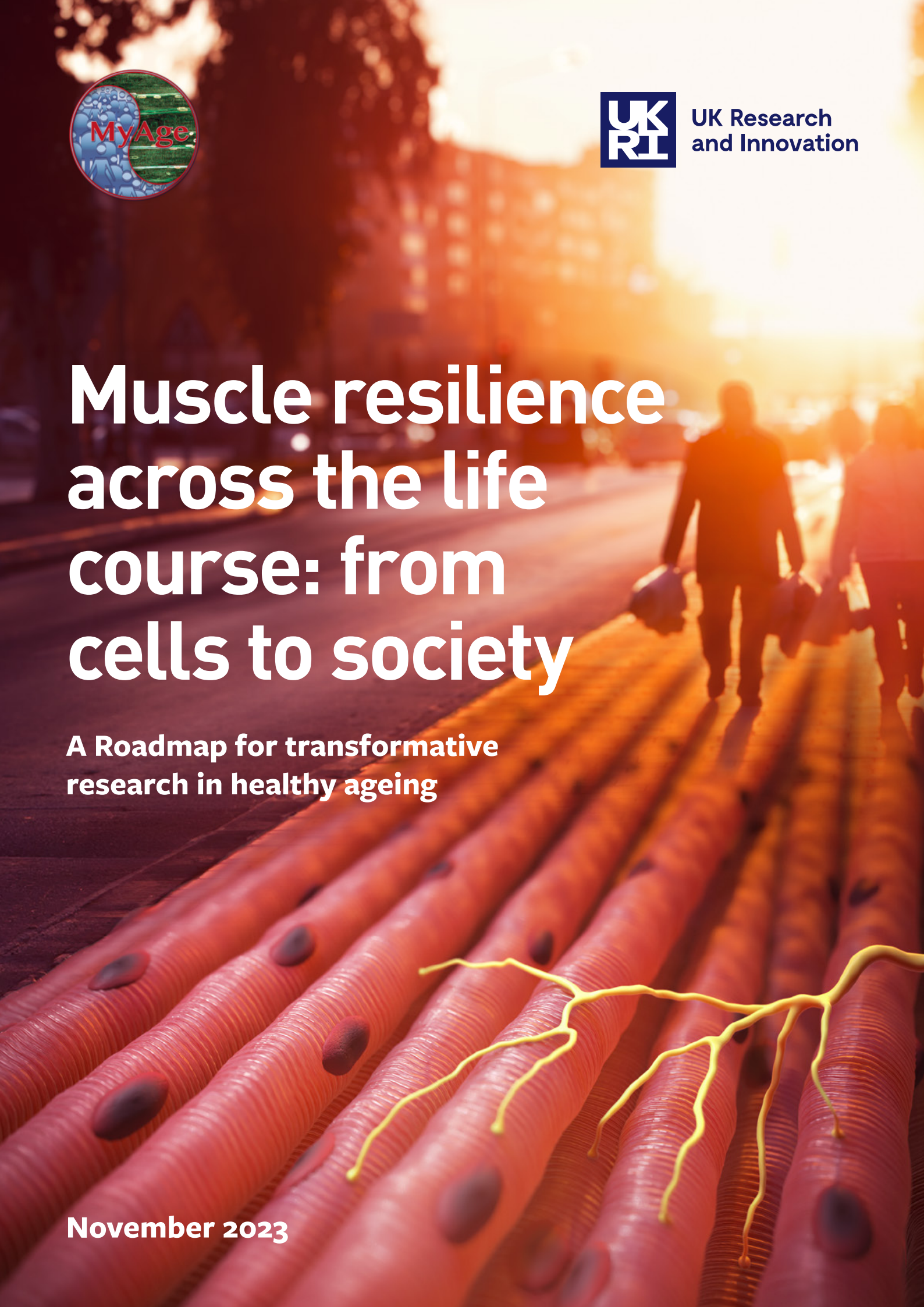


UK Research and Innovation

Muscle resilience across the life course: from cells to society

A Roadmap for transformative research in healthy ageing

November 2023

Executive Summary

Muscle resilience is important for health and well-being across the life course, from childhood to later life. A lack of muscle resilience contributes to the significant and growing health and social care burden, to health disparities, and to economic disadvantage through early exit from the workplace.

The MyAge roadmap identifies the most important knowledge gaps and best approaches for strengthening muscle resilience research across the life course.

