

# CENTRES FOR MUSCULOSKELETAL AGEING

## IMPACT REPORT



**RESEARCH  
VERSUS  
ARTHRITIS**



Medical  
Research  
Council



# LIVING HEALTHIER FOR LONGER

A decline in musculoskeletal function is a well-recognised feature of ageing. When our musculoskeletal function declines, it can lead to life-limiting changes, such as loss of mobility and independence, that can have a detrimental effect on our quality of life.

As our life expectancy increases, so does the need for dedicated research to better understand how we can live healthier for longer. Investigating why and how age-related musculoskeletal changes in our body occur is crucial to developing and implementing lifestyle and pharmacological solutions that have the greatest potential for older people living with arthritis.

## Enter our Ageing Centres

In 2012, the Medical Research Council (MRC) and Versus Arthritis established two centres of research excellence: the Centre for Integrated Research into Musculoskeletal Ageing; and the Centre for Musculoskeletal Ageing Research. They have since received over £3.4 million of infrastructure funding from Versus Arthritis and over £4 million from the MRC. This has supported network creation, capacity building, tackling unanswered scientific questions, obtaining additional funding, and integrating patient and public involvement.

From this investment, our Ageing Centres have generated world-leading research that improves our understanding of ways to delay and/or minimise the effects of ageing on our musculoskeletal system at both a tissue and whole-body level. Drawing on this research, they have debunked myths about ageing; empowered the public with accessible information and tools to maintain their musculoskeletal health as they age; advocated for funding into healthy ageing research to be prioritised in a way that matches its ever-growing significance across the globe; and primed a legacy of researchers with the skills, capacity and connections needed to tackle musculoskeletal ageing at scale.

**VERSUS  
ARTHRITIS**



## Our Ageing Research Centres of Excellence bring together world-class researchers to tackle the following questions:

### 1. What are the causes and mechanisms of musculoskeletal ageing?

Understanding how and why musculoskeletal tissues decline, as we get older, reveals important insights that could be used to halt or prevent frailty. Doing so opens opportunities to maximise our healthspan so that day-to-day quality of life can be improved in later life.

CIMA

### 2. How can we enhance musculoskeletal health in an ageing population?

Our musculoskeletal health is comprised of physiological features such as muscle mass, quality, and joint condition. These factors are all amenable to change through our lifestyle. Centre research is demonstrating ways to eat well and keep active that we can all apply in our lives to stay resilient as we get older.

CMAR

### 3. What policies need to be changed for older people living with arthritis to live well?

Our Centres are championing musculoskeletal ageing to remain high on the policy agenda using the highest calibre, evidence-based research; and improving musculoskeletal ageing disease-specific guidelines at all stages of the healthcare pathway.

CIMA

CMAR

### 4. How can we better empower people to take better control of their musculoskeletal health as they age?

Public involvement, engagement and education activities across our Centres are debunking common fallacies; boosting awareness of arthritis; and producing freely accessible evidence-based resources to equip everyone with the facts to help you take better control of your health.

CIMA

CMAR

### 5. How can we build a stronger future for healthy ageing research?

CIMA and CMAR have grown into more than a sum of their parts by working together to create a platform for healthy ageing research to thrive. They've trained many students; promoted researchers into permanent positions; acquired specialist equipment unparalleled anywhere else in the world; and established networks that will enable musculoskeletal ageing research to prosper.

CIMA

CMAR

# CENTRE FOR INTEGRATED RESEARCH INTO MUSCULOSKELETAL AGEING

The Centre for Integrated Research into Musculoskeletal Ageing (CIMA) is a collaboration between clinicians and scientists across three sites in the UK — University of Liverpool, University of Sheffield, and Newcastle University. CIMA was set up in 2012 and its mission is to undertake world-leading research into why our bones, joints, and muscles function less well as we age and why older people develop diseases of bones, joints, and muscles, such as arthritis or osteoporosis.

Investment from Versus Arthritis and the MRC has allowed us to answer important questions such as how our lifestyle can impact our bones, joints, and muscles as we age, and is there anything we can do to prevent or improve this. It has also enabled us to train over 100 post-graduate researchers who will become the future of musculoskeletal research and has led to the creation of more than 30 new staff posts across the three universities focused on musculoskeletal ageing. These achievements will ensure that this vital area of research remains a priority.

One of our main objectives was to increase our engagement with the public, patients, and representatives of the older population. As part of this commitment, we have participated in more than

70 engagement events and have cemented the involvement of patient partners in the development and evaluation of our research.

CIMA researchers have been appointed as editors to several musculoskeletal-focused journals, invited as speakers at multiple international conferences focused on musculoskeletal health and ageing, developed guidelines for the treatment of musculoskeletal conditions, and sat on numerous panels and advisory groups, including appearing as expert witnesses at the House of Lords Science and Technology Select Committee into Ageing: Science, Technology and Healthy Living.



**Professor Eugene McCloskey,**  
Director of CIMA



**Professor Malcolm Jackson,**  
Director of CIMA



**Professor John Loughlin,**  
Director of CIMA



# CENTRE FOR MUSCULOSKELETAL AGEING RESEARCH

The MRC Versus Arthritis Centre for Musculoskeletal Ageing Research (CMAR) is a collaboration between the University of Birmingham and the University of Nottingham. Its mission is to increase understanding of the biology of age-related musculoskeletal deterioration, including identifying the factors influencing an individual's trajectory towards frailty and determining the processes underpinning the transition to musculoskeletal disease.

Over the lifetime of CMAR, we have built an internationally recognised and globally networked research programme, operating across three research themes (Mechanisms of Musculoskeletal Ageing, Ageing and Progression of Musculoskeletal Disease, Interventions to Improve Musculoskeletal Health and Function), which has collectively constructed new technology platforms and generated novel and clinically testable approaches to reduce musculoskeletal ageing and disease.

Investment from Versus Arthritis and the MRC has underpinned significant leveraging of grant income for musculoskeletal ageing research in CMAR. Importantly, this investment also underpinned and accelerated capacity building with the training and progression of CMAR staff and postgraduate students at our institutions and beyond. The establishment of CMAR also played a significant role in the creation and successful renewal of our two National Institute for Health Research Biomedical Research Centres in Birmingham and Nottingham.

Both centres contain musculoskeletal ageing and health themes, facilitating the translation of CMAR knowledge and know-how to practical advice for health service providers and patients.

Through strategic collaboration with other centres of excellence in the UK and overseas, CMAR has leveraged expertise, resources and facilities to ensure traction in musculoskeletal health research and translation for the future. This has included CMAR playing leading roles in several UK Research and Innovation Musculoskeletal Ageing Research Networks. We have also partnered with policymakers and contributed to substantive ageing research policy reports, ensuring accelerated adoption of our joint findings to maximise public health impact. To date, CMAR has achieved a step-change in mechanistic understanding of musculoskeletal ageing and the testing and implementation of interventions to ensure positive impact on musculoskeletal health as we age.



