. Versus Arthritis. November 2018.

¹⁵ <https://www.versusarthritis.org/research/our-current-research/our-research-centres/>

how MSK health should be considered as part of multiple long-term conditions¹⁶, the unmet needs of people living with arthritis¹⁷ and the economic costs of arthritis for the UK economy.¹⁸

Versus Arthritis led the way among research charities in ensuring that public and patient involvement is routinely incorporated into the research funding decision-making process. Initially achieved through the USER stakeholder committee established in 2008, this approach has been refined over time, and patient voice is now integrated fully into all research activities through close collaboration with Patient Insight Partners.¹⁹

In 2007, the Arthritis Research Campaign led the MSK community in a new vision to work in partnership with the UK Clinical Research Network (UK CRN), industry and other funders, to develop a comprehensive programme that would permit the testing of both new and existing interventions, based on a nationally agreed and scientifically robust research agenda, across the major disease areas within the charity's remit.²⁰ Seven Clinical Study Groups (CSGs) were established, to obtain consensus from all relevant stakeholders on the most relevant and important therapeutic questions, and translate these into methodologically sound and feasible proposals.²¹

Since 2019, this vision has continued through the work of Versus Arthritis' three Research Advisory Groups (RAGs) and the existing Paediatric Rheumatology CSG which remains in operation within the National Institute for Health Research (NIHR) CRN and addresses conditions including juvenile idiopathic arthritis and associated uveitis (JIA), Juvenile Dermatomyositis, scleroderma, vasculitis, bone disease and juvenile SLE. The three Versus Arthritis RAGs focus on -

- 1) adult inflammatory arthritis including rheumatoid arthritis and related inflammatory conditions including axial spondyloarthritis and psoriatic arthritis;
- 2) autoimmune rheumatic diseases (or connective tissue diseases) including scleroderma, vasculitis and systemic lupus erythematosus, and
- 3) musculoskeletal disorders including osteoarthritis and related degenerative disorders, conditions of bone including osteoarthritis and conditions of pain including lower back pain and fibromyalgia.

The RAGs have an important role in identifying key issues and opportunities to develop and influence research funding, with a multidisciplinary membership representing specialist researchers, people with arthritis and health professionals.²² Regular review and analysis conducted by the RAGs provides critical oversight of the current state of play of MSK research.

From a historical model of open or response-mode research funding, Versus Arthritis has increasingly moved towards identifying strategic research priorities, leading to investment into pioneering research areas. Over the last eight years, these priorities have included 'stacking the odds towards a cure' and 'pushing frontiers in health research'; research into bacteria which live in or on the human body which are collectively known as the 'microbiome', to understand how they impact the immune system and potentially lead to diseases such as rheumatoid arthritis; research to accelerate the delivery of experimental and translational medicines, new treatments or cutting-edge

¹⁶ Musculoskeletal conditions and multimorbidity. Versus Arthritis. 2017.

¹⁷ Arthritis Research UK Unmet Needs of People with Arthritis. Revealing Realities. 2015.

¹⁸ The economic costs of arthritis for the UK economy. Oxford Economics on behalf of Arthritis Research UK. 2010.

¹⁹ [Our patient insight partners | Versus Arthritis](#)

²⁰ Silman AJ. A new paradigm for musculoskeletal clinical trials in the UK: the Arthritis Research Campaign (ARC) Clinical Studies Groups initiative. *Rheumatology* 2008;47: 7779.

²¹ Silman & Rudkin, A national strategy for UK musculoskeletal clinical research: Arthritis Research UK clinical studies initiative. *Rheumatology* 2011; 50:640-642

²² <https://www.versusarthritis.org/research/research-funding-and-policy/research-advisory-groups/>

improvements for people with arthritis, and research to gain a greater understanding of the role of pain and fatigue in MSK disease.²³

1.4 Versus Arthritis support for careers

Versus Arthritis is committed to building a world-class workforce to continue the fight against arthritis through supporting research careers and building skills capacity within the MSK research community UK. Of 434 Versus Arthritis Fellows for whom data was available in June 2020, at least 68 (15%) are Professors within their MSK specialty. Three Versus Arthritis Centres of Excellence have former Fellows as their Directors and at least 15 former Fellows contribute to the MSK sector as expert members of Versus Arthritis RAGs. 20% of the members of the Versus Arthritis College of Experts are former Fellows.²⁴ Since 1978, Versus Arthritis has established nine Endowed Chairs at universities across the UK to promote excellence in academic rheumatology at a cost of over £6.5 Million.²⁵

1.5 Versus Arthritis partnerships

Versus Arthritis works in partnership with others to maximise its approach to and impact of research funding, in order to achieve more than could be done individually. This includes other research funders, universities, hospitals and commercial organisations.²⁶ Versus Arthritis has established a partnership with NIHR through Programme Grants for Applied Research to address Pain Roadmap priorities in disease management and applied health research²⁷ and a longstanding partnership with Medical Research Council to support three Versus Arthritis Research Centres. Innovative cross-disciplinary funding opportunities have been developed through partnership with other charities including Connect Immune²⁸, a new initiative to radically change how autoimmune conditions are researched and understood, and joint fellowships with MQ: Transforming Mental Health to conduct research investigating the impact of MSK conditions on mental health. Versus Arthritis is seeking to support innovation and translation in medical technologies with clearly defined commercialisation routes through research funded in partnership with the Medical Technologies Innovation Knowledge Centre.²⁹ Beginning in April 2020, Versus Arthritis selected technology company Razor as a strategic partner to deliver new and innovative AI technologies. Razor will build upon existing business intelligence that exists around the Versus Arthritis research portfolio, revolutionising the way that the charity maximises its research investment to improve the quality of life for people living with arthritis. Research funded jointly by Versus Arthritis and British Society for Rheumatology is currently investigating the impact of 'lockdown' on individuals with arthritis or other long-term MSK conditions as a funded extension to the established MAintaining MuscuOskeleTal Health (MAmMOTH) study.³⁰

Availability of robust population data for the prevalence of MSK conditions is limited because most treatment occurs in primary care, where data are not consistently collected. Versus Arthritis partnered with Imperial College London to develop the Musculoskeletal Calculator³¹, a tool designed to produce prevalence estimates which is now available on Public Health England's Musculoskeletal Conditions

²³ [Our plans for 2020/21 | Research | Versus Arthritis](#)

²⁴ Internal data compiled. June 2020.

²⁵ Internal data compiled. June 2020.

²⁶ <https://www.versusarthritis.org/research/research-funding-and-policy/working-in-partnership/>

²⁷ <https://www.nihr.ac.uk/documents/nihr-themed-call-on-the-management-of-chronic-pain-nihr-programme-grants-for-applied-research-in-partnership-with-versus-arthritis/20388>

²⁸ <https://www.immunology.org/news/connect-immune-research-new-initiative-support-autoimmune-research>

²⁹ <https://www.versusarthritis.org/media/21992/medical-technologies-proof-of-concept-call-2020.pdf>

³⁰ <https://w3.abdn.ac.uk/hsru/mammoth/>

³¹ <https://www.versusarthritis.org/policy/resources-for-policy-makers/musculoskeletal-calculator/>

website.³² Versus Arthritis has recently partnered with the Nuffield Foundation to fund two new research projects which will create new datasets and exploiting existing data. These will include drawing together data on diagnosis and treatment from GPs, rheumatologists, social care and community service providers and information collected directly from patients and the wider population.³³

2. The individual, societal and economic impact of medical research

2.1. Evidence of the impact of Versus Arthritis-funded research activity

Since genetics was first shown to play a role in rheumatoid arthritis in 1953, through to the licensing of the first anti-TNF therapy in 2000 and approval of the first cartilage cell transplantation for early knee osteoarthritis by the NHS in 2017, Versus Arthritis-funded research has delivered life-changing breakthroughs which directly have improved the quality of life of people with arthritis and related MSK conditions.^{34,35}

Research outputs are not limited to traditional biomedical treatments. Versus Arthritis funding supported the initial development of ESCAPE-pain, a non-drug intervention involving group physio and peer to peer support which has been shown to reduce pain, increase function and improve the ability to self-manage their condition in people with knee osteoarthritis (OA). ESCAPE-pain went on to be supported by the Health Innovation Network (HIN) from 2014 before being adopted by the Academic Health Science Networks (AHSN) as a national programme in 2018.³⁶ By March 2019, ESCAPE-pain had spread from 50 to 154 sites and from 20 to 42 NHS Trusts, with a 482% increase in participation with 32,758 patients referred and a reported 498% increase in patients benefitting.³⁷ The Versus Arthritis-supported STarT Back Tool, an example of evidence-based implementation of stratified care for chronic back pain, led to a significant reduction in disability and halved the time off work without increasing health care costs.^{38,39} Versus Arthritis funded the REmote MOnitoring of Rheumatoid Arthritis (REMORA) project which was the first study to demonstrate that patient-reported symptoms can be collected using a smartphone app and successfully transferred directly into NHS electronic health records.⁴⁰

Versus Arthritis actively seeks opportunities to improve and promote research impact. Versus Arthritis investment in MSK research is focused on translation and improved outcomes for people with arthritis through the UK Musculoskeletal Translational Research Collaboration (The UK MSK TRC), a joint collaboration with NIHR. The UK MSK TRC creates an opportunity to work collaboratively with all sectors of the health and care ecosystem to further research and implementation in MSK disorders and provides industry with streamlined access to MSK clinical and academic experts.⁴¹ Research supported by Keele University and Primary Care Centre Versus Arthritis is captured in a recent

³² [Musculoskeletal Conditions - PHE](#)

³³ <https://www.versusarthritis.org/news/2020/april/working-with-others-to-maximise-the-impact-of-research-funding/>

³⁴ <https://www.versusarthritis.org/media/17906/research-timeline-poster-sept19.pdf>

³⁵ [Our research achievements | Versus Arthritis](#)

³⁶ I Walker, A., Boaz, A., Gibney, A. *et al.* Scaling-up an evidence-based intervention for osteoarthritis in real-world settings: a pragmatic evaluation using the RE-AIM framework. *Implement Sci Commun* 1, 40 (2020). <https://doi.org/10.1186/s43058-020-00032-6>

³⁷ The Academic Health Service Network. Impact Report. Office for Life Sciences/NHS. 2018/2019.