MyAge makes the following recommendations to funders and to the research community:

1. Engage with policy makers at an early stage to establish dialogue and pathways to influence.

The economic and societal impacts of muscle resilience across the life course and musculoskeletal ageing are not fully understood by decision makers. The research community can work more closely with large national charities who are resourced for advocacy work with people at different stages of life, to help inform the population[1,2]. Robust cost-benefit analysis is needed to demonstrate the societal benefit/value of muscle resilience and musculoskeletal ageing research, to policy makers and funders.

2. Invest in basic mechanisms of ageing and chronic disease

UK researchers have a deep understanding of the key role of muscle resilience and healthy muscle ageing for increasing healthspan. However, much stronger investment is needed, notably into understanding the basic mechanisms of muscle resilience and ageing in association with chronic disease. This will allow discovery of commonality of pathogenic mechanisms between diseases, enabling translation through new interventions in partnership with the life sciences industry.

3. Invest in pilots and trials of interventions

Lack of resources for pilot and full-scale trials of interventions hampers translation of muscle resilience and ageing biology into clinical trials. Furthermore, a greater risk appetite is required to support high quality, disruptive research, including appropriate interdisciplinary review processes.

4. Encourage and support collaboration between life science and social science.

Recognise the value of social science for muscle resilience research. Embed social science expertise from the outset, for example by co-production of interdisciplinary research questions and the co-design of methods. Generate a research culture that promotes collaboration and provide mechanisms to help train early career researchers to engage with social science and other disciplines important for the translation of experimental science into practice.

5. Encourage private sector investment in research and development.

Improve commercialisation of outputs from UK muscle resilience and ageing research. Support the research community in achieving buy-in from industry[3] and provide funding mechanisms to promote collaboration in activities that industry would not otherwise undertake, and to timescales consistent with business cycles.

6. Strengthen and support international partnerships.

Accelerate the impact of research through working with international experts and pooling funding resource. Promote dialogue between UK funding bodies and overseas funders to help align administrative processes and encourage international collaborations.

Cover:
Image designed by NEXU Science Communication

About MyAge

MyAge is a UK interdisciplinary network researching *muscle resilience across the life course: from cells to society*. Funded by the Biotechnology and Biological Sciences Research Council and the Medical Research Council, we aim to improve understanding of the mechanisms leading to reduced muscle function and set the direction of future research leading to effective interventions.

We work with policy makers, funders, healthcare professionals, inequality experts and the public, to tackle the biggest questions in muscle ageing.

A roadmap for transformative research in healthy ageing

One of the highest impact changes during ageing is the loss of muscle mass and function, termed sarcopenia. Approximately 50% of muscle is lost by the eighth decade of life[4]. As muscle is critical for normal physical function and metabolic homeostasis, loss results in multiple adverse outcomes, directly linked with impairment of multiple systems. This results in increased risk of several long-term conditions as well as falls, fractures, frailty and physical disability; all of which are associated with reduced muscle resilience. It is the main driver of loss of independence in old age and is associated with substantial societal and economic costs through the life course. In addition, the effects of muscle loss are not experienced evenly across society, because sex, ethnicity and both physical and social environments strongly drive health inequalities in ageing. As a leading cause of sickness absence from work, reduced muscle resilience also impacts health and economic productivity at a relatively young age. Investing in muscle resilience and preventing muscle loss from a younger age will enable individuals with good muscle health and reduced economic inequalities throughout life.

> **“I think that it’s important for young people to learn about muscle resilience because our actions just now are likely to have a very large impact on our future selves, and our muscle resilience.”**
>
> *Member of the LifeLab Youth Panel*

Understanding the drivers of sarcopenia and developing interventions to combat declining muscle resilience at key time points during the life course, are central to delivering effective policies to promote independent living in later life, to enhancing health and reducing health inequalities, decreasing the societal costs, and benefiting people of all ages.

Key numbers

470,000

approximate number of British people of working age suffering from musculoskeletal symptoms[6]

12.5 million

approximate number of people over 65 in the UK[7-9]

Twice as many years without disability for those living in the wealthiest parts of England compared to the poorest areas, beyond the age of 65.[10]

£2.5 billion

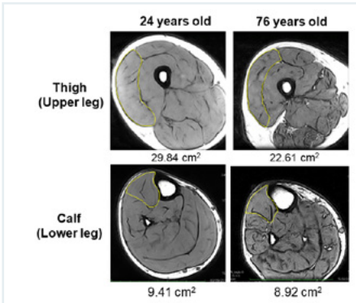
estimated annual UK excess healthcare costs associated with muscle weakness[11]

Less than **5%**

of the NHS budget is spent on prevention of ill health[12]

MyAge: Responding to scientific and societal challenges

The complexity of the ageing process requires an innovative and interdisciplinary research approach that shifts away from studying single systems in isolation, towards an integrative and holistic understanding of muscle ageing. This approach is not only a scientific conduit to improving health; it impacts upon pressing societal issues and political imperatives. The MyAge network has brought together a new grouping of key experts in disparate areas to combine strengths and resources in muscle ageing research. This enables a shift away from treatment alone, to include prevention of the adverse consequences of a decline in muscle resilience. We present an evidence-based Roadmap to guide research aimed at improving muscle health and resilience across the life course. The Roadmap is the output of two years of network activities to inform policy and the funding landscape for muscle resilience research, translation and innovation.