**Professor Janet Lord CBE,**  
Director of CMAR (2012-2023)



**Professor Simon Jones,**  
Training Lead (2012-2023). Deputy  
Director of CMAR (2023 - Present)



**Professor Paul Greenhaff,**  
Deputy Director of CMAR (2012-  
2023). Director (2023 - Present)



# RESEARCH IMPACT AREAS



New Knowledge



Influence on Policy & Practice



New IP, Products & Services



New Networks



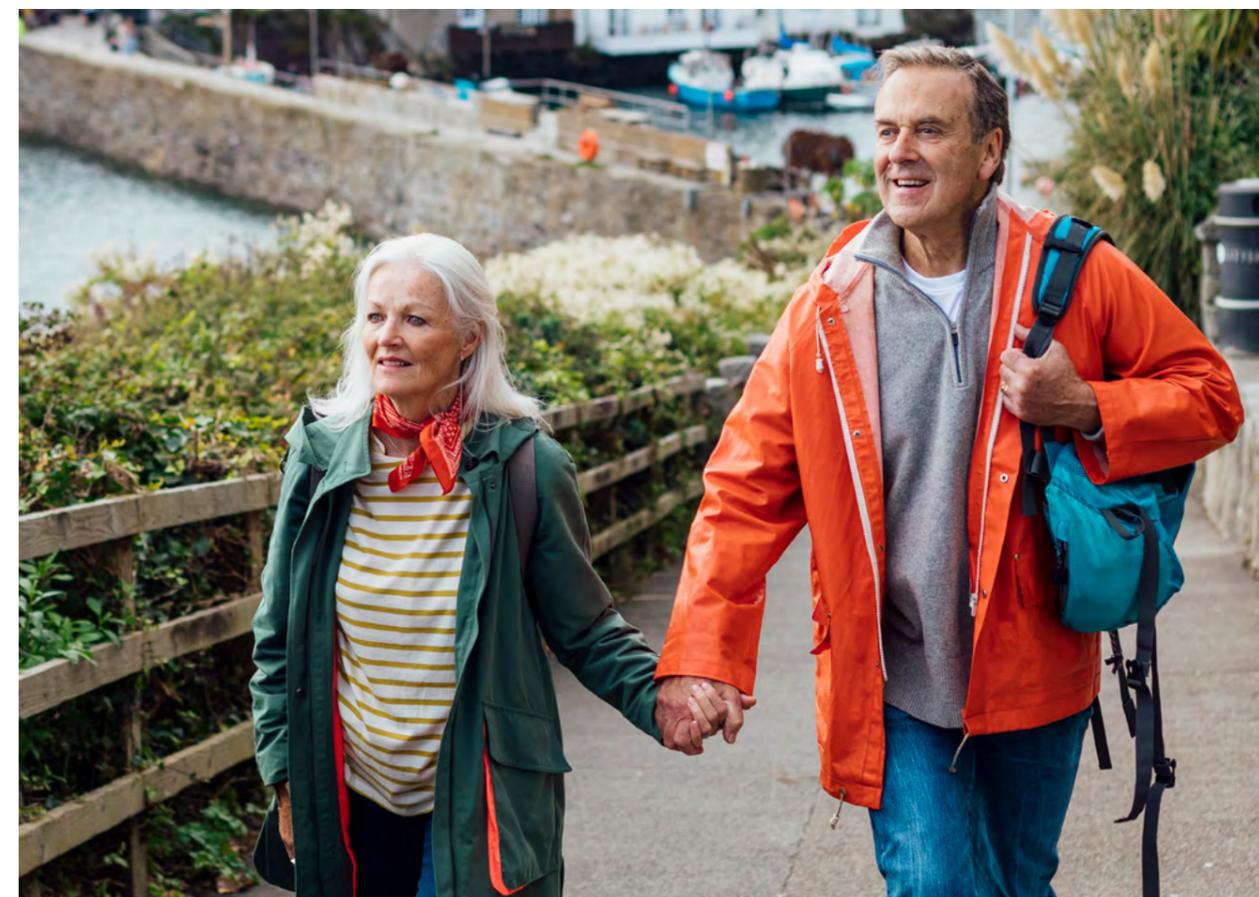
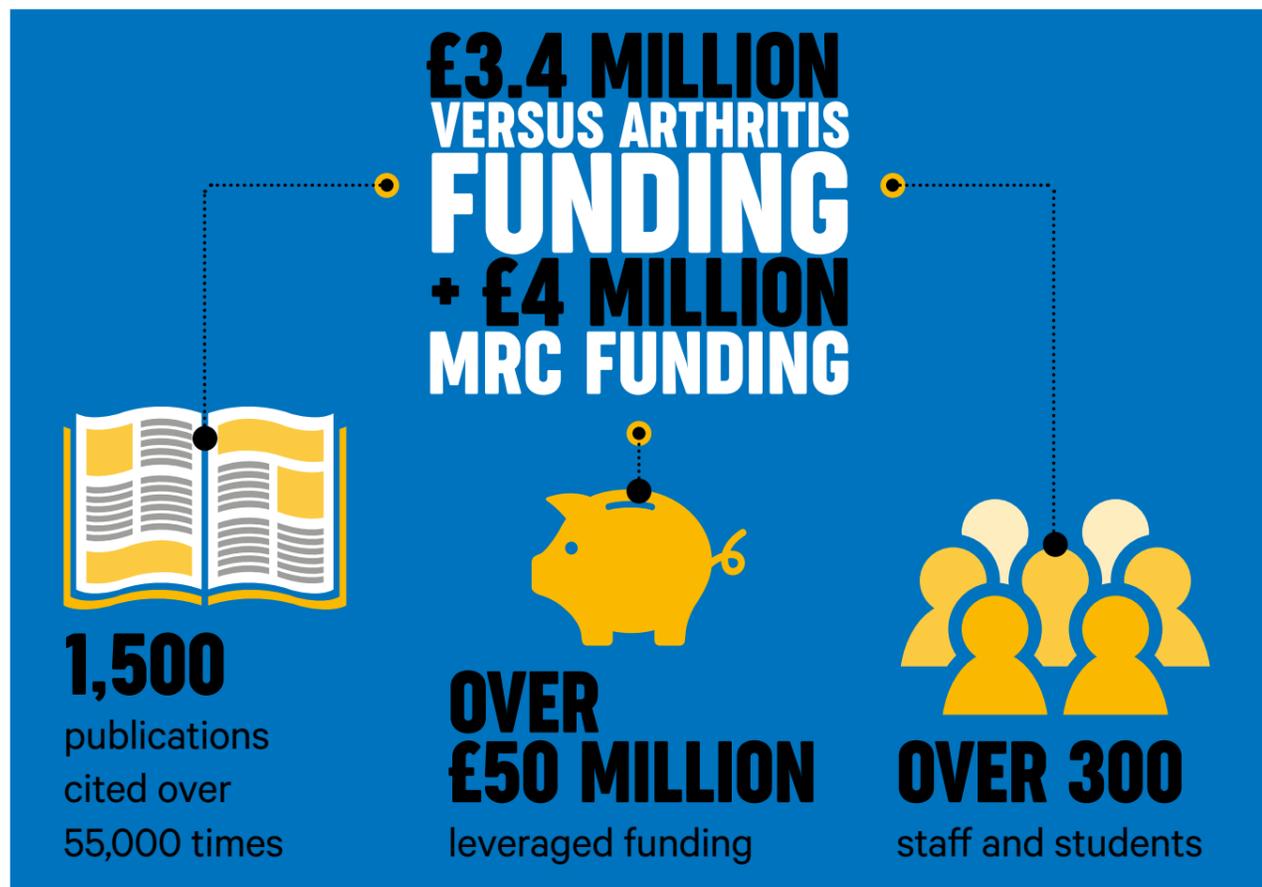
Increased Capacity to Conduct Research



Leveraged Funding



Patient and Public Involvement



# THE CAUSES AND MECHANISMS OF MUSCULOSKELETAL AGEING

## Why is this important to people with arthritis?

As we age, our musculoskeletal system works less well and our risk for developing musculoskeletal conditions, such as arthritis, increases. A decline in musculoskeletal health can lead to life-limiting changes like loss of mobility and independence. That's why CIMA research is identifying the causes and drivers of the musculoskeletal ageing process, so that the effects of ageing on our musculoskeletal tissues can be minimised and our day-to-day quality of life can be improved.

## The origins of ageing

To understand how best to enhance musculoskeletal health as we age, it is important to first know what molecular changes occur with age. Before CIMA was established, in 2012, there was limited insight into biomarkers specific to musculoskeletal ageing. CIMA research has since shown that there are several important processes that drive musculoskeletal ageing within our cells. These findings could open up opportunities to prevent or treat age-related musculoskeletal diseases.



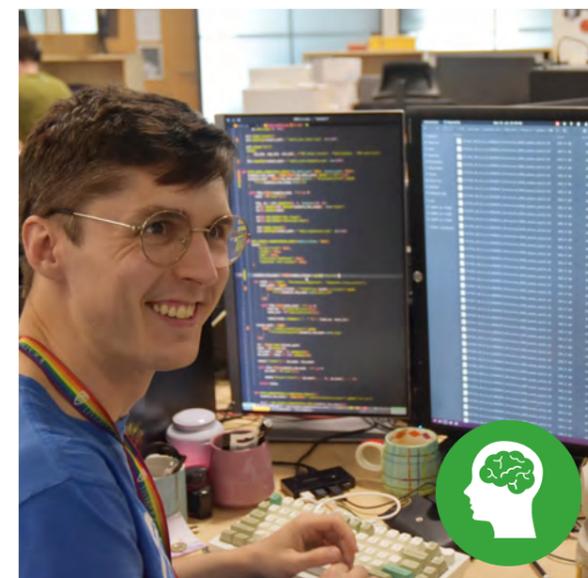
### New knowledge:

- [Mitochondria](#), the energy powerhouses of our cells, are critically linked to a process called senescence, which is a driver of ageing. Senescence occurs when cells begin to function less well and stop dividing in a healthy way. This discovery was supported by a CIMA pump-priming award and is now widely accepted in the field. Several textbooks, which have been accessed over 4,000 times, refer to this particular research.
- As human knee joints age, cells experience several changes that can cause disease such as cell number decline, protein damage, cell death, and cell recycling. Centre researchers built a [computational model](#) to observe these changes. This model can be applied to many different situations and tests, enabling more discoveries to potentially be found more quickly and easily, based on simulations, using existing data.
- Several ageing markers have been identified for [mesenchymal cells](#), a kind of cell that plays an important role in maintaining joint health. They have the ability to form connective tissues such as cartilage-producing cells.



## The role of DNA in osteoarthritis

One misconception surrounding osteoarthritis is that it is an inevitable effect of ageing, driven by 'wear and tear'. This is not the case — the development of osteoarthritis is underpinned by a much more complicated process in which our DNA plays a role. To push back against misinformation such as this, CIMA research investigates how much of our ageing trajectory is inherited in our biology, from birth as well as acquired over time through our DNA. This has led to several discoveries.



### New knowledge:

- The [genetic-based likelihood](#) of developing osteoarthritis is laid down early in the life course. This means that a person's risk doesn't simply activate later in life, as some might expect.
- Genetic insights derived from a computational model built by the Centre have enabled researchers to identify a [set of genes that might be targeted for future therapies](#).
- There is a [programmed link](#) in our DNA through which heritable traits (that we inherit from our parents) and acquired traits (changes that happen over our lifetime) impact our susceptibility for developing osteoarthritis.



**New intellectual property:** The methylation study has been cited in a patent for [pain management](#) and another for [treating arthritis](#).