³⁸ <https://startback.hfac.keele.ac.uk/>

³⁹ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/670211/musculoskeletal_conditions_return_on_investment_final_report.pdf

⁴⁰ <https://clahrcprojects.co.uk/resources/projects/remote-monitoring-rheumatoid-arthritis-remora>

⁴¹ <https://www.nihr.ac.uk/partners-and-industry/industry/collaborate-with-us/ukmsktrc.htm>

overview of physiotherapy treatment or exercise plans developed through research. This provides a simple and accessible tool for patients to use to understand how research can benefit them.⁴²

2.2. Evidence of the wider impact of MSK research

An analysis of the rate of return of UK public MSK research spend in the period 1978-1997 and the interventions resulting from research in the period 1994-2013 demonstrates that every £1 invested in MSK research historically delivered a return equivalent to 22-25% per year.⁴³ This is a combination of a 7% internal rate of return specifically for monetised health gains resulting from MSK research investment added to an estimated 15-18% return from broader economic or 'spillover' impact of biomedical and health research in the UK.^{44,45}

A number of Academic Health Service Networks (ASHN), which were designed to spread innovation at pace by acting as regional catalysts to connect public and private stakeholders, have funded successful MSK research innovation and implementation programmes. These include Health Innovation Networks' support for regional adoption and scale-up of the ESCAPE-pain programme⁴⁶; Oxford ASHN's support to improve outcomes for early inflammatory arthritis (EIA) patients through the 'angry hand' public awareness campaign to reinforce need for early diagnosis and treatment, and working with rheumatology teams across the Oxford ASHN area to address delays in access to secondary care⁴⁷; and development by the South West AHSN of a programme to give clarity and understanding on the use of biological therapy for rheumatoid arthritis (RA) and the impact that early intervention can have on the local health economy.⁴⁸

NHS Research Scotland promotes and supports excellence in clinical and translational research in Scotland so that patients can benefit from new and better treatments. Within MSK health, its remit is to support research that deals with interventions that can be applied to the prevention and treatment of patients with MSK diseases including medicines as well as lifestyle interventions, medical devices and comparison of surgical approaches for prevention & treatment.⁴⁹

MSK research in the UK has improved health and clinical outcomes across the EU and globally. UK researchers are involved in almost all rheumatoid arthritis research programmes at EU level.⁵⁰ 146 Research Excellent Framework 2014 impact case studies reported MSK health impact globally, with 124 reporting impact across the EU and 118 reporting impact in the UK.⁵¹ Across the EU, the Innovative Medicines Initiative (IMI) is the world's biggest public-private research partnership⁵², with MSK priority diseases represented across a number of IMI programmes including prevention of RA through an understanding of the earliest events in disease progression⁵³, more personalised treatments at earlier stages of inflammatory autoimmune diseases through revised disease

⁴²Moving Forward A guide for the public on the latest physiotherapy research for the health and wellbeing of people with muscle, bone and joint pain. NIHR. August 2020.

⁴³ Estimating the returns to United Kingdom publicly funded musculoskeletal disease research in terms of net value of improved health outcomes. Glover et al. Health Research Policy and Systems 16:1. 2018.

⁴⁴ Medical Research: What's it worth? A briefing on the economic benefits of musculoskeletal disease research in the UK. Wellcome. 2018.

⁴⁵ Quantifying the economic impact of government and charity funding of medical research on private research and development funding in the United Kingdom. Sussex et al. BMC Medicine 14:32. 2016.

⁴⁶ Adoption and spread of innovation in the NHS. The Kings Fund. 2018.

⁴⁷ Establishing networks to improve patient care in early inflammatory arthritis: Case Study. Oxford Academic Health Science Network. 2018.

⁴⁸ Rheumatoid Arthritis Project: Case Study. 2016. South West Academic Health Science Network

⁴⁹<https://www.nhsresearchscotland.org.uk/research-areas/musculoskeletal-health>

⁵⁰ The Impact of Collaboration: The Value of UK Medical Research to EU Science and Health. A review of existing evidence and views from the EU. Technopolis Group. May 2017.

⁵¹ The Impact of Collaboration: The Value of UK Medical Research to EU Science and Health. A review of existing evidence and views from the EU. Technopolis Group. May 2017.

⁵² <https://www.imi.europa.eu/>

⁵³ <https://www.rtcure.com/>

classification⁵⁴ and creation of an osteoarthritis platform containing data from over 10,000 patients and healthy volunteers to support clinical trials for personalised treatments.⁵⁵

Internationally, MSK research has resulted in innovation that has directly lead to novel therapeutic interventions that improve patient outcomes and standard of care, including the development of new biomaterials and biomechanics to improve replacement joints, advanced imaging to revolutionise diagnosis and treatment and stem cell therapies to open up opportunities for regenerative technologies.⁵⁶ Broader healthcare initiatives such as the National Institutes of Health (NIH) Helping to End Addiction Long-term (HEAL) Initiative to provide scientific solutions to the opioid crisis and offer new hope for individuals, families, and communities maintain close links to major research projects such as back pain projects led by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).⁵⁷

2.3. Evidence of the positive impact of UK medical research

MSK research in the UK operates within the context of an ecosystem of researchers, funders and policy makers with deep connectivity of universities, frontline NHS hospitals and independent UK charities/foundations.⁵⁸ The UK Life Sciences sector generates an annual turnover £73bn and supports 482,000 jobs.⁵⁹ Overall, every additional £1 of public research expenditure is associated with an additional £0.83–£1.07 of private sector R&D spend in the UK, 44% of which occurs within a year of public investment⁶⁰ and in 2018, UK biotech SMEs raised £2.2bn from private investors.⁶¹

Medical research charities have a vital role to play within the system. Versus Arthritis is a member of the Association of Medical Research charities (AMRC) whose members have invested £14 billion in research in the UK since 2008, with £1.9 billion in 2019 alone.⁶² In 2019, Association of Medical Research Charities (AMRC) member charities funded half of all publicly funded medical research nationally (increased from 41% in 2018)⁶³, while 32% of non-commercial research supported by the NIHR CRN was funded by AMRC charities. 213,000 people in the UK were recruited into over 1200 clinical studies or trials funded by AMRC charities.⁶⁴

Robust evidence is emerging that research not only has academic and economic benefits but is directly associated with improved patient outcomes.⁶⁵ Even patients who are not directly involved in trials themselves benefit from being treated in research-active hospitals.⁶⁶

3. Challenges faced by the MSK research community and the wider research sector

3.1. The scale of MSK disease

⁵⁴ <https://www.imi.europa.eu/projects-results/project-factsheets/precisesads>

⁵⁵ <https://www.imi.europa.eu/projects-results/project-factsheets/approach>

⁵⁶ Innovations in MSK Research (Orthopaedic Research Society). Accessed online May 2020.

⁵⁷ NIH HEAL Initiative Research Plan. Accessed online May 2020.

⁵⁸ The Impact of Collaboration: The Value of UK Medical Research to EU Science and Health. A review of existing evidence and views from the EU. Technopolis Group. May 2017.

⁵⁹ Life Sciences: Catalysing Investment and Growth. Interim Report. UK BioIndustry Association. 2019.

⁶⁰ Quantifying the economic impact of government and charity funding of medical research on private research and development funding in the United Kingdom. Sussex et al. BMC Medicine 14:32. 2016.

⁶¹ Life Sciences: Catalysing Investment and Growth. Interim Report. UK BioIndustry Association. 2019.

⁶² AMRC. Medical Research Charities: Our Sector's Footprint in 2019. June 2020.

⁶³ Medical research charities: Our Sector's Footprint in 2018. Association of Medical Research Charities. 2019.

⁶⁴ AMRC. Medical Research Charities: Our Sector's Footprint in 2019. June 2020.

⁶⁵ Recognising research - how research improves patient care. Van't Hoff & Selvaratnam: Royal College of Physicians. 2018. Accessed online April 2020

⁶⁶ High hospital research participation and improved colorectal cancer survival outcomes: a population-based study. Downing et al. Gut 66:89–96. 2017.

Musculoskeletal conditions comprise more than 150 diagnoses that affect muscles, bones, joints and associated tissues such as tendons and ligaments. The most common and disabling musculoskeletal conditions are osteoarthritis, back and neck pain, fractures associated with bone fragility, injuries and systemic inflammatory conditions such as rheumatoid arthritis.⁶⁷ The impact of impaired MSK health on individuals and society globally is profound and the burden is predicted to rise markedly in coming decades.⁶⁸ Around 1 in 3 people worldwide live with chronic MSK conditions, rising to 1 in 2 people in America which is comparable with the combined prevalence of cardiovascular disease and chronic respiratory disease.⁶⁹ Following submission of a report by Osteoarthritis Research Society International in 2016,⁷⁰ in 2018 the US Food and Drug Administration recognised OA as a serious disease with an unmet medical need for therapies that could modify the underlying pathophysiology of the disease and potentially change its natural course to prevent long-term disability.⁷¹

Musculoskeletal conditions were consistency ranked second for Years Lost to Disability (YLD) globally over a 15 year period⁷², while low back and neck pain are the greatest cause of Years Lost to Disability in each of the individual UK nations and 18 other 'comparator' countries.⁷³ MSK conditions affected an estimated 18.8 million people across the UK in 2017.⁷⁴ While MSK conditions are considered to largely contribute to morbidity rather than mortality, there is a relationship between chronic pain (high impact or interfering) and mortality which is not well understood. Participants in a UK study including a MSK cohort, who reported being often troubled by moderate or severe pain that interferes with daily life, had an increased risk of mortality.⁷⁵

Research in 2008 estimated that rheumatoid arthritis and osteoarthritis resulted in a combined annual cost to the UK economy of £30.7bn.⁷⁶ Work-related MSK conditions are the most commonly reported cause of occupational ill-health in Great Britain. They account for 41% of all ill-health cases and 34% of working days lost to ill-health.⁷⁷ In Northern Ireland, 29% of all absences from work were due to musculoskeletal problems or back and neck problems while back pain and muscle/joint pain accounted for 53% of all work-related illnesses reported over a 12-month period.⁷⁸

The impact of impaired MSK health on individuals and society globally is profound and a multilevel, integrated response is required including collaboration between groups working on MSK conditions to address this effectively.⁷⁹ In a survey conducted for Versus Arthritis in 2015⁸⁰, 62% of people with MSK conditions felt that the NHS doesn't give their condition a high enough priority and 53% felt that GPs lacked specialist knowledge in their condition. 48% felt they had to 'fight' to get the best treatment and/or care. Although their condition was not life threatening, 88% reported that it was debilitating and limited how they lived their lives.

⁶⁷ World Health Organization Musculoskeletal Conditions - Key Facts. Accessed online May 2020.

⁶⁸ Musculoskeletal Health Conditions Represent a Global Threat to Healthy Aging: A Report for the 2015 World Health Organization World Report on Ageing and Health (Briggs et al 2016; Gerontologist)

⁶⁹ Bulletin of the WHO: Reducing the global burden of MSK conditions. Briggs. 2018. Accessed online May 2020.

⁷⁰ OARSI White Paper- OA as a Serious Disease. Report submitted to US Food and Drug Administration. November 2016.

⁷¹ Osteoarthritis: Structural Endpoints for the Development of Drugs, Devices, and Biological Products for Treatment Guidance for Industry. Food and Drug Administration. 2018.

⁷² Sebbag E, Felten R, Sagez F, et al. The world-wide burden of musculoskeletal diseases: a systematic analysis of the World Health Organization Burden of Diseases Database. *Annals of the Rheumatic Diseases* 2019;78:844-848.

⁷³ The Burden of Disease in England compared with 22 peer countries. A report for NHS England. Public Health England. 17th Jan 2020.

⁷⁴ Global Health Data Exchange, Institute for Health Metrics and Evaluation. 2017.

⁷⁵ Smith et al 2018. Pain and Mortality in Older Adults: The Influence of Pain Phenotype. *Arthritis Care Res (Hoboken)*. 70:236-243.