Magnetic resonance images of thigh and calf muscles: comparison of muscle cross-sectional area between young and older individuals. Image courtesy of Dr Mathew Piasecki, University of Nottingham.

The Roadmap

1. **Articulates** research questions arising from our challenge, and proposes the best approaches to address them
2. **Identifies** strategies for muscle resilience research across disciplines to gain a better understanding of healthy ageing
3. **Provides** recommendations to generate an evidence base underpinning policymaking in this area

Definitions used in this report

Muscle resilience

The ability of muscle to recover from a challenge, such as ageing, inactivity, a period of immobility, poor nutrition, illness, or injury. By building and maintaining muscle mass, quality and function across the life course, we are better able to respond to challenges and to ameliorate the effects of muscle loss.

Muscle ageing

Age related dysregulation of any aspect of muscle function at a molecular, cellular or tissue level, which may result in a decrement of muscle mass, quality or function, but which may not necessarily result in sarcopenia.

Sarcopenia

Age-related loss of muscle strength, quantity and quality. It is a progressive and generalised skeletal muscle disorder that is associated with increased likelihood of adverse outcomes including falls, fractures, physical disability and mortality[5]. In practice, sarcopenia is detected by low muscle strength, confirmed by identifying low muscle quantity or quality, and its severity graded by physical performance tests.

1. Applying insights from cells to society, how do we improve muscle resilience from childhood to later life?

The most important research questions underpinning improvement in muscle resilience across the life course, were synthesised from MyAge in-person meetings and a qualitative analysis of the online responses of the MyAge membership to a survey (Figure 1). Respondents included both early career and established researchers, as well as representatives from industry and third sector organisations.

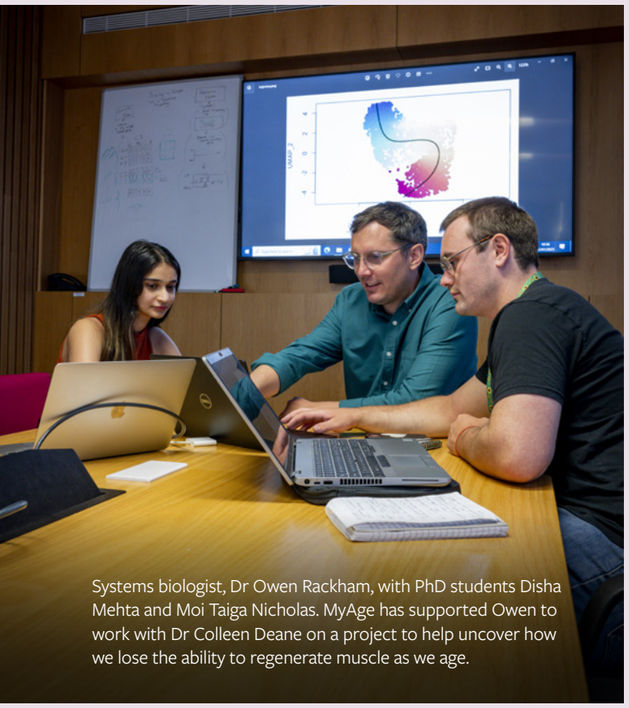
The responses represented the MyAge network's three main themes: (i) molecules, cells and tissues (ii) systems, organisms, populations and (iii) environment, genes, epigenetics.

A **How can we unlock new preventive and therapeutic approaches to attenuate muscle ageing?**

Research into the biological mechanisms underlying sarcopenia should include neural decrements (both central and peripheral), as well as the positive and negative 'memory mechanisms' responsible respectively for triggering a hypertrophic response or for mediating the influence of early life adversities on muscle ageing. We need to take an interdisciplinary approach by harnessing mathematical and engineering expertise in data analytics, while also investigating the extent to which behaviours and perceptions held earlier in life impact muscle health in later life.