“**There's a balancing act between eradicating pain and halting the progression of disease in arthritis. If you just get rid of pain, there's a risk that joints will become severely diseased and degraded. That's why it's so important to better understand the underlying mechanisms of disease, like our research is doing.**”

Professor John Loughlin



## MANDY'S STORY

### Who is Professor Mandy Peffers and how is she linked to CIMA?

I am a Professor of Musculoskeletal Ageing Research and Head of the Department for the Musculoskeletal and Ageing Sciences at the University of Liverpool. I am a Senior Principal Investigator at CIMA but first joined as a PhD student.

### How and why did Mandy first join CIMA?

The Centre awarded me two pump-priming grants to cover bench fee costs for my Wellcome Trust Integrated Fellowship. I was lucky to receive these grants from CIMA because my research involved using a combined approach, known as multi-omics, that few were doing at the time.

During my PhD, I found that genetic molecules called snoRNAs experience change in ageing horse cartilage. That led me to a 3-year research project supported by CIMA to investigate these molecules in more detail in the blood and joints of young, old and osteoarthritic mice. This work has since expanded into many new projects that are supported by CIMA. The snoRNA research my laboratory group are doing is extremely niche — snoRNAs in a musculoskeletal setting are only really studied by us at Liverpool and my long-term collaborator Professor Tim Welting at Maastricht Medical Centre.

### How has CIMA benefitted Mandy?

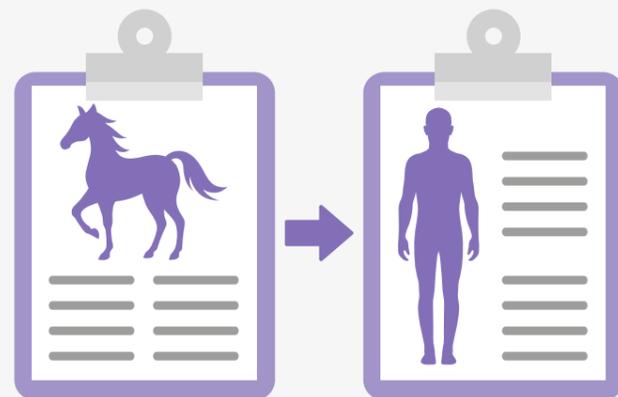
Without early-stage funding and support from the Centre, I wouldn't have progressed to where I am now in senior roles at the University of Liverpool, making strategic decisions, leading a research laboratory group, and supervising students.

I was mentored by Professors Malcolm Jackson and Professor Peter Clegg, who helped me develop collaborations with researchers from different universities whom I would not have met any other way because these scientists were outside my field.

My experience at the Centre supported me to make an out-of-the-ordinary career leap, 'skipping' through intermediate researcher roles, from Senior Lecturer to Professor. I also got tenure, a permanent position at the University of Liverpool.

### What are some key successes of CIMA?

As a veterinarian originally, I feel really privileged to be a part of the CIMA family. One of the key successes from CIMA is that it has increased the capacity of musculoskeletal ageing researchers. My research skills were developed through CIMA and now I develop the skills of others, specifically by supervising PhD students. I find this incredibly impactful — it makes you feel like you're changing the world for the good because you are building the skills of 'new' researchers who will find out the next best things in science. Developing the next generation of researcher leaders is vital to keep musculoskeletal research alive.



## JOHN'S STORY

### Who is Professor John Loughlin and how is he connected to CIMA?

I am a Co-Director for CIMA and oversee all Centre research programmes taking place at Newcastle University.

### What research is John involved with at CIMA?

My research is focused on the genetics of osteoarthritis. We investigate the role of genes that we all inherit from our parents and also explore non-genetic variables, known as epigenetic factors. Even identical twins don't necessarily all develop the same disease or exhibit the same characteristics of disease. There are sections of our DNA that are amenable to modulation and manipulation, which interact with the environment and our lifestyle habits. This is where epigenetic research comes in. It is the result of slight chemical modifications that occur to parts of our DNA and cause transient changes to our genome.

### What has John's research discovered?

Our research has played an integral part in demonstrating that part of a person's risk for developing osteoarthritis originates from birth. This investigation built on research first conducted at Harvard by Professor Terence Capellini, which showed that a particular locus, growth differentiation factor 5 (GDF5), is associated with osteoarthritis. We then investigated this at a deeper level. Turns out, there is a particular change of expression within this gene that leads to an increased risk of developing osteoarthritis.

Following on from this, we and other researchers found several intermediate factors that drive this process, which ultimately revealed that these genetic changes influence a person's joint shape. The way that a person's hips and knees are shaped vary

between one and another very slightly. One reason why this may occur is because these variations were once drivers of bipedalism in humans. If so, these variations may have been beneficial to humans to start with, but as we've evolved and our life expectancy has increased, they may have a negative effect as we age. In summary, this means that the risk factors for osteoarthritis as a disease are laid down during development, but only manifest as we get older.

### How has CIMA enabled growth in the wider epigenetics osteoarthritis research field?

CIMA sponsored the world's first ever epigenetics workshop for osteoarthritis. This was held in the Netherlands. It brought young and senior investigators together and built up such a momentum that a follow-on event was held in Dublin. The third is in Toronto.

During my time at CIMA, I was involved in several European Union research projects. One was the IMI-APPROACH knee osteoarthritis study totalling nearly €18 million. My increased understanding surrounding the importance of epigenetics in musculoskeletal diseases, that I gathered through CIMA, influenced the inclusion of an epigenetics arm into this study.

### Why is CIMA a success?

CIMA is a success because it is borne out of collaborations with other universities that are working on musculoskeletal research but not necessarily with the same focus as us. In Newcastle, we are particularly strong on osteoarthritis research; at Sheffield they lead on osteoporosis; and at Liverpool they are particularly good at muscle decline and diseases. As a consortium, we have come together to tackle these three broad areas in a holistic way from several perspectives.

# RESEARCH ACHIEVEMENTS

At CIMA



2012

The MRC Versus Arthritis Centre for Integrated Research into Musculoskeletal Ageing is established.

2013

A [£4.9 million grant](#) is awarded by the Engineering and Physical Sciences Research Council for CIMA to work with JRI Orthopaedics and Smith & Nephew on a musculoskeletal engineering modelling project.

2014

CIMA research demonstrates the effect of muscle ageing on a key process within our metabolism. Several [oxidant proteins](#), involved with muscle contraction and regulating essential pathways in our cells, become less active, efficient and adaptive to change. This is one reason why our muscles are not able to contract as quickly in old age.

2016

CIMA researchers show that [several age-related changes](#) occur in our knee joints that make osteoarthritis more likely to develop. These changes include cell number decline, protein damage, cell death, and cell recycling.

2015

The [world's first osteoarthritis epigenetics workshop](#) takes place in Amsterdam with support from CIMA. The workshop was a success and two more have since been held.

2014

Centre researchers find that [fewer than a third](#) of people with osteoporosis registered at a Newcastle GP, who were requiring treatment, were receiving adequate treatment. This discovery prompted the National Osteoporosis Guidelines Group to adjust intervention thresholds in their updated guidelines.

2016

Ageing markers are identified for [mesenchymal cells](#), a certain kind of cell that plays an important role in maintaining joint health.

2018

CIMA and CMAR build a [toolkit](#) that monitors the age of our musculoskeletal system, to gauge how 'old' your joints, muscles, and bones are.

2018

A systematic, community-based screening programme of fracture risk in older women in the UK is shown to be [feasible](#) and [cost-effective](#).

2019

CIMA researchers produce a massive open online course titled [The Musculoskeletal System: The Science of Staying Active into Old Age](#) that over 33,000 people have enrolled onto.

2021

Professor Malcolm Jackson wins an [outstanding contribution award](#) from the International Society for Free Radical Research.

2020

[JointCalc](#), the first complete web decision support tool for joint replacement, is launched.

2020

A [toolbox](#) of research study plans, known as protocols, is created to allow the healthspan of mice to be assessed by specific research techniques in a consistent way.

2020

CIMA supports the establishment of a new Wiley open access journal called 'Lifestyle Medicine'. They appoint two patient editors to this purpose.

2021

Human muscle cells are sent into space to learn about ageing, which is reported on BBC Radio 4, Sky News and [CBBC Newsround](#).

2022

Professor Mark Wilkinson is on the committee for the NICE osteoarthritis diagnosis and management guideline.

2023

CIMA researchers discover that the [genetic-based likelihood](#) of developing osteoarthritis is laid down early in the life course.

THE FUTURE!

# ENHANCING MUSCULOSKELETAL HEALTH IN AN AGEING POPULATION

## Why is this important to people with arthritis?

People with arthritis deserve to live full and healthy lives, well into their later years. Life expectancy in the UK is increasing, and so promoting ways to enhance musculoskeletal health across the whole life course is now more important than ever. Two aspects of musculoskeletal health that are important to maintain as we age include muscle mass and musculoskeletal quality. When these decline, there is an increased risk of frailty and falls, as well as prolonged recovery.

To address this, Centre researchers are investigating why musculoskeletal health can decline as we age and what we can do to stop it from happening.

## Why can muscle be lost with age?

Muscle mass refers to the size of your muscles. It is maintained by a balance between muscle proteins being grown, achieved through protein consumption or strength-training exercise, and the breakdown of muscle proteins, which can occur due to injury, inadequate nutrition or physical inactivity. How this balance is regulated, however, becomes less effective as we age. This can result in muscle size, strength, and the quality of remaining muscle, declining as we age. Several, significant breakthroughs surrounding the exact causes of age-related muscle mass and quality loss have been discovered by CMAR.