⁷⁶ The economic costs of arthritis for the UK economy. Oxford Economics on behalf of Arthritis Research UK. 2010.

⁷⁷ Health Priority Plan: Musculoskeletal Disorders. Health and Safety Executive (HSE). 2017.

⁷⁸ Guidance on the Prevention and Management of Musculoskeletal Disorders (MSDs) in the Workplace. Health and Safety Executive for Northern Ireland (HSENI) and the Health and Safety Authority (HSA). 2013.

⁷⁹ Musculoskeletal Health Conditions Represent a Global Threat to Healthy Aging: A Report for the 2015 World Health Organization World Report on Ageing and Health (Briggs et al 2016; Gerontologist)

⁸⁰ Arthritis Research UK Unmet Needs of People with Arthritis. Revealing Realities. 2015.

The COVID-19 pandemic is creating new and unexpected challenges for MSK health which are still not fully understood. An interim report found a significant increase in MSK complaints among home workers. More than half of the survey respondents reported new aches and pains, especially in the neck, shoulder and back, compared to their normal physical condition. A third of respondents reported eating a less healthy diet while 60% were exercising less. Poor sleep, fatigue, mental health concerns also reported.⁸¹ While there is an expectation of overall reduced mortality in the UK, as a result of lockdowns, increases in MSK conditions are estimated to impact both morbidity and mortality outcomes. Social distancing resulting in a requirement to work from home without ergonomic office equipment is the reason for predicting an increase in MSK conditions.⁸² Lockdown had immediate negative consequences for people with pre-existing MSK disease, based on findings from an online survey. 52% of respondents said that their symptoms had worsened since lockdown measures were introduced.⁸³

The impact of contracting COVID-19 on MSK health is also becoming apparent. It is now known that COVID-19 is a disease affecting multiple systems, including the respiratory, cardiovascular, renal, nervous, MSK and metabolic systems.⁸⁴ A review of published clinical data from over 12,000 patients collected during the first 5 months of the COVID-19 pandemic found that from the onset of the symptoms and to the most severe stages of COVID-19 disease, MSK symptoms, including muscle pain, joint pain, and fatigue, were a nearly constant presence.⁸⁵ There is growing evidence of the long-term health effects of COVID-19, which include long-term respiratory complications, thrombosis, heart failure, kidney injury, fatigue, joint and muscle pain, and metabolic abnormalities.⁸⁶ NHS guidelines recognise that being ill with COVID-19 may make pre-existing MSK pain worse, and that further support may be required if these symptoms do not resolve within 3 months.⁸⁷

Long-term health impacts are still to be determined. Research including the PHOSP-COVID study has been prioritised through Urgent Public Health status, to gain a comprehensive picture of the impact COVID-19 has had on longer term health outcomes across the UK for hospitalised patients, and develop trials of new strategies for clinical care, including personalised treatments for groups of long COVID patients based on the particular disease characteristics.⁸⁸ NICE guidelines which address long-COVID health effects including MSK symptoms are in development.⁸⁹

3.2. Gaps and imbalance in MSK research activity

Some specific examples identified through the evidence review are summarised below.

Recruitment to clinical trials. In 2018, 212,000 people in the UK were recruited into over 1300 clinical studies or trials funded by AMRC charities but only 10,000 people were recruited into MSK clinical studies or trials compared to 17,000 into dementia/ neurodegeneration studies.⁹⁰ Currently Versus Arthritis does not provide a mechanism to support people with MSK conditions who are

⁸¹Homeworker wellbeing survey. Interim Findings. Evan et al. Institute for Employment Studies. 2020.

⁸²Direct and Indirect Impacts of COVID-19 on Excess Deaths and Morbidity: Executive Summary. Department of Health and Social Care, Office for National Statistics, Government Actuary's Department and Home Office. 15 July 2020.

⁸³ Toby O Smith, Karen Durrant, Linda Birt, Pippa Belderson, Jackie Chipping, Max Yates, Jordan Tsigarides, Caitlin Notley, Felix Naughton, Lee Shepstone, Alex Macgregor, Accessing health services for musculoskeletal diseases during early COVID-19 lockdown: results from a UK population survey, *Rheumatology Advances in Practice*, rkaa047, <https://doi.org/10.1093/rap/rkaa047>

⁸⁴ Rapid Response: Short and Long Term Health Effects of COVID-19. UK Parliament. 7th September 2020.

⁸⁵ Cipollaro et al. Musculoskeletal symptoms in SARS-CoV-2 (COVID-19) patients. *Journal of orthopaedic surgery and research*, 15: 178. 2020 <https://doi.org/10.1186/s13018-020-01702-w>

⁸⁶ Rapid Response: Short and Long Term Health Effects of COVID-19. UK Parliament. 7th September 2020.

⁸⁷ Your COVID Recovery: Musculoskeletal, shoulder & back pain. National Health Service. 2020.

⁸⁸ <https://www.phosp.org/>

⁸⁹ NICE & SIGN announce latest rapid Covid-19 guideline will address Long Covid. October 2020. Accessed online 17th November at <https://www.nice.org.uk/news/article/nice-sign-announce-latest-rapid-covid-19-guideline-will-address-long-covid>

⁹⁰ Medical research charities: Our Sector's Footprint. Association of Medical Research Charities. 2019.

interested in taking part in research studies or researchers who find recruiting to their studies challenging. 68% of people with MSK conditions are interested in taking part in research but only 15% have taken part in research to do with their MSK condition while 82% of MSK researchers have experienced challenges with recruitment.⁹¹ Failure to recruit sufficient numbers of participants to MSK clinical trials or to recruit in a timely manner risks the success and impact of trials.

One specific example of a gap within MSK research is availability of clinical trials addressing children's MSK health. In 2017-18, the NIHR spent £11.1 million on research studies into MSK disorders. The NIHR CRN supported 429 MSK studies, 136 of which were new studies, and recruited 38,120 patients to studies in 2019/20. However, in November 2020, just under half of studies currently recruiting new patients are open to those under the age of 18 (80/164 studies) and this is further reduced when individuals are stratified into infants, children or adolescents (22%, 17% and 20% studies respectively).⁹² In the period 2011-2016, Versus Arthritis funding for children's health research was up to 9% per year.⁹³ The Paediatric Task Force for Global MSK Health, part of the Global Alliance for Musculoskeletal Health (G-MUSC), aims to raise awareness about unmet needs for Children & Young People with MSK conditions, promotion of MSK health through lifestyle and the avoidance of injury. One of the aims of the Task Force is that greater awareness and collaboration can harness existing and emerging knowledge, innovations and technical advances to make real impact and achieve 'better MSK health for all'.⁹⁴

Addressing the imbalance between types of research activity. Versus Arthritis restructured its funding committees following a review in 2015 with three new strategic funding Sub Committees (SCs) addressing the themes of Disease, Treatment and Health established in 2016 to stimulate insight-driven, challenge-led funding across the domains of discovery, translational, clinical and health research. While this has gone some way towards addressing a recognised imbalance towards early stage, biomedical science research activity, more still needs to be done. The five-year strategic framework for MSK health, published by the Department of Health and Social care working with Public Health England and Department for Work and Pensions and supported by Versus Arthritis, recognises that the public health system is not as effective as it could be to prevent, maintain and improve MSK health and activities to address this will require commissioning and influencing MSK public health research.^{95,96}

The Health Research Classification System (HRCS) codes types of health research activity from 1 (underpinning research) through to 8 (health and social care services research); to capture the continuum of activity required from basic discovery bioscience activity through to applied, translational research.⁹⁷ An analysis of MSK Fellowships showed that the focus of rheumatology fellows from 2009 to 2017 changed dramatically with respect to HRCS types of activity. In 2009 ~50% were coded to 'aetiology' (2), with no fellowships coded to 'prevention' (3) or 'health and social care services' (8). In 2017, however, more than 10% of fellowships were coded to 'underpinning research' (1), less than 20% to 'aetiology' (2), with 70% coded to activity codes 3-8 and all codes represented. However, 'prevention' (3) and 'health & social care services' (8) combined only represented ~5% of

⁹¹ Versus Arthritis Mass Participation Project Final Report (INTERNAL: DRAFT)

⁹² <https://www.nihr.ac.uk/explore-nihr/specialties/musculoskeletal-disorders.htm>

⁹³ Turning the tide - five years on. Royal College of Paediatrics & Child Health. 2018.

⁹⁴ Foster, H.E., Scott, C., Tiderius, C.J. et al. The paediatric global musculoskeletal task force - 'towards better MSK health for all'. *Pediatr Rheumatol* 18, 60 (2020). <https://doi.org/10.1186/s12969-020-00451-8>

⁹⁵ Musculoskeletal Health: A 5 year strategic framework for prevention across the life course. Department of Health and Social care working with Public Health England and Department for Work and Pensions; supported by Versus Arthritis. June 2019.

⁹⁶ Musculoskeletal Health: 5 year strategic framework logic model

⁹⁷ <https://hrcsonline.net/research-activities/>

fellowships⁹⁸, indicating that there are still improvements to be made in achieving balance across all types of research activity within the MSK sector.

Rare diseases research. Rare autoimmune rheumatic diseases include conditions such as scleroderma, vasculitis and systemic lupus erythematosus.⁹⁹ The UK Strategy for Rare Diseases includes 51 Commitments, 17 of which relate to research activities, from meaningful patient involvement in research to ensuring specialist centres prioritise research and facilitating international research through shared databases.¹⁰⁰ In 2018, the Rare Autoimmune Rheumatic Disease Alliance (RAIRDA) specifically called for health-services research to be undertaken to assess what benefits have accrued for people living with rare autoimmune rheumatic diseases since 2013, as a consequence of the UK Strategy for Rare Diseases and introduction of Specialised Services Commissioning.¹⁰¹

Attracting and retaining MSK clinical researchers. Rheumatology was one of 9 specialities with less than 50 clinical Fellows in 2017, and among those, there was a high proportion of Early Career Researchers and a lack of senior academic leaders. In 2017, only 20% of rheumatology Fellowships were coded to Health Research Classification System (HRCS) code 'MSK' while 60% were coded to HRCS 'inflammation & immune system', suggesting an imbalance of expertise across the Versus Arthritis disease remit.¹⁰² In late 2019, Versus Arthritis shared an outline of the charity's evolving new approach to research funding and leadership in which investing in and supporting teams, talent and future leaders in MSK research was identified as one of its near-term research priorities.¹⁰³

MSK conditions are often undervalued. Both with respect to their prevalence and impact on individuals¹⁰⁴ and their contribution to the experience of living with multiple long-term conditions.¹⁰⁵ Historically, there has been a perception that "there's not much that can be done", with the result that the impact of MSK disorders is not appreciated or addressed in ways which would maximally benefit individuals and the economy.¹⁰⁶

3.3. Inequalities in funding for MSK research

Financial donors to Versus Arthritis overwhelmingly (65%) consider that "*researching new or better treatments*" is the best answer to the problem which prompted them to donate, regardless of what they considered the problem to be.¹⁰⁷ However, 55% of people with arthritis believe that arthritis does not receive the same level of research and investment by drug companies compared with other diseases while 58% felt there would be a significant or moderate positive impact on their quality of life if greater investment into cures and treatments was encouraged.¹⁰⁸ Only 20% of survey respondents

⁹⁸ UK-Wide Survey of Clinical and Health Research Fellowships. Medical Research Council. 2017.