B **How can we enhance our knowledge of disease-associated muscle loss to design targeted interventions to improve muscle resilience?**

A greater depth of knowledge and understanding of the processes that influence muscle loss in chronic disease (for example, inflammation), and which associated phenomena associated with muscle loss are cause or effect, integrated with knowledge of the experiences and perceptions of adults living with disease, will inform acceptable and feasible interventions.



Systems biologist, Dr Owen Rackham, with PhD students Disha Mehta and Moi Taiga Nicholas. MyAge has supported Owen to work with Dr Colleen Deane on a project to help uncover how we lose the ability to regenerate muscle as we age.

C **Which rehabilitation strategies are most effective at improving mobility in a diverse, multicultural society?**

Experimental science can inform on muscle degenerative/ regenerative responsiveness to catabolic crises, including acute/ high impact traumatic injury, chemotherapy and hospitalisation, as well as the biological after-effects. Harnessing an interdisciplinary approach would also enable investigation of the influence of social factors such as ethnicity and socio-economic deprivation on these phenomena, alongside the technological augmentation of rehabilitative efforts in the home and the community.

D **What is 'natural' ageing, i.e., what are the relative contributions of chronological ageing and environment/lifestyle to muscle ageing?**

For example, how does inactivity impact on muscle metabolic and functional decline? What social, economic and environmental factors influence muscle loss through the life course? Knowledge of what constitutes primary ageing with other causes of muscle loss throughout the life course would inform transformative methodologies to improve muscle health and resilience.

E **Why do women live longer, yet experience greater deconditioning and frailty than men?**

An interdisciplinary approach to addressing knowledge gaps around the female health paradox could combine physiological investigation of muscle metabolism and hormonal status with studies of sexual differences in relation to behaviours impacting muscle function. This could inform the design of tailored interventions aimed at maintaining or improving muscle resilience at critical periods in the female life span.

F **How and when can we intervene, in order to enhance muscle resilience across the population?**

Understanding which mechanisms underly exercise-induced muscle adaptation, including responsiveness of muscle to exercise and diet, combined with investigation of the barriers and facilitators to improving muscle resilience across diverse groups across different ages, ethnicities and settings, will inform optimum interventions at an individual, family or community level.

"The UK has a strong basic science understanding of muscle ageing processes, internationally well-established fields of research, and a deep understanding of the key role of healthy muscle ageing for living well, for longer. We are well placed to transform muscle resilience research across the life course."

Professor Carolyn Greig, School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham

Within these higher-level research questions, a number of individual responses at a mechanistic level emerged, covering the following basic science topic areas:

(i) influence of mitochondrial function on sarcopenia and the potential for nutritional and pharmaceutical therapeutics targeting this;

(ii) intercellular anti-ageing signalling pathways to alleviate muscle ageing;

(iii) the impact of the microbiome on muscle/ immune cell crosstalk and the effect of age and diet on the microbiome;

(iv) epigenetic changes to homeostasis to increase understanding of individual variability in muscle resilience;

(v) muscle stem cell dysregulation to understand the transition to sarcopenia;

(vi) adiposity and longevity pathways in skeletal muscle to understand the impact of obesity on muscle resilience across the life course;

(vii) the importance of the extracellular environment on muscle cell function;

(viii) hallmarks of ageing and multimorbidity/ disease to understand how the biological mechanisms of ageing may reduce polypharmacy by preventing disease clusters;

(ix) identifying tissue and cellular signatures that define muscle ageing to deliver meaningful targets for therapeutic development;

(x) understanding the influence of drug interactions on musculoskeletal health to inform patient management;

(xi) mapping proteome and transcriptome changes across the healthspan to determine at what level of control do perturbations influence health;

(xii) the influence of ethnicity on the time course and degree and mechanisms of muscle ageing, to enable targeted interventions to reduce muscle health inequalities.

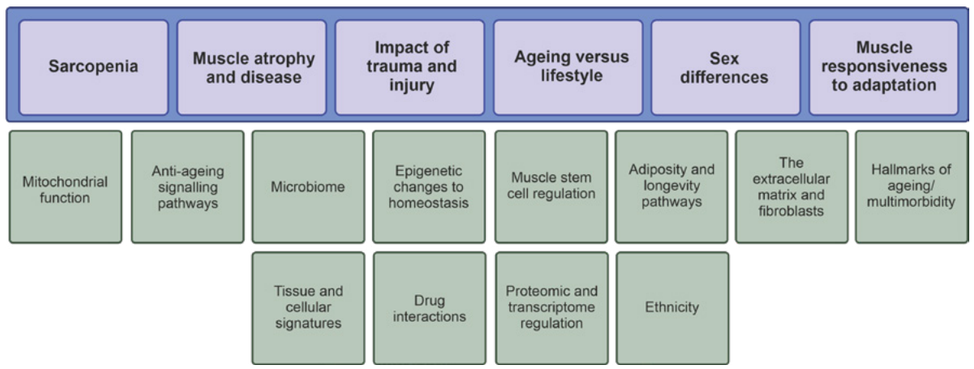


Figure 1: The most important research questions in muscle resilience research. The top row identifies 'higher level' topic areas identified by several MyAge network members, while the middle/ bottom rows show individual member- level responses identifying priorities for basic mechanistic research.