**New knowledge:** Contributed in a significant way to world-wide acceptance that a biological process which underpins muscle mass balance, known as [anabolic resistance](#), is fundamental to age-related muscle mass loss. This resistance to muscle growth stimuli, such as food and physical activity, negatively affects signals to effectively mediate between muscle mass increasing and decreasing, causing a blunted growth response.



**New knowledge:** Two [main drivers of muscle mass and functional loss](#), as we age, are our muscle fibres thinning (atrophy) and the junctions between our nerves and muscles losing connection (muscle fibre loss leading to denervation).



**New intellectual property:** This knowledge contributed to a patent being registered for an innovative gene therapy vector to treat a [muscle degenerative disease](#) called Duchenne. This potential therapy is now being investigated by US biotechnology company and patent owner, Regenxbio, in a Phase 1/2 human trial called AFFINITY DUCHENNE™.



**Leveraged funding:** Over **£2.5 MILLION** grants to further [anabolic resistance](#) research across the world.



## Why can the condition of our joints decline as we age?

Musculoskeletal function relates not only to how well our muscles work but the condition of our joints. Our joints importantly connect our bones together and are comprised of several, specialised types of cells. The state and configuration of our joints determine how freely our body can move and how healthy our musculoskeletal system is. Several CMAR discoveries have been fundamental to our understanding, at a cellular level, of why our joints can become damaged as we age.



**New knowledge:** A type of cell in our connective tissue, called [fibroblasts](#), function in different, defined ways. Some promote inflammation whilst others are responsible for joint destruction, which contributes to the development of arthritis.



**Leveraged funding:** This study led to CMAR researcher Professor Chris Buckley co-founding a company called [Mestag Therapeutics](#). This company is developing therapies for treating inflammatory disease and cancer which has received £40+ million of investment from SV, Johnson & Johnson, Google Ventures, Forbion and Northpond Ventures.



**New knowledge:** Distinct [fibroblast](#) populations within the joint lining tissue of our knees, the synovium, is significantly associated with painful knee osteoarthritis.



**Leveraged funding:** This study, funded by Versus Arthritis, led to a £1.3 million UKRI grant involving the University of Birmingham, the Versus Arthritis Pain Centre and the industry partner Eli Lilly Global Pain Discovery.

## Keeping active to stay resilient



**New knowledge:** Extensive research has previously suggested a relationship between age and physiological function, but this was ill-defined because there is no single, consistent, and comprehensive marker of human ageing. Centre researchers have since robustly demonstrated, by combining a wide range of human ageing biomarkers, including muscle mass, strength and insulin resistance, that [keeping active into old age prevents many aspects of musculoskeletal decline](#).



**New knowledge:** Before CMAR established in 2012, older people were encouraged to exercise to aid healthy musculoskeletal ageing, but it was unclear what form of exercise is best. CMAR research has demonstrated that [resistance exercise training is one of the most effective ways to prevent decline in musculoskeletal muscle mass and strength as we age](#).



## Eating well to stay resilient



**New knowledge:** 1.5g of [leucine](#), an essential amino acid found in fish, nuts, and legumes, stimulates muscle protein synthesis as much as 40g of whey protein in older women.



**New knowledge:** A nutritional supplement called [nucleoside riboside](#), a form of vitamin B3 found in milk and yeast, reverses many effects of ageing on our muscles.



**New knowledge:** Obesity in [older, non-frail men](#) causes anabolic resistance; obesity [coupled with inactivity](#), exacerbates anabolic resistance across both sexes despite age; and obesity is associated with significant [inflammation in synovial fibroblasts of joints](#), an important cause of pain and disease progression in people with osteoarthritis.



**New intellectual property:** The nucleoside riboside research has been cited in two patents, one to treat [Parkinson's](#) and another as a supplement to improve physiological state by reducing metabolic fatigue and improving [lifespan](#).



## CHRIS' STORY

### Who is Professor Chris Buckley and how is he linked to CMAR?

I am the lead for a theme of research at CMAR surrounding the role of inflammation in ageing and the progression to disease and frailty in synovial joints. Inflammation and ageing are very strongly linked. My research explores how these separate processes are integrated at a cellular level, how these driving forces interact with each other, and what pro-ageing effects they have on our body. Knowing these things could help us find ways to slow down or stop ageing in joints.

### What have been the major research successes for CMAR as a whole?

In my opinion, CMAR has been very influential in progressing the research field of healthy ageing in three main areas.

Firstly, by showing that there is a malleable component to how our body ages as we get older — regular exercise has the power to reset our ageing clock for certain organs. Professor Janet Lord led a project involving regular cyclists which showed that if you stay active and keep your muscles strong as you get older, then you can halt the ageing process in those organs. Loss of muscle mass, strength and immunity did not occur in people who exercised regularly, whereas it did in those who didn't exercise regularly.

Secondly, by showing that both inflammation and cellular damage play an important role in driving ageing, and that these different processes are carried out by certain types of cells known as fibroblasts. Fibroblasts are cells found in the joint-lining and, like sweets, we've found that they come in distinct 'flavours'.

Thirdly, by improving our understanding of how exercise affects our muscle biology in real-time. CMAR researchers, using specialist technologies and innovative methodologies, have been able to follow in real-time the biochemical changes that occur in our muscles during exercise. Doing so gives researchers a much clearer and fuller story of what happens to our muscles in our body as we age, more so than simply capturing snapshots of changes before and after exercise.

### What research has Chris been involved with at CMAR?

I led our fibroblast programme of work which discovered that one 'flavour' of fibroblast causes inflammation, another causes damage, and yet another causes pain in knee osteoarthritis. Researchers used to think that all fibroblasts were multi-functional, and each one was responsible for driving pro-ageing mechanisms. Knowing about the distinct 'flavours' of fibroblasts, though, is important because it means that there is potential to target one distinct flavour to counter its specific pro-ageing effect, without affecting the rest.

### How is Chris' work influencing the wider research landscape?

On the back of our fibroblast work, our research has expanded in many ways and more discoveries are being made. For each new avenue of research that we're now exploring, we have been successful in leveraging further funding.

Firstly, our fibroblast work has implications for cancer research. Often, many of the things we do to treat cancer are the opposite of what we do to treat inflammation. But there are inflammatory forms of cancer that our research could help better explain and shape, to potentially find new targets for cancer treatment.

Secondly, we've since found that each 'flavour' of fibroblasts has a different type of metabolism and uses fuels such as glucose and fatty acids differently. Moreover, we've known for a while that the joints at the tips of your fingers can get osteoarthritis but not rheumatoid arthritis, for example, but we've never fully known why. Turns out, it's based on the presence of different ratios of fibroblast 'flavours'.

Finally, we have recently demonstrated that there is an embryonic origin for rheumatoid arthritis and osteoarthritis. The propensity to develop these diseases is laid down in the embryo stage of our life because of the fibroblast 'flavour' ratio in our joints. This ratio dictates whether a person is more at risk of developing osteoarthritis or rheumatoid arthritis.

### How might Chris' work benefit people with arthritis?

One potential clinical implication from our research is that it could help us find a one-stop solution to treat people with arthritis. Fibroblast subsets located in our gut, joint, skin and eyes share similarities to one another. This is partly why many people with arthritis also experience issues across these parts of their body. If we can find a way to target harmful fibroblast 'flavours', then we could deal with multiple problems in one fell swoop.

### How is Chris' research influencing industry?

Researchers like me are driven by ideas; we think up many ideas all the time. Conventionally, you get an idea, create a product and then put intellectual property on it and hope that it'll develop. However, venture capital companies are moving away from this approach into a more parallel approach that focusses on intellectual capital. This is when they invest in platforms and people that deliver ideas with multiple avenues of potential, rather than specific products.

After our fibroblast paper came out, a venture capital company contacted us about the ideas in the paper. SV Health Investors gave us seed funding. Then, other venture capital companies invested in Mestag Therapeutics.

### What are some key strengths of the Centre model?

Centres allow collaboration whilst also forcing you to communicate your research simply so that researchers, who aren't experts in your particular field but are specialists in their own right, can understand and contribute. Centres break down the silos of scientific fields so that common mechanisms, pathologies or processes, such as inflammation or arthritis, can be investigated from many angles at once.



## DANIEL'S STORY

### Who is Dr Daniel Wilkinson and how is he linked to CMAR?

I am a Principal Research Fellow at the University of Nottingham. I joined as a postdoc in 2012 when CMAR was first established. My role is to devise new techniques and methods that help researchers better understand the underlying mechanisms of ageing in humans, so that we can potentially find a target that enables muscle mass to be maintained in older people.

### What research is Daniel involved with at CMAR?

One type of methodology that our team have continued to improve involves the use of stable isotopes, a special type of atom with unique properties. Using these stable isotopes, labels can be attached to amino acids, the building blocks of our muscles, to act like tracers. This allows us to monitor how quickly or slowly our muscles are being built up or broken down. By measuring this, we can see how the muscle building capacity of older people is affected by age and test therapies that may be able to assist to maintain muscle in older age.