⁹⁹ Reduce, improve, empower: Addressing the shared needs of rare autoimmune rheumatic diseases. Rare Autoimmune Rheumatic Disease Alliance. February 2018.

¹⁰⁰ UK Strategy for Rare Diseases. Department of Health. 2013.

¹⁰¹ REDUCE, IMPROVE, EMPOWER: Addressing the shared needs of rare autoimmune rheumatic diseases. Rare Autoimmune Rheumatic Disease Alliance. February 2018.

¹⁰² UK-Wide Survey of Clinical and Health Research Fellowships. Medical Research Council. 2017.

¹⁰³ <https://www.versusarthritis.org/research/research-funding-and-policy/our-approach-to-research/>

¹⁰⁴ COVID may deepen the hidden human and economic cost of arthritis. EULAR President Professor Iain McInnes writing in EU Reporter. October 2020.

¹⁰⁵ Just One Thing After Another - Living with Multiple Conditions. A report from the Taskforce on Multiple Conditions. 2018.

¹⁰⁶ Let's dispel the myth that "not much can be done" to treat Musculoskeletal disorders. Martin McShane (NHS England's National Medical Director for Long Term Conditions). November 2015. Accessed online at <https://www.england.nhs.uk/blog/martin-mcshane-20/>

¹⁰⁷ Internal: Versus Arthritis Audience Donor Insight self-selecting survey. 2018.

¹⁰⁸ Arthritis Research UK Unmet Needs of People with Arthritis. Revealing Realities. 2015.

felt research into arthritis was *less* important than research into diseases such as diabetes or Alzheimer's disease.¹⁰⁹

There are inequalities in public funding for research across underserved health conditions, including MSK health.¹¹⁰ In the US, funding for MSK conditions received least National Institutes of Health funding compared to other disease conditions.¹¹¹ UK public funding for arthritis research* has been essentially static since 2014, with these conditions accounting for 22.4% of Years Lost to Disability in the UK but only receiving 3.4% of public health research funding.¹¹² Total funding (in direct, real terms) by the twelve large public and charity funders of health research which comprise the UKCRC Health Research Analysis Forum (HRAF) in the period from 2014 to 2018 was £2.17bn or a 7.3% increase from the previous reporting period.¹¹³ Within the context of this modest increase, there was an £8m decrease in funding specifically allocated to arthritis research* from the core 12 HRAF funders.¹¹⁴ While the average funding proportion allocated to each Health Research Classification System (HRCS) category was 4.7% in the UK Health Research Analysis 2018 dataset, the arthritis research* funding proportion was 3.4%. This is substantially lower than the funding proportion for cancer (18.9%), cardiovascular disease (6.1%), mental health (6.1%) and neurological disease (9.7%).

Disability Adjusted Life Years (DALY) are frequently used as a measure of the burden of disease. 2016 DALY rates (2016)¹¹⁵ were used to investigate the proportion of funded allocated to different Health Categories in the UK Health Research Analysis 2018. While correlation analysis shows relatively poor matching of the UK's burden of disease in DALY rates and the research funding available, and a number of Health Categories received a funding allocation lower than the comparative burden of disease, MSK was one of five categories where this difference was considered significant (along with Respiratory, Oral & Gastrointestinal and combined group Blood/Cardiovascular/Stroke). In contrast, four disease categories (Metabolic & Endocrine, Reproductive health, Childbirth and Infection) received a higher proportion of research funding than the corresponding UK DALY rating.

3.4. Sector-wide research funding uncertainties

COVID has substantially impacted research activity and research careers across the sector.

The Versus Arthritis research portfolio was severely impacted in March 2020 by the COVID pandemic as universities closed and all face-to-face meetings stopped. In late March, it was estimated that between 75% and 100% of active awards had either been paused or research had been delayed. At that time, approximately 80% of clinical researchers paid from the charity's funding awards had been seconded to patient care with the impact appearing to be greatest for more junior researchers.

*The scope of 'arthritis research' is broader than the MSK definition of the Health Research Classification System (HRCS). The Versus Arthritis 2018 portfolio is categorised by HRCS code as 42% MSK, 53% Immune & Inflammatory System (I&IS) and 5% 'other' codes. A detailed keyword search was developed to interrogate the UK Health Research Analysis 2018 dataset and identify all research activity which fitted the Versus Arthritis remit. This is designated 'arthritis research' and is used to understand funding trends as they relate to the Versus Arthritis remit when the UKCRC Health Research Analysis Forum datasets are referred to throughout this document. ¹⁰⁹ Arthritis as a Compelling Cause. Research report on qualitative and quantitative work conducted by Ipsos MORI on behalf of Arthritis Research UK. 2013.

¹¹⁰ Delivering the Science-based economy. The Role of Health Research. Thomas & Nanda; Institute for Public Policy Research. July 2020.

¹¹¹ Lewis, R., Gómez Álvarez, C.B., Rayman, M. et al. Strategies for optimising musculoskeletal health in the 21st century. BMC Musculoskelet Disord 20, 164 (2019). <https://doi.org/10.1186/s12891-019-2510-7>

¹¹² Trends in Arthritis and Related Conditions Research: The Past, Present and How to Influence the Future. Tammy Cheng, Versus Arthritis. Accessed online 12th November 2020 at <https://www.versusarthritis.org/media/22701/arthritis-research-trends-key-messages-2020.pdf>

¹¹³ UK Health Research Analysis 2018 (UK Clinical Research Collaboration, 2020) ISBN 978-0-903730-29-7

¹¹⁴ Trends in Arthritis and Related Conditions Research: The Past, Present and How to Influence the Future. Tammy Cheng, Versus Arthritis. Accessed online 12th November 2020 at <https://www.versusarthritis.org/media/22701/arthritis-research-trends-key-messages-2020.pdf>

¹¹⁵ Global Health Estimates 2016: Disease burden by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018.

Researchers demonstrated exceptional flexibility and resilience: a number volunteered their time to COVID testing efforts while a large proportion were able to use the initial period of lockdown to undertake data analysis and write manuscripts. Research protocols were adapted where possible to collect data remotely. Some researchers returned to work over the summer, but at September 2020, it was calculated that approximately 35% of the Versus Arthritis research portfolio remained paused.

Recruitment of patients to trials was still severely impacted at the time of writing, with only a few studies able to make amendments or restart. A number of trials funded by the charity paused in the set-up phase and the slow return of elective surgery will continue to impact both patient recruitment and the supply of human tissue for research. There will be unavoidable costs and delays to re-establish other essential biological resources.

The experience of Versus Arthritis funded researchers is reflected across the sector. AMRC charities play a vital and unique role in the UK's research sector¹¹⁶ but have projected an average 41% decrease in their medical research spend over the next year due to the COVID-19 pandemic, leaving a predicted £310 million shortfall.¹¹⁷ Modelling to consider lost charitable income, reductions in leveraged income from private sector investment and the wider impact of adverse economic conditions predicts that £7.8 billion in medical research funding is at risk between now and the end of 2027.¹¹⁸ In addition to funding concerns, the Academy of Medical Royal Colleges has shared deep concerns about the risk of a long-term gap in the academic clinical workforce as a result of a depleted COVID-19 generation and notes that where paused research cannot be resumed, there will be gaps in scientific evidence to inform clinical practice, service provision and policies.¹¹⁹ The career progression of junior researchers will be greatly impacted for years to come by a reduced capacity to generate the preliminary data necessary to secure future funding through lost laboratory time.¹²⁰ It is clear that COVID-19 will continue to have a substantial impact on medical research careers across the sector, with a risk of long-term inequality as the specific impact for individuals will vary dependent on personal circumstance.¹²¹

Government funding commitments and research priorities. The NHS Long Term Plan acknowledges the benefits research and innovation can make to patients and the critical importance of research and innovation to drive future medical advance.¹²² However, a recent analysis estimated an underinvestment in UK R&D of £222 billion since 1985 when compared to OECD averages, despite the life sciences outperforming the UK economy on productivity over the previous 20 years¹²³. New opportunities for R&D funding outlined in the UK' Industrial Strategy in 2017¹²⁴ were broadly considered to represent a "*once-in-a-generation opportunity to set our science and research budget on a new path.*"¹²⁵ The March 2020 Budget reiterated plans to increase UK investment in R&D to 2.4% of GDP by 2027 and increase public funding for R&D to £22bn per year by 2024/25.¹²⁶ Government's stated vision for the UK to be a global science superpower and its funding

¹¹⁶ Without Charities. Association of Medical Research Charities. Sept 2020.

¹¹⁷ <https://www.amrc.org.uk/Handlers/Download.ashx?IDMF=3916cef3-3f16-437e-9cb7-7dbcbd5c0c33>

¹¹⁸ Research At Risk: Mitigating the Impact of Covid 19 on Health R&D Investment. Institute for Public Policy Research. 2020.

¹¹⁹ Mitigating the impact of COVID-19 on research and clinical academia. Academic Leads Group statement on behalf of the Academy of Medical Royal Colleges. October 2020. Accessed online 17th November 2020 at <https://www.aomrc.org.uk/statements/mitigating-the-impact-of-covid-19-on-research-and-clinical-academia/>

¹²⁰ <https://acmedsci.ac.uk/more/news/covid-and-careers-what-does-the-future-hold>

¹²¹ <https://royalsociety.org/blog/2020/05/science-in-lockdown-part-one/>; <https://royalsociety.org/blog/2020/05/science-in-lockdown-part-two/>

¹²² The NHS Long Term Plan. NHS England. 2019.

¹²³ Delivering the Science Based Economy. The Role of Health Research. Thomas & Nanda; Institute for Public Policy Research. July 2020.

¹²⁴ Industrial Strategy: Building a Britain fit for the future. HM Government. 2017. Accessed online on 17th November 2020 at

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/664563/industrial-strategy-white-paper-web-ready-version.pdf

¹²⁵ The Road to 2.4%. David Willetts: The Policy Institute; Kings College London. 2019.

¹²⁶ <https://www.gov.uk/government/publications/budget-2020-documents>

commitments were broadly welcomed within the sector although it was noted that to be effective, this commitment needs to increase public R&D investment, incentivise private R&D investment and invest in people and skills.¹²⁷

The UK's Industrial Strategy set out four Grand Challenges for research and innovation: Artificial Intelligence, ageing society, clean growth and future mobility. UKRI's Strategic Plan for 2020/2021 builds on this to set out priorities for each of the nine Research Councils. These include advancing the frontiers of bioscience discovery (BBSRC); addressing disease prevention and health inequalities; accelerating the early detection of diseases, catalysing novel approaches in precision medicine and advanced addressing the increasing burden of multimorbidities (MRC) and working in partnership to transform healthcare through the new materials, sensors, imaging and analytical techniques needed to improve prediction, diagnosis and treatment of disease (EPSRC). The UK's Business Energy and Industrial Strategy Committee is currently holding an inquiry to determine whether the Industrial Strategy remains fit for purpose in the light of the COVID-19 pandemic.¹²⁸

A Roadmap for UK R&D was published by BEIS in July 2020.¹²⁹ The Roadmap built upon the existing commitments to increase UK investment in R&D to 2.4% of GDP by 2027 and increase public funding for R&D to £22bn per year by 2024/25. It was intended to test the detail of stated Government intentions, as the start of a conversation with all stakeholders in the research system. Government funding commitments were due to be finalised as part of the Comprehensive Spending Review (CSR) in July 2020. As a result of the coronavirus pandemic, the CSR was first delayed¹³⁰ and then reduced to a one-year settlement, due to conclude in late November 2020.¹³¹ This has created ongoing uncertainty about how public investment in urgent, non-COVID-19 health-related research including MSK health and multiple long-term conditions may be impacted.