Note: the divisions between individual boxes are artificial; there is interaction between topic areas across each level; the high level questions are interdisciplinary, integrating social science with STEM.

The proposed best experimental approaches to address the important research questions were ascertained using the same process.

1 Development of ageing and disease relevant pre-clinical models/ tissue engineering

To include, for example, the development of muscle tissues to mimic different ageing stages, as well as induced pluripotent stem cell models (for example, to study myoblast/neuromuscular junction function/ muscle rejuvenation), to advance knowledge and understanding of mechanisms underlying muscle changes across the life course.

2 Biomarker discovery

Harness pre-clinical models and transformative technologies to identify and validate early detection markers and methods (including the development of meaningful metrics), to monitor muscle tissue loss.

3 Transformative technologies

To include wearable devices/ digital applications/ remote monitoring/ kinematics/ imaging/ exploitation of multi-platform data sets, to optimise the management of chronic long-term conditions.

4 Innovative therapeutic approaches (pharma/nutraceuticals)

Including targeted acute/ chronic interventions (exercise/ physical activity, nutritional, psychological-behaviour change) to develop optimal lifestyle-based maintenance, rehabilitation and recovery strategies across diverse groups and settings.

5 Integrative study methodologies with standardised outcome measures to generate an evidence base informing translation and implementation

Well designed and controlled studies (mechanistic, cohort, longitudinal, dose-response), incorporating harmonised protocols and robust outcome measures, are necessary to inform the translation of basic science to clinical trials and other interventions, to facilitate drug discovery, step-changes in technology or environmental drivers that will impact on muscle resilience. These need to be integrated (where appropriate) with qualitative methodologies, including surveys, interviews and focus groups, to generate greater knowledge of the 'bigger picture' and help us to better understand why some interventions may be effective, while others may not.

Early career researcher, Paul Muckelt, and Physiotherapy MSc student, Rebecca Cannon, conducting muscle ultrasound investigations.

2. Strategies to drive muscle resilience research

1 Building an international and interdisciplinary research community

Currently, clinical trials and patient engagement across a broad spectrum of areas, operate in partial to complete isolation from disciplines that address the mechanistic properties of single living cells. These properties are the foundation of performance in health and disease. Advanced mathematical insights also sit largely apart from omics, physiological and trial data. We need to stop working in silos and to continue building an interdisciplinary, global community of knowledge and expertise, to work together on transformative solutions to improve muscle resilience and prevent redundant research. We need to be strong advocates for the interdisciplinary approach – multimodal, multiscale and cross disciplinary. MyAge recognises the importance of social science to muscle resilience research, and we therefore need to promote closer collaborations between life and social sciences. We recognise that building a research community able not only to drive but sustain transformative ageing research requires training and support and this needs to start as early as possible in the career pathway. Equipping early career researchers with interdisciplinary research skills and encouraging cross- sectoral working in career development will enable the next generation of scientists to deliver research utilising cutting edge methods and techniques to provide game changing insight into human ageing activities.

2 Incentivise sharing of resources

Alongside Strategy 1, there should be mechanisms to incentivise and facilitate greater sharing of samples and data sets to support collaborative research. There are challenges to this and as a consequence, they are rarely sustained. Working with organisations that already exist, are well-resourced and which hold directories, (for example, The National Council of Universities and Businesses) may represent an alternative to starting anew.

3 Supporting strategy development by engagement with stakeholder/ advocacy groups

MyAge has produced value proposition documents for potential partners in industry[3] as well as a brief for policy makers/ influencers[1], which was presented to MPs and members of the House of Lords at Westminster during Evidence Week, July 2023 (see Recommendation 1, Section 3). Of course, the public represent our major stakeholder: MyAge has undertaken several public involvement and engagement activities with participants of all ages. We have also included public contributors in our Steering Committee, who have supported our progress and provided input to our schedule of activities and to the Roadmap. We need to continue to support and scale up public contributor input, including those from under-represented groups, via town hall meetings to discuss ideas and co-design opportunities to maintain a strong strategic focus which will improve chances of research success.