Through the work funded by the Centre, we've been able to develop and improve these tracer techniques so that we can gather the information we need in a less restrictive and less burdensome way for the research volunteer. Previously, these tracers had to be administered intravenously, and required the research

volunteer to spend several hours stuck in a laboratory or clinical room. Now, with Centre research, we have improved this procedure so that it can be completed relatively easily and non-invasively. This means that the subject can return home and go about their daily business, which allows us to gain measures that are more representative of real-life than sitting in a laboratory.

### How does Daniel's research benefit the wider research community?

Thanks to Centre funding and follow-on grants from external bodies, we have purchased an extensive number of specialist technologies and equipment. Our analytical capability has vastly expanded. This enables us to investigate at a deeper level than we've ever been able to before. CMAR is a unique analytical Centre — there aren't many places in the world that can do what we do. Because of this, lots of people from across the world come to us for advice. We help analyse samples for research collaborators nationally and across Europe, Canada and the USA.

Our technological expertise has been recognised by leading scientific bodies. For example, the Physiological Society and British Mass Spectrometry Society have both funded us to run courses so that we can share and promote our methodological knowledge with researchers nationwide.

# RESEARCH ACHIEVEMENTS

At CMAR



2012

The MRC Versus Arthritis Centre Musculoskeletal Ageing Research is established.



2014

The CMAR Director contributes to Versus Arthritis' [Musculoskeletal Health: A Public Health Perspective](#) report.

2016

CMAR research leads to worldwide acceptance that the biological processes which underpins muscle mass balance, known as [anabolic resistance](#), is fundamental to age-related muscle mass loss.

2017 ONWARDS

CMAR advances in non-invasive MRI and oral stable isotope tracer development at the University of Nottingham provide unprecedented insight and research opportunity in human musculoskeletal ageing and research from structural, metabolic and physiological perspectives.

2018

CMAR Director becomes an Institutional Lead for [UK SPINE](#), a £6.5 million knowledge exchange network funded by Research England to improve the healthspan for patients with multiple age-related conditions.

2018

The Student Patient Alliance, an initiative where research students are paired with people with lived experience of musculoskeletal diseases, is piloted successfully at the University of Birmingham.

2017-2018

Centre researchers show that [physical activity](#) has a protective effect on many aspects of our immune system, [neuromuscular system](#) and [muscle metabolism and function](#) as we age.



2019

Professor Carolyn Greig contributes to the revised definition of sarcopenia for the Writing Group for the European Working Group on Sarcopenia in Older People (EWGSOP).

2019

Professor Greenhaff leads the Physiological Society Ageing Report [Growing Older, Better](#). This includes expert contributions from Professor Malcolm Jackson and Professor Janet Lord on how science and technology can enable healthier living in old age.

2019

Centre members Professor Afroditi Stathi and Dr Sally Fenton respectively contribute to the [UK Chief Medical Officer's Physical Activity Guidelines](#) for the Older Adult and Sedentary Behaviour sections.

2022

Professor Carolyn Greig launches a massive online open course in 2022, entitled [Healthy Ageing: Concepts, Interventions and Preparing for the Future](#), which over 2,500 people have enrolled onto.

2020-2021

The CMAR Director acts as special advisor to the House of Lords inquiry [Ageing: Science, Technology and Healthy Living](#).

2021

Centre member Dr Amy Naylor, alongside Professor Roy Bicknell, publishes a [worldwide patent](#) for an osteopenia/osteoporosis treatment.

2023

Professor Janet Lord writes a chapter of the Chief Medical Officer's [annual report](#) on the ageing biology approach to improving health, and is awarded a CBE in the New Year Honours list for her service to older adults.

ONWARDS

Significant capacity continues to be built in the field of musculoskeletal ageing research — 36 PhD students directly funded by MRC and Versus Arthritis have been trained in CMAR; several promotions to Associate and full Professor level achieved; and over 20 permanent staff appointments made since the Centre began.

THE FUTURE!



# RESHAPING POLICY

## Why is this important to people living with arthritis?

There are many policies that directly influence the health of people living with arthritis, from healthcare guidelines that determine who receives what care, to public funding frameworks that determine how much is invested in specific areas of research. To ensure that these policies are continuously up-to-date and fit for purpose, they are regularly reviewed, revised, and improved using the highest calibre, evidence-based research. Our Ageing Centres have played a pivotal role in generating high-quality research findings that inform these policies. Their research has advocated for people living with arthritis so that their unmet needs can be recognised and embedded into life-improving policies.

CAMPAIGNS

## CIMA

Osteoporosis is a condition that causes your bones to become quite fragile and weak. People with osteoporosis are at risk of a fragility fracture, which is when you get a broken bone from a force that would not normally result in a fracture, such as a fall from standing height or less. More than 3 million people have osteoporosis in the UK.

CIMA research has been highly influential in reshaping osteoporosis policies at several key stages of the healthcare pathway.

## Pre-diagnosis screening



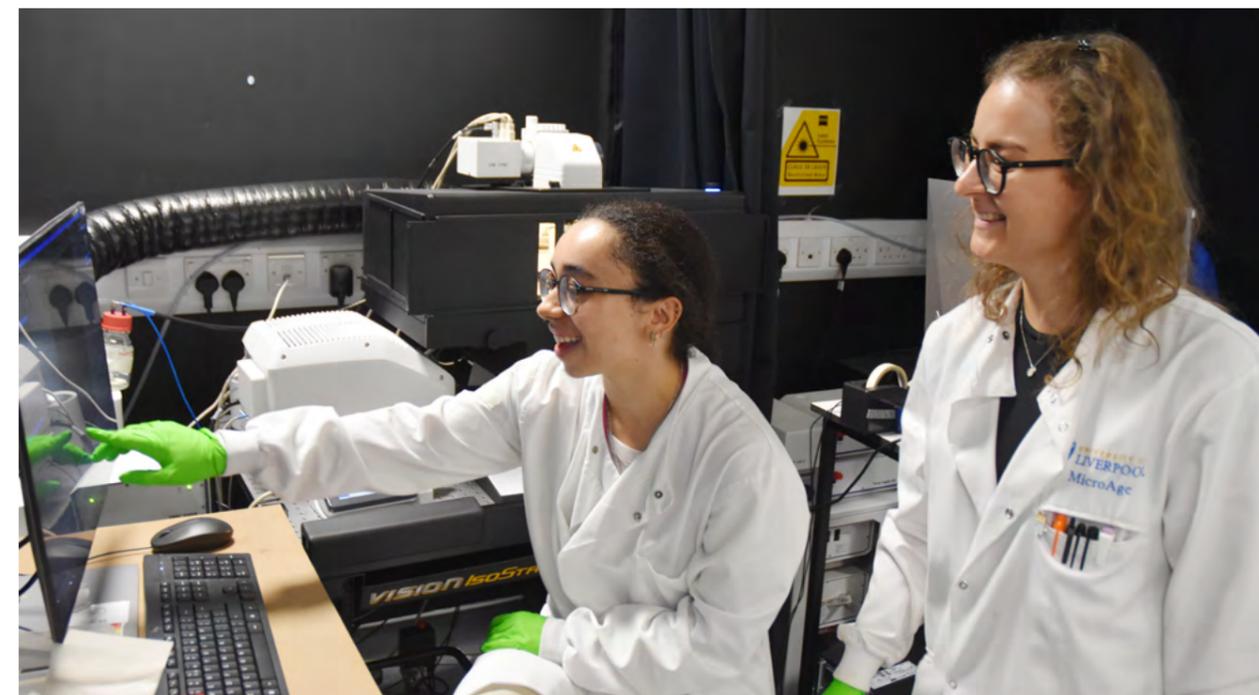
**New knowledge:** CIMA Director, Eugene McCloskey, worked with UK academics to demonstrate that a systematic, community-based screening programme of fracture risk in older women, known as [SCOOP](#), would be [cost-effective](#). Recruitment for SCOOP began in 2008 but its follow-up data collection and analysis was supported by the Centre. This was the first study worldwide to demonstrate that community screening for fracture risk is feasible and could be effective in reducing hip fractures. Specifically, if such a screening programme was implemented across the UK, at least 8,000 hip fractures could be prevented annually.



### Policy and practice impact:

The SCOOP studies have since been mentioned in three reports by the World Health Organisation (WHO), a United Nations agency that promotes health to help keep the world safe. First, as a recommended action to strengthen health systems in response to noncommunicable diseases. Secondly, in a [policy brief](#), to highlight the cost-effectiveness of screening as an example to improve health and prevent disease. Thirdly, in a report on [Better Help for Europe](#) which tells the story of how public health priorities and strategies were shaped between 2010-2020.

Now, several studies are ongoing or planned to implement the SCOOP strategy in primary care across the UK.



## Diagnosis and management



**Policy and practice impact:** CIMA Director, Professor Eugene McCloskey has co-authored several influential papers, including:

- A fifth of all research publications used to inform the production of 2019 European guidance for diagnosing and managing osteoporosis in postmenopausal women.
- A [position paper](#) on assessing muscle function and physical performance which was endorsed by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases. This paper has been accessed over 42,000 times.

## Treatment



**New knowledge:** Only [28.6%](#) of people with osteoporosis registered at a Newcastle GP practice, who were requiring treatment, were receiving adequate treatment. This reiterates the importance of implementing a fracture risk screening programme, such as SCOOP, because [making GPs and patients aware of their fracture risk can rapidly increase the uptake of osteoporosis treatments](#).

**FEWER THAN A THIRD**

of people with osteoporosis in Newcastle received adequate treatment in 2015.