COVID has fundamentally altered the way medical research is funded and supported by the UK Government at least in the short term. Rapid response initiatives launched jointly by MRC and NIHR feature rapid submission and evaluation timescales, agile responsiveness and aggressive timeframes for impact.¹³²

Further uncertainty stems from the proposed changes to Public Health England, which has a commitment to public health research, translation and innovation; to do research, to support research and to use evidence from research.¹³³ It is not yet clear how this will be impacted by the announcement in August 2020 of the creation of the new National Institute for Health Protection. The NIHP, whose primary focus is public health protection and infectious disease capability will focus on a 'rigorous science-led approach' to public health protection, working with local government, the NHS and the devolved administrations.¹³⁴

The Scottish Government's Research Strategy five-year plan published in 2015 promoted research in pursuit of quality improvement and health and social care integration, with a closer focus on research proposals of direct patient, or health services or public health, benefit. It includes three key priorities – informatics, precision (stratified) medicine and digital health – with a commitment to ensure relevant funding outputs are suitably evaluated through research to warrant their adoption in the NHS and

¹²⁷ Building on Scientific Strength. The Next Decade of R&D Investment. Campaign for Science and Engineering. July 2019.

¹²⁸¹²⁸ <https://committees.parliament.uk/work/469/postpandemic-economic-growth-industrial-strategy/>

¹²⁹ UK R&D Roadmap. HM Government. July 2020.

¹³⁰ <https://www.gov.uk/government/publications/comprehensive-spending-review-2020-representations-guidance#history>

¹³¹ <https://www.gov.uk/government/news/spending-review-to-conclude-late-november>

¹³² <https://blogs.bmj.com/bmj/2020/07/29/fiona-m-watt-covid-19-a-new-disease-has-forced-a-re-think-of-how-we-fund-medical-research/>

¹³³ <https://www.gov.uk/government/publications/doing-supporting-and-using-public-health-research-phe-strategy>

¹³⁴ <https://www.gov.uk/government/news/government-creates-new-national-institute-for-health-protection>

International partnership – to address global strategic research issues.¹³⁵ Scotland's Life Sciences Strategy prioritised SubSectors include Digital Healthare, Regenerative Medicine, Medical Technologies and Pharmaceutical Services.¹³⁶ An updated Scottish research strategy for 2021 and beyond has yet to be announced.

Considerable under-investment in Welsh Government-funded research and innovation activity in Wales has been reported despite investment levels increasing at the UK level and in England and Scotland. Wales was found to lack critical-mass and research base size due to a deficit of STEM researchers.¹³⁷ The Welsh Government's research and innovation strategy was launched in 2019.¹³⁸ Public Health Wales set its key priorities as tackling persistent inequalities in healthy life expectancy, childhood obesity, reducing the overall consumption of healthcare and preparing services and communities for the challenges of an increasingly ageing population.¹³⁹ Health care research is funded under a different mechanism via Health and Care Research Wales¹⁴⁰, a networked organisation, supported by Welsh Government, which brings together a wide range of partners across the NHS in Wales, universities and research institutions, local authorities, and others. HCRW promotes research into diseases, treatments, services and outcomes that can lead to discoveries and innovations which can improve and even save people's lives.

Uncertainty over the impact of Brexit on UK R&D remains. The UK research sector continues to vigorously support efforts to ensure the UK and EU reach agreement to ensure continued participation in joint research activity beyond January 2021; advocating that clinical trials are reliant on EU-UK collaboration, close research partnerships accelerate life changing medical research and shared global challenges require joint solutions.¹⁴¹ With respect to EU and international engagement beyond January 2021, Wellcome Trust advocates that the UK must build networks globally, must be strategic, using its available resources efficiently to maximise impact and must use its influence to contribute to global good.¹⁴²

Guidance for the Life Sciences sector prepared by the UK Government raises a number of uncertainties for UK researchers and for the MSK community more widely as the end of the transition period approaches in Jan 2021. Data restrictions may impact personal data sharing if the EU's data adequacy assessment does not find UK Regulations to be adequate. MHRA will become the UK's standalone medicines and medical devices regulator and will be responsible for orphan medicines and regulation of biosimilar products. The UK will undertake its own independent certification of batches of biological medicines while imported biological medicines from the EEA will require a NIBSC certificate. MHRA will introduce a Conditional Marketing Authorisation (CMA) scheme for new medicinal products that fulfil and unmet need. The current system for clinical trial registration on a public access database will not change, with international registers continuing to be used.

4. Delays and inconsistencies in the translation and implementation of research outputs.

¹³⁵ Delivering Innovation through Research Scottish Government Health and Social Care Research Strategy. Chief Scientist Office. 2015.

¹³⁶ Life Sciences Strategy for Scotland 2025 Vision: Accelerating Growth, Driving Innovation. Life Sciences in Scotland. 2017.

¹³⁷ Research and Innovation in Wales. National Assembly for Wales Economy, Infrastructure and Skills Committee. April 2019

¹³⁸ Research and Innovation: the Vision for Wales. Higher Education Funding Council for Wales. May 2019.

¹³⁹ Research Strategy 2015-2018. Public Health Wales. Accessed online on 17th November 2020 at http://research.publichealthnetwork.cymru/files/7014/8708/7189/PHW_Research_Strategy_report.pdf

¹⁴⁰ <https://healthandcareresearchwales.org/>

¹⁴¹ Securing a strong outcome for research in the EU-UK future relationship: Reaching an agreement on UK participation in Horizon Europe. Wellcome Open Letter, signed by 100+ organisations including AMRC. 22 July 2020.

¹⁴² The UK's role in global research. Wellcome Trust. October 2020.

4.1. MSK-specific examples

There are many varied reasons for delays and inconsistencies in the translation and implementation of MSK research outputs. These include safety concerns, for example in the case of cell-based therapies for skeletal disease¹⁴³, translational gaps as may exist between success treating inflammatory pain in preclinical animal models and subsequent lack of demonstration of efficacy in human clinical trials¹⁴⁴, and lack of time, resource, communication, knowledge and trust when implementing changes to prevent MSK diseases in the workplace.¹⁴⁵

Analysis of UK public MSK research spend in the period 1978-1997 found that the elapsed time between research spend and an associated health gain was 16 years. This lag time in demonstrable benefit is similar to that reported separately for cancer and CV disease.^{146,147} Simple low-cost non-drug interventions such as the ESCAPE-pain programme can be transformative in health and care services but their rapid adoption and spread is dependent on access to continued funding at key points.¹⁴⁸

4.2. Sector-wide challenges

While examples of delays and inconsistencies in research translation exist within MSK research, this is a sector-wide issue. The AMRC recognises that “*it is rare that the path to impact is linear*” and suggests that research outputs focussed on one disease area are often applicable more widely. With “*a complex web of interactions*” required over a lengthy period of time to achieve successful implementation of research outputs, early engagement in partnerships both within and beyond the medical research charity sector is essential.¹⁴⁹ The Academy of Medical Sciences considers that biomedical research as currently conducted does not have the capacity to address increasingly diverse and complex issues, and the full societal value of research for the health of the public will not be realised until it is translated into improved health and health equity.¹⁵⁰

A lack of translation of research outputs into health and social care innovation is widely recognised.¹⁵¹ The first annual report of the Industrial Strategy Council (ISC) in early 2020 noted that Government funding is available at scale in the Industrial Strategy to support R&D, particularly linked to the four Grand Challenges but while it is useful to acknowledge the level of R&D spend, what matters is the outputs of this increased R&D activity. The ISC suggests going forward, it is important to consider how this funding should be used to “*crowd-in*” private funding, help incentivise industry co-investment and sustain the flow of ideas from the research base into commercial uses.¹⁵² Investment in research implementation is also essential to improve the success of embedding non-drug research interventions into healthcare settings. The Council for Science and Technology noted that some challenges do not require new research and innovation, but instead require implementation

¹⁴³ The promise and challenges of stem cell-based therapies for skeletal diseases: stem cell applications in skeletal medicine: potential, cell sources and characteristics, and challenges of clinical translation. Diederichs et al. *Bioessays*. 35: 220–230, 2013.

¹⁴⁴ Preclinical assessment of inflammatory pain. Muley et al. *CAN Neurosci Ther* 22:88-101. 2016.

¹⁴⁵ Barriers for implementation of successful change to prevent musculoskeletal disorders and how to systematically address them. Yazdania & Wells. *Applied Ergonomics* 73: 122-140. 2018.

¹⁴⁶ Estimating the returns to United Kingdom publicly funded musculoskeletal disease research in terms of net value of improved health outcomes. Glover et al. *Health Research Policy and Systems* 16:1. 2018.

¹⁴⁷ Medical Research: What's it worth? A briefing on the economic benefits of musculoskeletal disease research in the UK. Wellcome. 2018.

¹⁴⁸ Adoption and spread of innovation in the NHS. The Kings Fund. 2018.

¹⁴⁹ Making a Difference: Impact Report. Association of Medical Research Charities. 2019.

¹⁵⁰ Improving the Health of the Public by 2040: Optimising the research environment for a healthier, fairer future. Academy of Medical Sciences. September 2016

¹⁵¹ The Biomedical Bubble: Why UK research and innovation needs a greater diversity of priorities, politics, places and people. Jones & Wilsdon: NESTA. 2018.