Dr Colleen Deane, one of the next generation of investigators takes a collaborative, interdisciplinary approach to muscle resilience research.

4 Maintaining cohorts and muscle samples from well characterised cohorts

The UK is a world leader in biobanked human samples from well characterised ageing cohorts. There is, however, a lack of resource to renew/replace/augment ageing cohorts; notably most of the banked tissues do not include muscle. An accessible national sample repository with comprehensive metadata to support ageing research is needed, although we recognise that this will be a significant endeavour and investment. Human material, under either selective or controlled conditions could feed a pipeline of STEM investigation.

MY AGE ROADMAP

HOW DO WE IMPROVE MUSCLE RESILIENCE ACROSS THE LIFECOURSE?

THE PROBLEM

LOSS OF MUSCLE RESILIENCE IS ASSOCIATED WITH A NUMBER OF ADVERSE OUTCOMES WHICH HAVE A SUBSTANTIAL IMPACT ON HEALTHY AGEING

IT IS THE MAIN DRIVER OF LOSS OF INDEPENDENCE IN OLD AGE

IT IS ASSOCIATED WITH SUBSTANTIAL SOCIETAL AND ECONOMIC COSTS

IT IS A LEADING CAUSE OF SICKNESS AND ABSENCE FROM WORK

AN INCREASED RISK OF MULTIPLE LONG-TERM CONDITIONS AND AN IMPAIRMENT OF MULTIPLE SYSTEMS

INCREASED RISK OF FALLS, FRACTURES, FRAILTY, AND PHYSICAL DISABILITY

THE EFFECTS OF MUSCLE LOSS ARE NOT EXPERIENCED EVENLY ACROSS SOCIETY

THE IMPORTANT RESEARCH QUESTIONS

(A) HOW CAN WE UNLOCK NEW PREVENTIVE AND THERAPEUTIC APPROACHES TO ATTENUATE MUSCLE AGEING?

(B) HOW CAN WE ENHANCE OUR KNOWLEDGE OF DISEASE-ASSOCIATED MUSCLE LOSS TO DESIGN TARGETED INTERVENTIONS TO IMPROVE MUSCLE RESILIENCE?

(C) WHICH REHABILITATION STRATEGIES ARE MOST EFFECTIVE AT IMPROVING MOBILITY IN A DIVERSE MULTICULTURAL SOCIETY?

(D) WHAT IS NATURAL AGEING? I.E. WHAT ARE THE RELATIVE CONTRIBUTIONS OF CHRONOLOGICAL AGEING AND ENVIRONMENT/LIFESTYLE TO MUSCLE AGEING?

(E) WHY DO WOMEN LIVE LONGER, YET EXPERIENCE GREATER DECONDITIONING AND FRAILTY THAN MEN?

(F) HOW AND WHEN CAN WE INTERVENE, IN ORDER TO ENHANCE MUSCLE RESILIENCE ACROSS THE POPULATION?

THE UK IS WELL PLACED TO **TRANSFORM MUSCLE RESILIENCE RESEARCH.**

IF THE UK IS SERIOUS ABOUT SUPPORTING ECONOMIC GROWTH, AND PIONEERING RESEARCH TO ADDRESS MAJOR SOCIETAL CHALLENGES WE NEED A MASSIVE INJECTION OF LONG-TERM INFRASTRUCTURAL FUNDING.

THIS WOULD ALLOW THE UK TO PIONEER A **TRULY INTERDISCIPLINARY APPROACH** IN AGEING RESEARCH, WITH **POPULATION WIDE INITIATIVES** TO IMPROVE MUSCLE RESILIENCE IN THE WORK FORCE, SUSTAIN HEALTH, AND CREATE PRECISION INTERVENTIONS FOR THOSE WITH MUSCULAR SKELETAL RELATED DISORDERS.

THE SOCIO-ECONOMIC IMPACT WOULD BE IMMENSE!

RECOMMENDATIONS

1. ENGAGE WITH POLICY MAKERS AT AN EARLY STAGE TO ESTABLISH DIALOGUE AND PATHWAYS TO INFLUENCE
2. INVEST IN BASIC MECHANISMS OF AGEING AND CHRONIC DISEASE
3. INVEST IN PILOTS AND TRIALS OF INTERVENTIONS
4. ENCOURAGE AND SUPPORT COLLABORATION BETWEEN LIFE SCIENCE AND SOCIAL SCIENCE
5. ENCOURAGE PRIVATE SECTOR R&D INVESTMENT
6. STRENGTHEN AND SUPPORT INTERNATIONAL PARTNERSHIPS