**Policy and practice impact:** These findings, alongside evidence from the FRAX UK tool and the National Osteoporosis Guidelines Group (NOGG), led to guidelines outlining the intervention thresholds for referral and access to osteoporosis treatment being adjusted. They are accredited by our national healthcare provider (NICE), provide greater equity in access to treatment at older ages, and encourage the identification of patients at very high risk of fracture who stand to greatly benefit from early access to bone-forming therapies.

# CMAR

The United Nations has declared 2021-2030 as the 'Decade of Healthy Ageing' and in response to this, several commitments have been made by the UK government to support this vision. To aid this cause, CMAR researchers have provided key evidence that has kept the pressure on our policymakers to make healthy ageing a national priority.



## Policy and practice impact:

- CMAR Director, Professor Janet Lord, co-wrote a chapter of the Chief Medical Officer's 2023 [annual report](#) on the ageing biology approach to improving health in old age. It is now focussed on tackling age-related ill health by addressing biological hallmarks of ageing, as opposed to treating specific diseases.
- Professor Carolyn Greig and Dr Mathew Piasecki, through their collaborative links with UKRI-funded network MyAge, co-authored a [policy brief](#) presented to parliamentarians in July 2023. This brief demonstrates the current crisis facing a lack of muscle resilience across the life course and provides recommendations for policymakers to drive change.
- CMAR Director, Professor Lord, wrote a chapter for the [Nuffield Council's Bioethics report](#) — the UK's leading bioethics agency in the UK. She was part of the working group and spoke with members of underserved communities to ensure that their perspectives were embedded into the report's recommendations. These suggestions are all focussed on ensuring that the goals of ageing research remain principled and realistic, rather than aiming towards unethical objectives such as 'wanting to live forever'.

## BOTH CENTRES

CIMA and CMAR have worked collaboratively to drive change at a national scale by reforming healthy ageing research policy. They have used their expertise to address one of the UK's ambitions related to healthy ageing is its Ageing Society Grand Challenge mission — to ensure 5 years of extra healthy life by 2035 whilst reducing inequalities.



## Policy and practice impact:

Professor Paul Greenhaff (CMAR) chaired the Physiological Society's report (Growing Older Better) with expert input from CIMA and CMAR colleagues into how science and technology can enable healthier living in old age.



## Capacity building:

This report contributed to the UK Government establishing a series of eleven UK Ageing Networks; a Centres of Research Excellence funding call for Enhancing Healthspan, and funding to stimulate new start-up and discovery research.



**Policy and practice impact:** Professor Janet Lord acted as Scientific Advisor and Professors Greenhaff, Mathers and Kemp provided evidence towards the 2021 House of Lords' inquiry titled: [Ageing: Science, Technology and Healthy Ageing](#). This report concluded that the UK Government was not on track to achieve its mission to extend healthspan by 5 years, and that significant investment should be made, urgently, to fund more research into the biology underlying ageing.



## What's next?

Our Ageing Centres are working with other leading musculoskeletal health experts and Versus Arthritis to advocate for the inclusion of musculoskeletal health into the NHS Health Checks programme. A working group was established to develop a set of questions and resources for consideration to promote public health messages about musculoskeletal health. Versus Arthritis continues to champion this cause and has recently called for this in its response to the [Major Conditions Strategy](#).





## PETER'S STORY

### Who is Professor Peter Clegg and how is he connected to CIMA?

I'm a Professor of Musculoskeletal and Ageing Science at the University of Liverpool, Dean of the Institute of Life Course and Medical Sciences, and Deputy Pro Vice Chancellor for the Faculty of Health and Life Sciences.

I'm also a qualified vet and a specialist equine surgeon. The cases I've seen in horses are like an extreme version of human orthopaedics. This has inspired the research, which I lead through the Centre, to evolve into human osteoarthritis and cartilage and tendon biology.

### What research has Peter been involved with prior to CIMA?

I have received multiple grants from Versus Arthritis for tendon and soft tissue musculoskeletal injury research since 2010 and, thanks to them, our tendon ageing research group has been extremely successful.

### How has CIMA benefitted the University of Liverpool?

CIMA has had a significant impact on our organisation. Having the Centre badge from Versus Arthritis and MRC has helped put our university's musculoskeletal research on the map and become recognised as world leading.

The University of Liverpool has historically been strong in many life science research areas such as infection biology, pharmacology, and drug safety science. Our musculoskeletal research expertise, however, was relatively less well-known and developed. With Centre funding, we received investment to establish the Department of Musculoskeletal Biology at the University.

This department has since grown into one of the biggest at the University, and with it a critical mass developed. This wouldn't have been possible without CIMA.

On the back of this growth, the University have invested more into us. They based this decision on seeing the credible growth, outputs and world-leading research coming out the Centre. This has led to us being a very attractive place for early career researchers — an influx of people come to us to complete their studies who, in the past, would have chosen to go to other leading universities.

### How has CIMA helped build capacity in the wider research field?

The University of Liverpool has been successful in leveraging an MRC-funded Doctoral Training Partnership grant to empower the next generation of researchers. The existing interactions that the University of Liverpool had with Newcastle and Sheffield, through CIMA, helped made this application a success.

Professor Mandy Peffers and Dr Kasia Whysall are just two career progression success stories that have come out of the Centre. I supervised Professor Peffers, a qualified veterinarian, to progress from a PhD student to a professor in 14 years. She has since grown into a well-respected leader here at the University of Liverpool. Dr Whysall, was a high-flying young academic who benefitted from the PhD students funded by CIMA who were generating great data. She is now the backbone for a research programme on age-related muscle decline in Ireland, has a big research group, and is an Associate Professor at the University of Galway.



## CAROLYN'S STORY

### Who is Professor Carolyn Greig and how is she linked to CMAR?

I am Professor of Musculoskeletal Ageing and Health at the University of Birmingham. I have been an active member of CMAR throughout its lifetime and lead a programme of research at the Centre themed around lifestyle interventions.

### What research has Carolyn been involved with through the Centre?

My research aims to better understand how we can improve muscle health in diverse groups of older people so that they can maintain their physical independence. I focus on ways to increase physical activity, reduce sedentariness and optimise nutrition. This research is globally important and involves researching with collaborators in low-, middle-, and high-income countries. Given that we are in the World Health Organisation's Decade of Healthy Ageing (2021-2030), this work is very timely.

On the back of a collaboration with the University of Sao Paulo in Brazil; I and colleagues Professor Janice Thompson and Dr Vicky Goodyear developed a free massive open online course (MOOC) around healthy ageing. Over 2,500 people have since enrolled.

### How has CMAR contributed to Carolyn's work in reshaping policy?

Policy work is something that a lot of academics feel they're not sufficiently well equipped to do effectively. They are unsure how or where to start. It is very challenging to get your foot in the door and have opportunities to present evidence to politicians. CMAR members, however, have managed to engage successfully with policymakers over the years, most recently contributing to the 2021 House of Lords'

'Ageing: Science, Technology and Healthy Ageing inquiry and the inception of the UK Ageing Networks'.

There are eleven UK Ageing Networks, and they are all pulling in the same direction to transform ageing research in the UK and drive policy change. I was Co-Director (for 2 years) for one of these networks, called MyAge, which seeks to understand muscle resilience across the life course. A measure of their success is that all the networks have been funded for a third year now. Through CMAR and MyAge, we have backing from societies who have connections to policymakers such as Versus Arthritis, the Physiological Society and the British Society for Research into Ageing. These policy connections are crucial for us to achieve our mission.

### What are the key discoveries from CMAR?

Before CMAR, there was little understanding about what type of physical activity, or what range of interventions in combination with each other, gives an older person more 'bang for their buck' to improve their muscle health. For example, there used to be a misconception that high intensity training wasn't possible for older people, but it is, and we've shown that it can be a safe and effective way to improve their musculoskeletal health.

The multidisciplinary nature of CMAR allows us to go one step further to maximise the reach of this finding. It's one thing to know what works best for a person but getting people to actually do exercise training or even increase their physical activity, consistently and at scale across the country, is another task and type of research in itself. This is possible though through the Centre — we are working with behaviour change specialists, people with lived experience, and community outreach researchers to do exactly this.

# EMPOWERING ALL BY SHARING KNOWLEDGE

## Why is this important to people living with arthritis?

Taking better care of ourselves, through self-management, is key to living healthier as we get older. To be able to self-manage your health, though, you must first understand your condition and the evidence-based ways that you can support yourself. Without this information and/or understanding, there is a barrier to self-management and a potential for misinformation to spread. That's why our Ageing Centres are embedding patient involvement and public education and engagement to their research, to boost awareness of arthritis and 'arm' you with the facts to help you take better control of your health.

## CIMA



### Patient and public involvement:

CIMA researchers have worked with patients to debunk many health myths surrounding osteoarthritis, by:

**1. Co-producing leaflets:** their [Behind Osteoarthritis leaflet](#), which has been distributed to approximately 1,000 people so far, challenges the false, misinformative idea that osteoarthritis is 'wear and tear'. The success of this leaflet led to the co-development on another entitled [Behind Rheumatoid Arthritis](#).

**2. Running workshops for the public:** their 'Behind the Headlines' [workshops](#) reveal the various ways that news stories have been spun to falsely exaggerate the truth.