¹⁵² Is the industrial strategy working? First Annual Report of the Industrial Strategy Council. 2020.

through public engagement, trust and regulation.¹⁵³ Innovation is one of four strategic priorities outlined in Public Health England's research strategy and includes commitments to accelerate translation through development of a model for translation of evidence into practice, a process to enable robust evaluation of public health interventions and working with partner organisations and private sector to support translation.¹⁵⁴ The Service Development and Commissioning Directives for Arthritis and Chronic Musculoskeletal Conditions in Wales highlight the need for new ways of working which are evidence-based, flexible, rooted in a cycle of evaluation and continual improvement, and which encourage innovation across organisational boundaries.¹⁵⁵ The Directive has not been updated since its publication in 2007. Despite specific service improvements, such as the setting up of clinical MSK assessment and treatment services in some health board areas, and better access to physiotherapy, there are concerns that MSK health in Wales is chronically underprioritised and stakeholders would like to see more timely access to the right treatments and services with a greater focus on prevention and early intervention.¹⁵⁶

Northern Ireland's 2016 Health and Social Care Strategy highlighted the benefits of increasing the capacity of the Health and Social Care sector to engage with research, by including increasing numbers of staff in research project teams which ensured that research projects focus on topics that are of real, current consequence for the staff who interact directly with patients and clients to provide services. It included an objective that the likelihood of delivering a return on investment as evidenced by clinical benefits and improved care for patients and service users as well economic development would contribute to decisions on which research projects to fund.¹⁵⁷

The 2016 Accelerated Access Review made a series of recommendations to enable the NHS to improve patient outcomes by using the UK's strong biosciences research and life sciences industrial base. The Accelerated Access Collaborative (AAC) was intended to bring breakthrough products to market and then to patients as quickly as possible.¹⁵⁸ However, this focus on innovative 'products' – therapeutics, medical devices, diagnostic and digital health tools – may not reflect the reality that most products are used within complex care pathways spanning different providers and clinical specialities, and new innovations need to be considered in relation to these.¹⁵⁹ Recent improvements to the AAC announced in May 2019 established a new dedicated unit within NHS England and NHS Improvement to oversee UK health innovation and implement a system to identify the best new innovations and make sure the NHS is ready to make use of them.¹⁶⁰

Technology plays a major role in shaping both demand (a new treatment makes it possible to address an unmet need) and supply (drug therapies replacing complex surgery). There is a role for the NHS in better understanding the forces shaping those decisions and the impacts this has on the health system. Although technological progress itself is largely outside the influence of NHS policymakers, it is shaped by decisions about investment and research, therefore how technology is adopted within the NHS can be influenced.¹⁶¹ A horizon-scanning activity considering the attractiveness and feasibility of innovations likely to reach market over a 10-year period found health-

¹⁵³Principles for science and technology moon-shots: Letter from Science & Technology Council to the PM. July 2020.

¹⁵⁴ Doing, supporting and using public health research. The Public Health England strategy for research, translation and innovation. July 2015.

¹⁵⁵¹⁵⁵ <http://www.wales.nhs.uk/documents/Service-Development-and-Commissioning-e.pdf>

¹⁵⁶ <https://seneddresearch.blog/2016/06/13/arthritis-and-musculoskeletal-conditions-chronically-underprioritised/>

¹⁵⁷ Research for Better Health & Social Care: A Strategy for Health & Social Care Research and Development in Northern Ireland (2016-2025). Department of Health, Social Services and Public Safety. 2016.

¹⁵⁸ <https://www.gov.uk/government/publications/accelerated-access-review-response>

¹⁵⁹ <https://www.phgfoundation.org/blog/accelerating-access-to-healthcare-innovations>

¹⁶⁰ <https://www.nice.org.uk/aac>

¹⁶¹ The bigger picture Learning from two decades of changing NHS care in England. The REAL Centre. Health Foundation. October 2020.

themed innovations were under-represented in its prioritised list. This appeared to be due to them having relatively focused, rather than cross-cutting, benefits within a rigid regulatory landscape.¹⁶²

5. The requirement for greater sophistication and coordination in the research sector.

5.1. Prevention research

New research is required to promote MSK health, prevent MSK conditions, develop systematic methods for the collation of data about MSK conditions and interventions, and explore gaps to improve services while encouraging innovative, new models of care.¹⁶³ Alongside cutting-edge treatments for arthritis, there are opportunities for a life-course approach to public health interventions in MSK health, with individuals improving and maintaining their MSK health; living healthy lives as well as longer lives.¹⁶⁴ There is currently no systematic collection of data about the extent of MSK conditions in the population and the interventions that people need. Systematic information on incidence, prevalence, treatment, referral and outcomes for population and people with MSK conditions is urgently needed.¹⁶⁵

In early 2020, The All Party Parliamentary Group on Longevity called for research funders to give the prevention of disease a much higher priority, saying that “*National health charities have a vital role to help improve our health and reduce health inequalities... Most focus on individual diseases and their cure rather than on primary prevention... All health and disease charities might review what more they can do to promote better health and support a social movement to do so.*”¹⁶⁶

5.2. Multimorbidity research

One in eight people in England report living with at least two long-term conditions, at least one of which is MSK related.¹⁶⁷ Four out of five people with osteoarthritis have at least one other long-term condition such as hypertension, cardiovascular disease or depression while one in six people with rheumatoid arthritis are affected by depression.¹⁶⁸ There is a demographic shift globally with people from all countries living longer with chronic disease. The burden shift is from communicable to long-term non-communicable disease, which commonly includes MSK conditions.¹⁶⁹

MSK health must be considered locally and nationally, both individually and as part of wider multiple long term condition (MLTC) planning; this includes developing a research framework which reflects the prevalence and impact of chronic diseases and emphasises the goal of healthy life expectancy.¹⁷⁰ Research needs to deliver improvements for people with MSK conditions through broader representation in clinical trials including people with multimorbidities and multi-joint disease, and wider consideration of the heterogeneity of treatment effects in order to better predict outcomes and tailor treatments. Research should also investigate more integrated and holistic approaches to

¹⁶² The Prioritisation of Future Innovations A Consultancy Study for the Department of Business, Energy and Industrial Strategy (BEIS) BEIS Research Paper Number 2020/042. October 2020.

¹⁶³ Musculoskeletal Health: A 5 year strategic framework for prevention across the life course. Department of Health and Social care working with Public Health England and Department for Work and Pensions; supported by Versus Arthritis. June 2019

¹⁶⁴ MSK Health: a public health approach. Arthritis Research UK 2013.

¹⁶⁵ Musculoskeletal Health: A 5 year strategic framework for prevention across the life course. Department of Health and Social care working with Public Health England. 2019

¹⁶⁶ The Health of the Nation - A Strategy for Longer, Healthier Lives. All Parliamentary Group for Longevity. 2020. Accessed online Feb 2020.

¹⁶⁷ The State of Musculoskeletal health 2019. Arthritis and other musculoskeletal conditions in numbers. Versus Arthritis. 2019

¹⁶⁸ The State of Musculoskeletal health 2019. Arthritis and other musculoskeletal conditions in numbers. Versus Arthritis. 2019

¹⁶⁹ Bulletin of the WHO: Reducing the global burden of MSK conditions. Briggs. 2018. Accessed online May 2020.

¹⁷⁰ Musculoskeletal conditions and multimorbidity. Versus Arthritis. 2017.

management rather than focussing on individual treatments in isolation.¹⁷¹ MSK research is specifically required within the context of rising levels of comorbidity and multimorbidity. The complex needs of the growing group of people affected by multimorbidity with an MSK component must inform the research agenda, and disease specific non-profit organisations should work together to develop resources, programmes, research and partnerships to meet the complex and changing needs of people with multimorbidity.^{172,173}

UK Government commitments to increase healthy life expectancy by 5 years by 2035, are particularly relevant in the light of COVID-19, which has shown this to be fundamental to the health of society.¹⁷⁴ A specific focus on R&D which promotes healthy life expectancy and management of multiple conditions is essential going forward.¹⁷⁵ There is an opportunity to achieve efficiencies of scale and maximise the impact of research investment by prioritising research which addresses complex health challenges such as healthy ageing.

The Innovative Medicines Initiative IMI2 Strategic Research Agenda 2014-2020 is aligned to EU Health Research Priorities and WHO's Priority Medicines for Europe and the World. It focusses on the unsustainability of current healthcare systems and the rising costs of disease of ageing and multimorbidity. It recommends that '*now is the time for change*' through next generation target identification, biomarkers, bioinformatics, -omics technologies and precision medicines, but also identifies the need to increase patient participation early in R&D to better understand needs and create integrated programmes tailored to maximising outcomes outside of traditional drug treatments.¹⁷⁶

5.3. Sector-wide challenges

The essential need for partnership and cross-sector working. Medical research charity investment catalyses and supports the whole research ecosystem, building capacity through supplying the skills pipeline, sparking further investment in R&D, funding from the patient perspective and acting as innovators and honest brokers.¹⁷⁷ The medical research charitable sector has an essential role to play within the wider research landscape, but its distinctive characteristics and priorities mean that it cannot work in isolation. The majority of charitable spend as measured in the 2018 Health Research Analysis dataset falls within HRCS codes 'Underpinning' (1) and 'Aetiology' (2) (27% and 37%, respectively), with approximately a quarter of spend in 'Detection and Diagnosis' (4) and 'Development of Treatments' (5) (10% and 14% respectively). This is in keeping with AMRC findings that in the period from 1999 – 2018, 51% of AMRC members' funding supported research into normal function and what causes disease, while 40% supported research into detection of disease and development of diagnostics/treatments and only 9% supported research into how to advance disease prevention, management and health services.¹⁷⁸

In the 2018 Health Research Analysis dataset, charity funding priorities were very similar to those of UKRI, which is consistent with a shared focus on basic science and early stage translational activity.

¹⁷¹ Challenges and controversies of complex interventions in osteoarthritis management: recognising inappropriate and discordant care. Dziedzic & Allen. *Rheumatol* 57:iv88-iv98. 2018.

¹⁷² The contribution of musculoskeletal disorders in multimorbidity: Implications for practice and policy. Duffield et al. *Best Practice & Research Clinical Rheumatology* 31; 129-144. 2017.

¹⁷³ Musculoskeletal conditions and multimorbidity. *Versus Arthritis*. 2017.

¹⁷⁴ APPG for Longevity. Business Coalition for a Healthier Nation - report of findings from round tables and summary presentation in May 2020. July 2020.

¹⁷⁵ Delivering the Science Based Economy. The Role of Health Research. Thomas & Nanda; Institute for Public Policy Research. July 2020.

¹⁷⁶ The right prevention and treatment for the right patient at the right time. Strategic Research Agenda for Innovative Medicines Initiative 2. IMI. March 2014.

¹⁷⁷ <https://www.amrc.org.uk/Handlers/Download.ashx?IDMF=c9dee4cb-5212-4e14-b1bf-dc0a22b9c5b5>

¹⁷⁸ Making a Difference: Impact Report. Association of Medical Research Charities. 2019.