STRATEGIES

TO DRIVE MUSCE RESILIENCE RESEARCH

1. BUILDING AN INTERNATIONAL AND INTERDISCIPLINARY RESEARCH COMMUNITY
2. INCENTIVISE SHARING OF RESOURCES
3. SUPPORTING STRATEGY DEVELOPMENT BY ENGAGEMENT WITH STAKEHOLDER/ADVOCACY GROUPS
4. MAINTAINING SAMPLES FROM WELL CHARACTERISED COHORTS

THE BEST PROPOSED EXPERIMENTAL APPROACHES

1. DEVELOPMENT OF AGEING AND DISEASE RELEVANT PRE-CLINICAL MODELS/TISSUE ENGINEERING
2. BIOMARKER DISCOVERY
3. TRANSFORMATIVE TECHNOLOGIES
4. INNOVATIVE THERAPEUTIC APPROACHES
5. INTERGRATIVE STUDY METHODOLOGIES WITH STANDARDISED OUTCOME MEASURES

JONNY GLOVER

3. Recommendations to generate an evidence base underpinning policy making: the MyAge 6-point plan

1 Engage with policy makers at an early stage to establish dialogue and pathways to influence

Despite efforts and initiatives, the economic and societal impacts of muscle resilience across the life course and musculoskeletal ageing are not fully understood by decision makers. MyAge has been proactively working at Governmental level with support from learned societies and Sense about Science, an independent charity that promotes the public interest in sound science and evidence, to focus on the societal and economic implications of poor muscle resilience. MyAge has produced a document 'A lifelong approach to muscle resilience: implications for policy and practice'[1], aimed at policy makers and influencers. As a research community we can work more closely with large national charities who are resourced for advocacy work with people at different stages of life, to help brief the population. We also recommend robust cost-benefit analysis to demonstrate the societal benefit/value of ageing research, including musculoskeletal ageing, to policy makers and funders.

> **"Promoting muscle strength and development at an early stage could improve childhood and adolescent health and wellbeing, reduce adult sickness and enhance productivity, and reduce frailty in older age."**
>
> *Professor Keith Godfrey, MRC Lifecourse Epidemiology Centre, University of Southampton & NIHR Southampton Biomedical Research Centre*

2 Invest in basic mechanisms of ageing and chronic disease

In the UK there is a strong basic science (cellular physiology linked to molecular processes) understanding of muscle ageing processes. In addition, UK researchers have a deep understanding of the key role of healthy muscle ageing for increasing healthspan. However, we need much stronger investment than at present, notably into understanding the basic mechanisms of muscle ageing as it occurs in association with chronic disease. This will allow discovery of commonality of pathogenic mechanisms between diseases, enabling translation through new interventions in partnership with the life sciences industry. Looking globally, longevity investment grew from $0.5 billion in 2013 to over $6.2B in 2021; the US National Institute on Aging has a budget of $4.4 billion p.a. It is vital that UK investment keeps pace with global trends.

3 Invest in pilots and trials of interventions

Lack of resources for pilot and full-scale trials of interventions hampers our ability to translate understanding of muscle ageing biology into clinical trials. Furthermore, a greater risk appetite is required to support high quality, disruptive ageing research, including appropriate interdisciplinary review processes.

4 Encourage and support collaboration between life science and social science

It is a challenge to foster engagement between life and social scientists, but doing so gives greater opportunities for successful translation of research to policy. The challenge may be due in part to negotiating different languages, perspectives and methodologies but this may be overcome by embedding social science expertise from the outset into life science research, for example by co-production of interdisciplinary research questions and the co-design of methods – noting that recognition of the value of social science should be more widely considered than an 'add-on' at the stage of translation. Appropriate training of early career researchers is important in this respect (see also Strategy 1), and mechanisms need to be in place to support this. With respect to funding, UKRI has supported several interdisciplinary programmes in the past but there remain obstacles to interdisciplinary research that crosses research council boundaries. It's not just about funding, however, but the generation of a research culture that promotes collaboration and which encompasses both funder and research community.

5 Encourage private sector R&D investment

There is perceived weakness in commercialisation of UK research in the muscle ageing. There is a lack of support to achieve buy-in from industry so that funding mechanisms support collaboration in activities that industry would not otherwise undertake, and to timescales consistent with business cycles.

6 Strengthen and support international partnerships

We have opportunities to accelerate the impact of research through working with international experts and pooling funding resource. MyAge includes national and international members and advisors and currently leads a UKRI funded Global Partnership Award working closely with Institutions in the USA and Canada. MyAge also contributes to activities led by other UK Ageing Networks partners in the global South. Better dialogue between UK funding bodies and overseas funders would help align administrative processes to strengthen support for international collaboration. This is of particular importance with respect to accessing US funded partnerships.