### Patient and public involvement:

One source of scientific knowledge is research publications. However, access to these papers can be limited when the journals that hold them are hidden behind a paywall. This can exclude the key people, who could benefit from understanding the research, from being able to read it.

One way that CIMA is addressing this inaccessibility is by supporting the appointment of two patient editors, Rita Stringfellow and Peter Johnson, to a new Wiley open access journal called 'Lifestyle Medicine'.

**Leveraged funding:** Grants totalling approximately £3 million were awarded to CIMA alongside the UK Space Agency and Kayser Space to use microgravity to understand what happens to human muscles as we age and why. Microgravity is a great test-bed environment for this research because it accelerates skeletal muscle ageing — astronauts lose up to 40% of their muscle after six months in orbit. A key part of this research involves sending lab-grown human muscle constructs out to space. Engagement for this project has been a success — media coverage has reached BBC Radio 4, Sky News, CBBC Newsround and many other news outlets.

## CMAR



### Patient and public involvement:

CMAR Centre Director, Professor Lord, and Professor Bethan Phillips have been involved with several

successful engagement campaigns to promote the importance of exercise in healthy ageing. This includes hosting a series of home-exercise videos during the COVID-19 lockdown, TV appearances, and speaking on several radio stations with patient representatives, targeted at older and ethnic minority communities. Professor Lord's long-term contributions led to her being awarded the CBE in the 2023 New Year Honours list for her services to older people.



**Capacity building:** Professor Lord works closely with an organisation called Move It or Lose It. Centre support, networks and funding from CMAR has helped springboard the organisation into a community where health, vitality and connection thrive. 1,200 specialist instructors have so far been trained by Move It or Lose It and they host 1.2 million exercise class interactions every year.



### Patient and public involvement:

CMAR researchers Professors Bethan Phillips and Simon Jones led a successful pilot of a patient and public involvement scheme known as the Student Patient Alliance. CMAR PhD students and patient partners were partnered together as buddies for the duration of their PhD to integrate patient and public involvement into the doctoral students' training. The scheme was such a success that it was then implemented at other centres, including the Research into Inflammatory Arthritis Centre Versus Arthritis (RACE) and the NIHR Birmingham Biomedical Research Centre. An [evaluation](#) of this pilot scheme illustrated that participating in the Student Patient Alliance had a positive, mutual benefit for students and patients on understanding, motivation and communication skills.

## BOTH CENTRES



### Patient and public involvement:

Researchers from both CIMA and CMAR each produced a massive open online course to amplify important information about how people can maintain a healthy lifestyle as they get older. Local public and patient groups were involved in their design, and both courses continue to receive very positive reviews.

Over  
**35,000**

people have enrolled to massive open online courses produced by CIMA and CMAR.



“

The course is aimed at anybody who is interested in making life a bit better for older people. Most people who have signed up for the course so far are older people themselves. One reason for this is because it was designed with them. We had some amazing involvement from public contributors to help shape the content. For example, focus groups took place in both the UK and in Brazil which feature in the course. Their perspectives on healthy ageing are shared as a talking point for a myth-busting discussion.

”

Professor Carolyn Greig



## JULIE'S STORY

### Who is Julie Robinson?

I'm CEO of Move It or Lose It, a company that empowers older adults to live life to the full. I founded Move It or Lose It in 2010 in response to experiences I'd faced as an exercise instructor. My class members inspired the company name and business idea to make an exercise DVD. Since then, we have released five DVDs and an exercise book that has reached over 80,000 people; provided training to support over 3,500 patients in hospital get stronger; and evolved into a community where health, vitality and connection thrives.

### How is Julie linked to CMAR?

I met Professor Janet Lord, CMAR Centre Director, at the University of Birmingham whilst I was producing our first exercise DVD in 2010. She was a breath of fresh air who saw potential in our DVD. She had many, research-based ideas to help us incorporate purposeful, functional exercises that would bring our members more benefits in their day-to-day life. Informed by her expertise in healthy ageing research, we focussed the DVD exercises on evidence-proven strength and balance-improving activities.

### Why is Move It or Lose It needed?

As some people get older, they can become isolated and less active. This leads to a decline in musculoskeletal health. Then, they may stop being active and social altogether. Once their musculoskeletal health deteriorates, they might become frail and have a fall. We want to prevent this from happening by empowering people to stay active as they get older.

For older people who may already be experiencing a decline in strength or balance, we want to help reverse this. Physiotherapists rehabilitate people

who've had a fall through a 6-week exercise programme but once this is over, they often go back home, become de-motivated and may end up falling again. They then need to redo the programme from the beginning. We want to help break this cycle.

### How has collaborating with CMAR helped Move It or Lose It grow?

CMAR part-funded one of our DVDs. Janet Lord also used her contacts to help us bring on board the physiotherapy falls and fracture team at University Hospital Birmingham, who have championed use of the DVDs for their patients. Janet's knowledge and my passion has helped us build collaborations with the NHS, the Royal Voluntary Service, UK Active, and many others. At one UK Active conference, we met Professor Sir Muir Gray who has volunteered to be our Chief Knowledge Officer. Having ambassadors like Janet and Muir Gray has helped propel Move It or Lose It's growth.

### How has Move It or Lose It helped people with arthritis?

Most of our class members have arthritis. We know this because everyone fills out a questionnaire when they first join. Our community has been shown to reduce loneliness and social isolation; improve strength, balance and confidence so they have the functional fitness of someone 10 years younger.

Move It or Lose It brings together empathy, patience and kindness along with some solid, evidence-based exercise. All of our resources and services are influenced by the research and evidence that Janet has passed on to us through CMAR. We're forever grateful for that.



## FRANCINE'S STORY

### Who is Francine and how did she start getting involved in CIMA research?

I live close to Liverpool, am now retired, but used to be a clerical worker. Whilst attending a COVID-19 vaccination session at my local church, I met some Liverpool University representatives. They asked me if I wanted to help them in shaping arthritis research. I agreed because coincidentally, I had just started experiencing arthritis symptoms.

### How does Francine get involved in CIMA research?

I participate in meetings every few months and we get to see an impressive variety of arthritis research — not only what people are finding under the microscope but also the best ways to deliver medicine that suits patients.

### What benefits does being involved in research bring to Francine?

I find the meetings exciting because they help me learn new things. For example, when I first joined, I didn't realise that there were different types of arthritis. I now know there are many types of arthritis and I have understood what my osteoarthritis diagnosis means. I recall one research presentation that I listened to that was looking at the components of cartilage. They debunked the misconception that I had heard for years before that arthritis was 'wear and tear'. This is folklore!

*"The patient and public involvement work led by Dr Helen Wright of the University of Liverpool is exemplary... The Patient Involvement Group (PIG) facilitates a dialogue between patients and researchers which I believe is mutually beneficial... While lay people may not understand all the complexities of molecular biology and immune system responses, the exercise of communicating research in terms that the PIG can appreciate, can help to strengthen and deepen the researcher's grasp of the science involved and ensure that the research aims are directed towards worthwhile goals.*



*I believe that participation in the PIG undoubtedly benefits patients in managing their own long-term musculoskeletal conditions. Medicine works best when there is a true partnership between the patient and the various practitioners involved in providing advice and treatment. The efforts which Dr Helen Wright and colleagues have put into developing patient information leaflets, glossaries and other communication vehicles is empowering people like me to take an active role in managing our musculoskeletal problems, resulting in a more productive dialogue with health practitioners and more effective engagement with treatment plans."*

**Len, member of the Liverpool Patient Musculoskeletal Group**

# EXPANDING THE POSSIBILITIES OF AGEING RESEARCH

## Why is this important to people living with arthritis?

A critical mass of researchers is needed with financial backing, expertise, connections, and equipment to discover and implement life-changing research breakthroughs that can benefit people living with arthritis. Our Ageing Centres, supported by infrastructure funding from Versus Arthritis, has provided all these conditions so that these arenas of research can thrive. By working collaboratively, CIMA and CMAR have flourished into a platform for a legacy of healthy ageing research to prosper now and in the future.

## CIMA



**Capacity building:** Dedicated, specialist laboratory staff were funded through CIMA to conduct vital work processing, analysing and sequencing tissues, cells, DNA material and proteins. With our consistent funding, these individuals were able to train other Centre members to carry out these specialist techniques for different kinds of research. This has greatly benefitted the quality of the science.

Many of the new knowledge discoveries featured in this report simply wouldn't have been possible without their work or knowledge transfer.



**New collaboration:** CIMA supported the [world's first ever workshop on osteoarthritis epigenetics](#) at Amsterdam in 2015. Scientists from 14 countries and 4 continents gathered to present and discuss their research. These [workshops](#) have become an established part of the osteoarthritis research community. Two more workshops have since followed — one in 2018 (Dublin) and another in 2024 (Toronto, at which Versus Arthritis is a partner).

## CMAR



Leveraged funding:

**NEARLY  
£30 MILLION**

from the MRC to purchase advanced equipment, such as mass spectrometers, bone density scanners and gene expression analysers, to work at the frontiers of human physiology ageing research.