In contrast a much higher proportion of funding from ‘other Government and public bodies’ was coded to ‘Evaluating Treatment’ (6), ‘Management of Disease’ (7) and Health and Social Care Services Research (8).¹⁷⁹ Balance is needed for charities to understand when to fund directly and when to work in partnership with other stakeholders to make a distinctive and effective contribution to research translation and implementation.¹⁸⁰

The UK BioIndustry Association estimates that private investment in R&D needs to increase by 70% to meet government targets towards R&D spend at a rate of 2.4% of GDP by 2027 and argues that partnership is required to de-risk innovative science, accelerate progress, facilitate onward investment and bridge the ‘*valley of death*’.^{181,182} Industry-led biotechnology research offers opportunities to improve health through earlier identification of disease risk and diagnosis, faster drug development and more accurate drug delivery and new treatments for previously untreatable conditions using engineered tissue and stem cell therapies. An analysis of the life and health sciences sector in Northern Ireland identified rheumatoid arthritis as an economic area of opportunity impacting on global demand for precision medicine, connected health, clinical trials, BigData and diagnostics.¹⁸³

However, increased funding for research on its own is not sufficient. Science spend can be wasteful; there is a need to avoid ‘boom & bust’ and it is essential that infrastructure and capacity building keep pace. A “*richer ecosystem*” is required with funding streams and institutional relationships that promote commercialisation.¹⁸⁴

A “*complex multi-organisational web of pathways*” is known to be necessary to deliver healthcare innovation.¹⁸⁵ The NHS is the biggest employer of scientists, and related scientific staff and over 15% of recruits embarking on a healthcare science career in the NHS already possess a research qualification such as an MSc or PhD. The Chief Scientific Officer’s strategy to contribute to delivery of the NHS Long Term Plan through research and innovation is multi-faceted and includes - further developing the research capacity and capability of the workforce, supporting the development and the implementation of technological and service innovation, providing scientific leadership for transformational change and partnering to improve and integrate information and knowledge in collaboration with academia, industry, charities, the health and social care system and government departments.¹⁸⁶

Wider integration and sophistication can also be addressed by creating a health system that values research and provides dedicated research time for NHS staff while building practical research capacities through healthcare curriculums and incorporating flexibility into postgraduate training.¹⁸⁷ Pragmatic co-creation is one way to address the ‘know-do’ divide between academics and practitioners/implementers, with creation and utilisation of new knowledge best achieved through dialogue and partnership. Researchers can become an integral part of the frontline healthcare delivery team to embed science-based service improvement and rapid evaluation of newly developed

¹⁷⁹ UK Health Research Analysis 2018 (UK Clinical Research Collaboration, 2020) ISBN 978-0-903730-29-7

¹⁸⁰ <https://pharmaboardroom.com/articles/uk-charities-the-funding-giants-of-medical-research/>

¹⁸¹ [Lost in translation: the valley of death across preclinical and clinical divide – identification of problems and overcoming obstacles | Translational Medicine Communications | Full Text \(biomedcentral.com\)](#)

¹⁸² Life Sciences: Catalysing Investment and Growth. Interim Report. UK BioIndustry Association. 2019.

¹⁸³ LIFE & HEALTH SCIENCES NORTHERN IRELAND. Capability Assessment & Foresight Report. MATRIX – Northern Ireland Science Industry Panel. February 2015.

¹⁸⁴ The Road to 2.4%. David Willetts: The Policy Institute; Kings College London. 2019.

¹⁸⁵ Innovation as a driver of quality and productivity in UK healthcare - Creating and Connecting Receptive Places. Emerging Insights Report. Marjanovic et al: RAND Europe. 2017.

¹⁸⁶ Science in Healthcare: Delivering the NHS Long Term Plan. The Chief Scientific Officer's Strategy. NHS England & NHS Improvement. 2020.

¹⁸⁷ Transforming health through innovation: Integrating the NHS and academia. Academy of Medical Sciences. 2020.

services.¹⁸⁸ Successful innovation in health system happens when combinations of drivers come together at local and national levels. Motivations of different stakeholders need to be taken into account to make progress across the health innovation pathway.¹⁸⁹ Mobilization of research to ensure implementation in practice requires integration of activities to achieve this within the research design. Knowledge mobilization requires common sense principles including co-design, collaborative working, recognition of context, impact of human relationships and communication styles and when successful, can make research by academics and care provided by healthcare professionals more relevant and meaningful.¹⁹⁰

The essential need for a change in research culture. A recent survey of academic (84%), industry and government (12%) and healthcare researchers (2%) identified a number of challenges for the UK research system. Respondents felt that the system may not always prioritise the right attributes when assessing research quality, with a focus on conservative research which is ‘retrofitted’ to fit funders requirements, and an emphasis on applicability rather than theory. Cross-disciplinary research may not be prioritised due to individual funder’s targeted priorities. Loss of innovation and blue skies thinking can result from a focus on impact. Finally, loss of talent across the research community is a genuine concern. The authors conclude that "*Those who fund, publish, evaluate or conduct research can now use this evidence as a starting-point to implement solutions in their own communities and working groups. Achieving a successful research culture will require collective responsibility and change at all levels.*"¹⁹¹ The Council for Science and Technology recommended that when seeking highly ambitious breakthroughs, ‘people, process and governance structures’ will be critical for success.¹⁹²

Improvements in research culture also extends to engagement between researchers and study participants. A recent report recognised that many trials struggle to recruit and fail to meet targets while patients and members of public are often not aware of opportunities to take part. Specifically, there are too few trial participants from poorer, black and minority ethnic communities.¹⁹³ Changes should be developed in partnership with patients and the public and be informed by what matters to patients, trial participants and their families.¹⁹⁴ A new strategy for health and social care research in the UK is designed to promote research transparency, champion openness and drive improvements in performance. Health Research Authority’s vision for research transparency is that trusted information from health and social care research studies is publicly available for the benefit of all.¹⁹⁵ In addition, there is recognition that clinical research needs to include under-served population groups more broadly, as groups may respond differently to an intervention due to differences in physiology or disease state. Only by ensuring the study population reflects the target population who live with the condition can results be generalisable to a broad population. New guidance and examples of best practice were released in 2020 to support this initiative.¹⁹⁶

6. Emerging opportunities in research

¹⁸⁸Bridging the Ivory Towers and Swampy Lowlands: increasing the impact of health services research on quality improvement. Marshall, M. International Journal for Quality in Health Care 26:1–5. 2014.

¹⁸⁹ Innovation as a driver of quality and productivity in UK healthcare - Creating and Connecting Receptive Places. Emerging Insights Report. Marjanovic et al: RAND Europe. 2017.

¹⁹⁰ Implementation research: making better use of evidence to improve healthcare. Ellis. Rheumatology 2020;0:1–3

¹⁹¹ What Researchers Think About The Culture They Work In. Wellcome. Jan 2020.

¹⁹²Principles for science and technology moon-shots: Letter from Science & Technology Council to the PM. July 2020.

¹⁹³ Vision for the Future of UK Clinical Trials: Patient, Public and Participant Perspectives. NIHR. 2020.

¹⁹⁴ Vision for the Future of UK Clinical Trials: Patient, Public and Participant Perspectives. NIHR. 2020.

¹⁹⁵ Make it Public: transparency and openness in health and social care research. Health Research Authority. July 2020

¹⁹⁶ Improving inclusion of under-served groups in clinical research: Guidance from the NIHR CRN INCLUDE group. The NIHR CRN INCLUDE Steering Group. July 2020

6.1. MSK-specific research underpinning research into emerging and diverse health conditions

In the late 1980s, ground-breaking research showed that a molecule called Tumour Necrosis Factor (TNF) which occurs naturally in the body plays a key role in inflammation. Early, innovative trials funded by Versus Arthritis led to the introduction of a new class of game-changing treatments known as biological therapies, with the first anti-TNF therapy licensed in 2000. The output from this research, which initially focussed on a single condition – rheumatoid arthritis - has since been shown to be beneficial for a range of common medical conditions known as inflammatory-mediated immune diseases (IMIDs). These conditions share some common genetic features, environmental triggers and inflammatory mechanisms and their prevalence in Western society is estimated to be 5-7%.¹⁹⁷ Versus Arthritis is a charity partner of IMID-BIO¹⁹⁸ a national consortium which seeks to enable more precise treatment of IMIDs including arthritis, psoriasis, liver and kidney disease, and identify common mechanisms which drive them.

Anti-TNF and other biologics are also being studied for the prevention and/or treatment of COVID-19. Preliminary findings from the COVID-19 Global Rheumatology Alliance found that patients who were already receiving anti-TNF therapies for rheumatic diseases had lower odds of hospitalisation.¹⁹⁹ There is a growing understanding of the potential of biological therapies but further work is needed to confirm their value in treating COVID-19. Arthritis research into the role of the anti-inflammatory and healing properties of mesenchymal stromal cells (MSCs) in the treatment of osteoarthritis is also helping COVID-19 research by seeking to determine whether MSCs can reduce the overreaction of the body's immune system to the COVID-19 infection.²⁰⁰

Profound and persistent fatigue with muscle aches has emerged as a frequent symptom of COVID-19. In partnership with the Kennedy Trust, Versus Arthritis is funding new research into this symptom which utilizes existing data. Participants enrolled in studies at King's College London who have previously had their immune systems studied will be encouraged to use the King's Covid19 Symptom Tracker App to help identify COVID-19 cases and associated symptoms. The aim of this research is to determine whether pre-existing differences in the immune system predict the onset of fatigue, its intensity and persistence both in COVID-19, and in MSK conditions.

MSK research funded over many years facilitates experts to respond at speed to emerging challenge. For example, researchers funded by Versus Arthritis were able to respond rapidly to refocus their research efforts and review the safety of hydroxychloroquine and azithromycin in the light of concerns raised through COVID-19. Hydroxychloroquine is most commonly used as the first-line treatment in patients with autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus. A multinational, retrospective study provided reassurance that short-term use of hydroxychloroquine did not appear to confer increased risk in COVID-19 patients with rheumatoid arthritis. The study also found that hydroxychloroquine, when used in combination with azithromycin appeared to be associated with serious cardiovascular adverse events and should therefore be used with caution.²⁰¹

There is an opportunity to achieve efficiencies of scale and maximise the impact of research investment by continuing to invest in cross-sector partnerships that can address common platforms

¹⁹⁷ Kuek A, Hazleman BL, Östör AJK. Immune-mediated inflammatory diseases (IMIDs) and biologic therapy: a medical revolution. *Postgraduate Medical Journal* 2007;**83**:251-260.

¹⁹⁸ <https://www.gla.ac.uk/research/az/imid/aboutus/>

¹⁹⁹ <https://ard.bmj.com/content/79/7/859.full>

²⁰⁰ <https://clinicaltrials.gov/ct2/show/NCT04397471>

²⁰¹ [https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913\(20\)30276-9/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30276-9/fulltext)

and mechanisms of disease. Whilst funding research to understand and tackle individual diseases will remain important, excellent collaborative research addressing common mechanisms underpinning clinically diverse diseases is essential.