Dr Mark Burton and other early career researchers from universities at Stirling, Edinburgh Napier, Liverpool John Moores and Southampton were supported by MyAge to map the differences between healthy individuals and those with muscle loss, at the level of individual cells.

Understanding these differences may give an opportunity to slow down or counteract muscle loss with lifestyle interventions or drug therapies.

Summary

The MyAge roadmap identifies the most important knowledge gaps and best approaches for researching muscle resilience across the life course. The UK has a strong basic science understanding of muscle ageing processes, internationally well-established fields of research, and a deep understanding of the key role of healthy muscle ageing for increasing healthspan. It has well-networked investigators and expertise in biobanking of human samples from well characterised ageing cohorts. As such, the UK is well placed to transform muscle resilience research across the life course and the UK Ageing Networks represent a positive step in this direction. There are however, challenges: there exists weakness in translating understanding of muscle ageing biology into clinical trials and commercialisation, alongside:

(i) lack of resource to monitor/renew/replace/augment ageing cohorts,

(ii) lack of suitable mechanisms to foster multiscale, multimodal, interdisciplinary collaborative research, particularly between life and social sciences, including growing international partnerships,

(iii) lack of an accessible national sample repository to support ageing research, and

(iv) weakness in administrative processes supporting international collaboration.

Muscle research, across the board, could act as an exemplar if properly funded with clear multimodal, collaborative and interdisciplinary goals. The UK should be serious about supporting economic growth through disruptive interdisciplinary research to address major societal challenges. We need a massive injection of funding, including support for longer term infrastructural funding to build capacity and encourage intellectual risk-taking. We already know that investment in medical research provides long term returns to the economy: every £1 spent delivers a return of about 25 pence p.a., forever[13].

Interdisciplinary collaboration doesn't succeed overnight but a substantial investment would allow the UK to pioneer a truly interdisciplinary to transdisciplinary approach in ageing research. Adopting a life course approach with population-wide initiatives to improve muscle resilience in the workforce and sustain health, would create enable the development of mechanisms-based precision interventions implemented at key life stages.

We cannot lose sight of the fact that investing in muscle resilience

- in childhood and adolescence
- in early adulthood
- in middle age

will benefit people throughout life, and in later years. Today's younger adults will be able to optimise their muscle health, will be less likely to leave the workforce earlier due to musculoskeletal problems and will be more resilient to the life limiting effects of physical frailty in those with musculoskeletal age-related disorders. The socio-economic impact of population-wide initiatives to improve muscle resilience would be immense.

> **"Understanding the hidden causes of muscle ageing and developing interventions to prevent declining muscle resilience across the life course, is central to helping people be more independent in later life, ease the economic pressure on our healthcare system and reduce health inequality. In a nutshell, it's important to make sure that old age is enjoyed and not endured!"**
>
> *Professor Janet Lord, FMedSci, CBE, MRC Versus Arthritis Centre for Musculoskeletal Ageing Research, University of Birmingham*

Authors

Professor Carolyn Greig, School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham

Dr Kambiz Alavian, Dept of Brain Sciences, Imperial College London

Professor Keith Godfrey, MRC Lifecourse Epidemiology Centre, University of Southampton & NIHR Southampton Biomedical Research Centre

Ms Josie Gray, University of Southampton

Professor Karen Lillycrop, School of Biological Sciences, University of Southampton

Dr Alexandra Mant, Institute for Life Sciences, University of Southampton

Dr Mathew Piasecki, Centre of Metabolism, Ageing and Physiology, University of Nottingham

Professor Peter JS Smith, Institute for Life Sciences, University of Southampton

The authors thank the Biotechnology and Biological Sciences Research Council and the Medical Research Council for funding and The Physiological Society for advice and support in the development of MyAge. At the time of writing, MyAge has over 120 members from universities in the UK and overseas, from industry, third sector, and members of the public. The authors thank all members for contributing to the development of the roadmap, through the membership survey, workshops and seminars, and through review, feedback and discussion.

To cite: Greig CA, Alavian, KN, Godfrey K, Gray J, Lillycrop KA, Mant A, Piasecki M, Smith PJS (2023). Muscle resilience across the life course: from cells to society. A Roadmap for transformative research in healthy ageing. Report, University of Southampton.

DOI: 10.5258/SOTON/P1128

Poster created by LifeLab Youth Panel member, Maria, to explain the importance of muscle resilience across the life course.

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