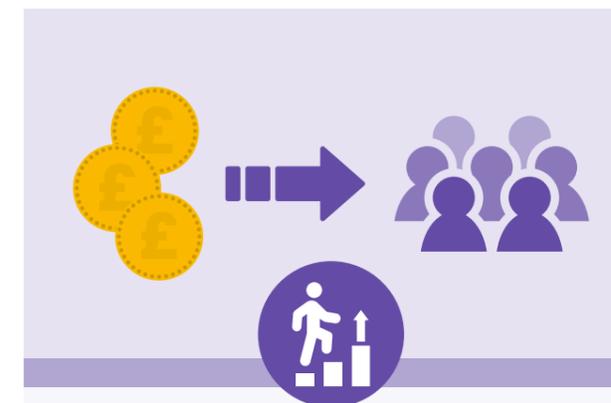


“Our lab is very technical and the feather in our cap is our mass spectrometry expertise. What sets us apart though, not just in the UK but across the world, is our ability to combine stable isotopes with mass spectrometry. There are very few labs in the world that can attempt this, but none anywhere near capable of doing what we can because of the equipment and people we have. Funding from Versus Arthritis and MRC for the Centre enabled us to purchase one of the specialist pieces of kit required, and things have propagated since then to attract more funding from others.”



Professor Philip Atherton

## BOTH CENTRES



**Capacity building:** Infrastructure funding from Versus Arthritis to CIMA and CMAR has enabled world-leading healthy ageing researchers to support and inspire the next generation of research leaders. Our Ageing Centres have been a central pillar in coordinating:

- Joint pump-priming schemes — smaller grants to kickstart new studies with the aim of leading onto further research.
- Connected PhD and early career researcher training placements, taking place across different host institutions.



**Capacity building:** The reach and influence of research stemming from CIMA and CMAR researchers is growing through their involvement in two additional research networks across the UK:

1. MRC National Centre for Musculoskeletal Ageing — this network spans nine universities to drive a step-change in musculoskeletal ageing research strategy and capacity. CIMA and CMAR are at the heart of this national network.
2. The UKRI-funded UK Ageing Network ([UKAN](#)), which comprises 11 interdisciplinary networks, each working to stimulate and transform ageing research in the UK. These networks bring together researchers, policymakers, industrialists and funders to tackle muscle loss in later life. CMAR members are on the management boards of several of these UKAN networks including [ATTAIN](#), [CARINA](#) and [FOOD4YEARS](#). CMAR and CIMA researchers are collective members of the [MyAge](#) network.



“**CMAR has enabled me to grow as a scientist, explore new areas of research and share our knowledge and expertise to build capacity in other countries globally.**”

Professor Carolyn Greig

## ABBY'S STORY

### Who is Abby Brumwell and how is she linked to CIMA?

In 2019, I joined CIMA as an entry-level research technician. Now, I'm a PhD student at Newcastle University.

### How did Abby's journey at CIMA begin?

I began as a technician fully funded by the Centre. My role involved collecting and processing samples derived from hip or knee joints, affected by osteoarthritis, that had been replaced through surgery. Control samples were also collected from people without osteoarthritis. RNA and DNA that I extracted from bone and cartilage were, and continue to be, a really vital resource for many research groups at CIMA institutions. The RNA and DNA samples are frozen, which means that they can be used for many years



from now. The exposure I got as a technician grew my interest in ageing and musculoskeletal disorders. That's why I applied for the PhD.

### What research is Abby involved with through CIMA now?

As a PhD student, I'm supervised by Dr Sarah Rice to explore the epigenetics of osteoarthritis and identify targets for novel therapeutics. This research is being substantiated by an expansion of sample collection work now taking place. Building off the collection that I managed as a technician, I now digest cartilage harvested from the joint samples and culture the cells from this tissue, which are a vital resource when testing drug compounds. mobilising and implementing the tool nationally.



## ELIZABETH'S STORY

### Who is Dr Elizabeth Sutton and how is she linked to CIMA?

I completed five years at CIMA and completed a combined Masters and PhD there.

### What research was she involved with at CIMA?

My PhD looked at the interaction between our body clock, circadian rhythms, and a key antioxidant factor in our body linked to a gene known as NRF2. My research explored the bi-directional interaction between these two variables across many different tissues in our body. We found that, because distinct tissues metabolise at different rates and at different times of day, there are certain windows of opportunity when treatment is most effective for each tissue. Outside these times, you may get a dampened response.

This was a particularly interesting finding because typically researchers draw conclusions from one tissue at a time in a siloed way. Being part of the Centre, where researchers with different areas of expertise work and collaborate, helped this project to grow and succeed.

### How has Elizabeth's research career through CIMA helped her?

I must thank my supervisor for building my professional confidence. She enabled me to complete and succeed in my studies. I'm typically a very introverted person but she was very supportive and encouraged me to present at conferences. I needed that push, and thanks to her, I was able to present at several national and international conferences. I even won a few awards. I recall one CIMA conference where many research fellows were all presenting, most of us for the first time ever. We were all very nervous beforehand, huddled together in a room, and practiced presenting to one another. It was a cohesive, bonding experience.

Other qualities that my PhD helped me grow are autonomy, maturity and adaptability. These have all really helped me build the independent thinking, questioning and actioning needed for my current role. I am now a post-doc based at Liverpool University, working with Professors Malcolm Jackson and Anne McArdle in a laboratory group for the Micro Age 2 space mission.



## MATHEW'S STORY

### Who is Dr Mathew Piasecki and how is he connected to CMAR?

I joined CMAR through the University of Nottingham in 2018 as an Assistant Professor. It was my first permanent position in academia. I have since been promoted to Associate Professor.

### What research has Mathew been involved with at CMAR?

We have identified several sex differences in the neuromuscular system between young and old people. This work is really important to help push the female agenda because most of our understanding of human muscle ageing stems from outdated, male-only studies. This doesn't show us the whole picture. You can't simply apply the same logic to men and women because there are many biological differences that happen across the life course between the two, such as menopause.

A key part of our muscular system is the neuromuscular junction, the connecting area between nerve cells and muscles. My research has shown that there are many components of our nerve cells and their connective activities with our brain that impair muscle function independently of the muscle itself. My work is continuing to find out what these causes are, and to try and identify ways that they can be targeted to improve muscle function as we age.

### How has CMAR supported Mathew?

The Centre has supported me in many ways. One way is financially — the type of research I do requires very specialist equipment. I have won three pump-priming awards through the Centre which covered the costs to purchase the equipment that I needed, which is now being used by several members of our group and contributes to several ongoing studies.

Another type of support I've received through the Centre are opportunities and experience to work collaboratively with international partners. I, like most early career researchers, was not specifically trained on how to start or maintain collaborations but this is crucial to advancing science. Being a part of CMAR though carries a lot of weight, which has helped me build the backing needed to form and sustain large networks.

Our research group has established links with researchers in Brazil, Canada and Denmark, and these collaborations are ongoing. We run scientific exchanges and, while learning together, set up future research projects. During one exchange with our Canadian collaborators, we developed a protocol to explore sex differences in neuromuscular function that can be used in each of our labs. This means we perform experiments in exactly the same way across the world, which will strengthen our combined findings.

### How has CMAR facilitated progress towards driving policy change?

Getting policy to change is a very long and challenging process. It takes years of convincing the right people, and to do that you need robust evidence delivered in a very compelling yet accessible way to policymakers. From CMAR, I became part of the management group of an international network of ageing researchers called MyAge. Through this, we presented evidence and gave recommendations to government on 'A lifelong approach to muscle resilience'. More than recommendations and presentations are needed to drive real-world change, but our work thus far has helped bring exposure to this important area of research.



## NICK'S STORY

### Who is Professor Nick Harvey and how is he linked to CIMA and CMAR?

I'm the Director of the MRC National Musculoskeletal Ageing Network. I have worked with CIMA and CMAR for a long time, through research funded by Versus Arthritis and the MRC, and continue to work with them to understand the ageing process of bones, muscles and joints.

### What is the MRC National Musculoskeletal Ageing Network and why is it needed?

Both CIMA and CMAR are also part of the MRC National Musculoskeletal Ageing Network. This network is vital because ageing is a complex topic and, to understand it better, we need the multi-disciplinary research which this provides. This National Network brings people together spanning many different disciplines, from molecule to population to policy, which is key because not one area of research is going to give us all the answers on ageing. Bringing these different types of networks of expertise together is so important.

### What qualities do CIMA and CMAR bring that benefit the National Network?

There is a fantastic range of skills across both centres and a real breadth of interlinked expertise, which has been crucial to the Network. They have helped us to plan what we should do, and their work complements our work.

The structures of both CIMA and CMAR are very supportive and collaborative. There is a strong sense of how these collaborations support and nurture young academics. A good example of this is how they have been able to bring in talented individuals from outside research with the right skills, provide them

with funding, and support them to complete PhDs and more. This sort of support is very hard to achieve elsewhere, and has been amazingly successful, for example one such individual is now a professor. A lot of researchers owe their careers to the support they've received from these structures.

### What difference does Nick think CIMA and CMAR have made to the wider healthy ageing research field?

The centres have made a massive difference in terms of scientific understanding and capacity building. They have helped bring on a new generation of researchers, who are hugely valued and appreciated in the field. They have undertaken internationally important research, including pioneering work in muscle physiology and molecular biology, and using cutting-edge molecular approaches to understand osteoarthritis development and progression. Aside from this early stage research, there is also a lot of research which is directly relevant in clinics and hospitals, such as how we can reduce fracture risks for people with osteoporosis through community-based screening. This is very impactful work, and it is now reaching UK and European policy guidelines. This research will help to prevent many people from getting fractures.



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