6.2. Consolidation of MSK research priorities

Priority setting exercises have been conducted in recent years by a number of research charities and others focussed on diseases which fall within Versus Arthritis' remit. Common priorities include earlier and improved disease diagnosis, new treatments, care and services, a greater understanding of causes, biomarkers and pathophysiology.^{202,203,204}

Other priority setting exercises have focussed on the quality of the proposed research, the outcome in terms of patient care, the opportunity to attract new researchers to the disease area or increase awareness and the balance basic and applied cross-disciplinary research.²⁰⁵ A current research prioritisation exercise being conducted by Arthritis Ireland aims to develop a strategy to influence research activities for better treatments, diagnoses and cures informed by the needs of patients.²⁰⁶ Of the 100 Priority Setting Partnerships published by the James Lind Alliance which define the top 10 priorities for future research agreed by patients, carers and clinicians, more than 10% feature MSK conditions. These range from osteoarthritis to fragility fractures, juvenile conditions, rare adult MSK conditions, surgical interventions, physiotherapy and multiple long-term conditions.²⁰⁷

The European League Against Rheumatism Taskforce (EULAR) developed RheumaMap in collaboration with stakeholders across the Rheumatic and Musculoskeletal Diseases (RMD) spectrum. RheumaMap identifies a number of cross-cutting themes that are relevant to all RMDs, from the 'unifying imperative' need is identified to seek preventive measures for RMDs through to a recognition of their negative impact on other chronic disorders and a common research focus to understand, identify and treat aggressively co-morbid conditions. However, greater EU-wide coordination is still required to achieve critical mass and address key research goals for MSK conditions more widely. Strategic coordination and integration of MSK R&D across Europe is required to better define priorities, make the most of limited funding and guide policy efforts and investment.²⁰⁸

A scoping review conducted by Australia and New Zealand MSK Clinical Trials Network of 49 articles published which considered priority setting exercises for MSK conditions noted that specific research questions were much more likely to relate to treatment than implementation or health services and systems research.²⁰⁹ Targeted global research in 15 priority areas of MSK research has been recommended to address the global threat to health ageing posed by MSK conditions. This includes varied types of research - worldwide epidemiological research, barriers to healthcare use, implementation of effective interventions, cost effectiveness of emerging models of care, evaluation of long term effect of biotherapies, association between MSK and psychological health, the role of sports injury in reduced MSK health, research into prevention and rehabilitation strategies,

²⁰² Research Priority Setting in Vasculitis. Mooney et al. *Rheumatology*, Volume 55, Issue suppl_1, April 2016, Page i176, <https://doi.org/10.1093/rheumatology/kew189.010>

²⁰³ Scleroderma & Raynaud's UK Research Strategy 2017-2022

²⁰⁴ Ardoin, S.P., Daly, R., Merzoug, L. et al. Research priorities in childhood-onset lupus: results of a multidisciplinary prioritization exercise. *Pediatr Rheumatol* 17, 32 (2019). <https://doi.org/10.1186/s12969-019-0327-4>

²⁰⁵ British Sjögren's Syndrome Association Research Strategy for the period to 2019 AGM.

²⁰⁶ Strategic Plan 2019-2023. Arthritis Ireland. 2019.

²⁰⁷ <https://www.jla.nihr.ac.uk/top-10-priorities/>

²⁰⁸ RheumaMap. European League Against Rheumatism Taskforce. 2019.

²⁰⁹ Scoping review of priority setting of research topics for musculoskeletal conditions. Bourne et al. *BMJ Open* 2018;8:e023962. doi:10.1136/bmjopen-2018-023962

effectiveness of conservative care and better data tool kits for surveillance to characterise burden and document benefits of intervention.²¹⁰

6.3. New opportunities in a post-COVID world

Data and digital technology. To meet rising demands, costs and expectations, the NHS increasingly needs to deliver healthcare innovation through digital technology. Integration of the technology agenda is a precondition for success of the NHS Long Term Plan.²¹¹ NHSX's vision includes researchers being viewed as an integral part of a modern and digitised NHS, with the NHS recognised globally as a valued and equitable partner in research.²¹² Scotland's Digital Health and Care Strategy addresses how care for people in Scotland can be enhanced and transformed through the use of digital technology across the whole range of health, social care and wellbeing services. Importantly, it extends as well to informal care, self-care, prevention and public health. The strategy recognises a real opportunity for researchers in Scotland to be at the forefront of one of the fastest growing fields in global healthcare delivery and promotes and facilitates appropriate, safe and secure access to clinical, biomedical, social care and other data about individuals for approved research in the public interest.²¹³ A project funded by Nuffield Foundation beginning in June 2020 will investigate the prevalence and outcomes of rheumatic and MSK disease (RMD) in rural and urban areas across Scotland and Wales using primary and secondary care datasets. To identify the key priorities in diagnosis, treatment and healthcare access for rural RMD patients, the researchers will undertake a priority-setting survey. The aim is to identify the priorities of patients with RMD conditions living in rural areas, as well as the priorities of healthcare professionals involved in their care.²¹⁴

Rapid implementation of technological innovation has been transformative during COVID-19 as health services have moved online at a dramatic pace.²¹⁵ Digital solutions such as virtual GP appointments have been critical to continued, effective health service delivery, and COVID-19 innovations have demonstrated the ability to pivot existing technology to meet new needs.²¹⁶ For example, Versus Arthritis rapidly developed Virtual Assistant 'COVA', the first coronavirus chatbot to be developed specifically for people with a long-term health condition in the UK, after experiencing unprecedented demand through our helpline, website, online community and social media channels.²¹⁷

In a post-COVID world, there are a number of opportunities resulting from a broader understanding of and engagement with technology platforms. As a charity, this has presented Versus Arthritis with opportunities to scale up the involvement of people with arthritis and related conditions in shaping our research. Previously, many people were unable to commit to face-to-face meetings due to mobility issues, severity of disease, fatigue, caring responsibilities or employment. Utilising technology to involve people has allowed us to increase the number of people and widen the range of experience represented in our engagement activities.

Healthcare and research sector transformation. COVID has required transformation at pace, often requiring collaborative work and with a 'different risk appetite' to deliver the best healthcare in a

²¹⁰ Musculoskeletal Health Conditions Represent a Global Threat to Healthy Aging: A Report for the 2015 World Health Organization World Report on Ageing and Health (Briggs et al 2016; Gerontologist)

²¹¹ Developing a plan for Tech in Health & Care - our vision. NHSX. 2020

²¹² Developing a plan for Tech in Health & Care - our vision. NHSX. 2020

²¹³ Scottish digital health and care strategy. Digital Health and Care Scotland. 2018.

²¹⁴ <https://www.nuffieldfoundation.org/project/mapping-rheumatic-and-musculoskeletal-disease-in-scotland-and-wales>

²¹⁵ Technology and innovation for long-term health conditions. Ben Collins (Kings Fund). August 2020.

²¹⁶ <https://charitydigital.org.uk/topics/tech-to-the-rescue-what-covid-19-means-to-the-future-of-tech-for-good-7497>

²¹⁷ <https://www.charitytoday.co.uk/launch-of-uks-first-condition-specific-coronavirus-chatbot/>

timely fashion. COVID-19 has significantly accelerated transformational change through partnership working. The NHS Reset campaign aims to contribute to the public debate on what the health and care system should look like post COVID-19. The intention is to understand, translate and adapt the best COVID-19-related innovations and initiatives into everyday practice – embedding positive change in a systematic and sustainable way.²¹⁸

The global research system has been changed in an unprecedented manner by the coronavirus pandemic and all near-term considerations are shaped by this reality. A recent statement by the Campaign for Science and Engineering recognises the invaluable connectedness of UK R&D and calls for this richness to be preserved through the recovery period ahead, concluding “*We can all think carefully about the shape of the research base that we want to see emerge, and how to sustain the highly networked research ecosystem on which we all rely.*”²¹⁹ UKRI’s Strategic Plan notes that the UK’s response to the COVID-19 crisis has demonstrated the critical importance of research and innovation to the stability of social and economic systems and that “*Fundamental to the success of the response has been a flexible, agile, empowered and interconnected network of innovators, scientists and researchers: the beating heart of our communities.*”²²⁰

New Government funding opportunities. Despite the ongoing uncertainties surrounding COVID-19, the Government has released its strategy setting out a vision to extend the UK’s leadership in genomic healthcare and research. Over a 10-year period, the strategy outlines an ambition to create the most advanced genomic healthcare system in the world.²²¹ This will include a focus on rare and inherited disease and a new era of ‘genomic prevention’: a prevention-first approach to healthcare.

The US Advanced Research Projects Agency has a singular mission to invest in breakthrough technology to catalyse development of new and surprising capability and it has been suggested that the UK needs to create a similar environment that will stimulate and sustain innovation, focussing on developing advanced technologies on a 10-15 year timescale.²²² The UK Government has made a commitment to spend £800M to set up a unique and independent funding body for advanced research. The House of Commons Science and Technology Committee led a formal inquiry into the nature and purpose of the new UK research funding agency in Autumn 2020.

A £10M Innovation Scholars Scheme announced by the Government’s Office of Life Sciences in February 2020) will support secondments for academics to develop new technologies and techniques to help NHS patients as soon as possible. The scheme offers investment to support collaboration in life sciences between researchers and industry. It will include developing new healthcare wearable technologies such as smartwatches and monitors, diagnostic devices like mobile health units, and new personalised medicines based on patients’ genetic information.²²³

Increasing public engagement in research. Public awareness of R&D is high, with 72% of people saying they know what it is and 86% able to identify the most straightforward examples.²²⁴ However, a sometimes narrow perception of R&D was identified as a risk for the sector. Supporting researchers to tell their story will be an essential factor in increasing public awareness of the tangible benefits of R&D. Medical research charities act as a direct link between the public and R&D and seek to put the patients’ voices at the core of their mission and use the delivery of patient outcomes as the

²¹⁸ NHS Reset Campaign Themes. NHS Confederation. June 2020.

²¹⁹ A voice for the whole research system. Dr Sarah Main, Campaign for Science and Engineering. 2020. Accessed online May 2020.

²²⁰ UKRI Corporate Plan. October 2020.

²²¹ Genome UK: The Future of Healthcare. HM Government. September 2020.

²²² Visions of ARPA: Embracing Risk, Transforming Technology. Policy Exchange 2020.

²²³ <https://www.gov.uk/government/news/10-million-boost-to-improve-patient-care-with-new-technologies>

²²⁴ Advocating R&D Investment. Public First on behalf of the Wellcome Trust and CaSE. July 2020.

touchstone of every decision.²²⁵ In 2019, 83% of AMRC charities included the patient voice in their research, strategy or influencing work.²²⁶ It is not yet clear to what extent the coronavirus pandemic might highlight the importance of science and prompt long-term support for basic research.²²⁷ The medical research community needs to clearly communicate why certain activities need to be prioritised in order to build engagement and inspire wider appreciation for the opportunities offered by research outputs.²²⁸

This is particularly important as part of the post-COVID recovery process, during which the R&D sector needs to work collaboratively to create a clear, bold new vision for continued public/private investment while recognising the need to make wise choices about how available funds are spent.²²⁹ COVID-19 has had a major impact on public involvement in R&D. The Academy of Medical Sciences recommends that an important feature of changing research culture is for research funders to actively encourage researchers to involve the public in research whenever possible. It further notes that there is a need for collective responsibility across the biomedical research sector to ensure that public involvement continues to make significant contributions to research throughout and beyond the pandemic.²³⁰

²²⁵ On the Front Foot: A Blueprint for Change in the Medical Research Charity Sector. AMRC. 2017

²²⁶ AMRC. Medical Research Charities: Our Sector's Footprint in 2019. June 2020.

²²⁷ Sputnik moment or budget breaker: How will the pandemic alter research funding? Nidhi Subbaraman. Nature.com June 2020. <https://www.nature.com/articles/d41586-020-01519-x>

²²⁸ Start With Why - a TED Talk. Simon Sinek. 2009. Accessed online March 2020.

²²⁹ Blog post: A bold plan for research will guide choices in a post-Covid economy. Beth Thompson; Wellcome Trust. Accessed online May 2020.

²³⁰ Public involvement and engagement in research during the COVID-19 pandemic. Summary of a FORUM workshop held on 19 May 2020. Academy of Medical Sciences. October 2020.

