

## Increasing healthy life expectancy: the policy implications of geroscience

The UK's demographic and health landscapes are undergoing a profound transformation characterised by a steadily ageing population and the rising prevalence of health conditions associated with older age. Geroscience offers a promising approach to extend healthy lifespan, reduce healthcare burdens and enhance economic productivity. A supportive research and innovation ecosystem is necessary for ensuring that the UK and its citizens benefit from breakthroughs in geroscience.

This policy briefing explores the emerging field of geroscience, a scientific discipline at the intersection of basic ageing biology, chronic disease and frailty, which offers the potential to revolutionise how we maintain health and independence in old age<sup>1</sup>. In the next 20 years, the number of people aged 85 and over in the UK will double to 2.6 million<sup>2</sup>, and two-thirds of adults aged over 65 are expected to be living with multiple long-term health conditions<sup>3</sup>. Caring for an ageing population will be one of the biggest clinical challenges facing the NHS and health systems around the world. There is therefore an urgent need to translate the current understanding of geroscience into extended healthy lifespan. This requires a shift from reactive healthcare to proactive measures and a greater focus on optimising health through combating the ageing process.

Implementing geroscience-informed interventions could lead to numerous benefits for the UK and its population. With a compression of illness towards the very end of life, individuals can experience an extended period of active and healthy living. This can also ease strain on the NHS, as fewer chronic diseases and frailties mean resources can be redirected to prevention and acute care.

Economically, improved health enables more individuals to remain in the workforce for longer, boosting productivity and alleviating financial pressures on the young to support the old. Given the significant inequalities in healthy life expectancy based on location and socioeconomic status, geroscience also holds promise in providing tools to help decouple deprivation from poor health. Finally, with increased investment appetite from the public and private sectors, geroscience emerges as a compelling financial avenue, poised to attract inward investment and generate revenue via the exportation of drug discoveries made in the UK.

This policy briefing was drafted by staff at the Royal Society in collaboration with biology of ageing expert Professor Dame Linda Partridge, Vice-President of the Royal Society, and Chair of the Royal Society's Geroscience Working Group, as an outcome of a conference that convened the UK's leading geroscientists and stakeholders across the health sector. It challenges the traditional view that ill health during ageing is inevitable, as demonstrated by many examples of healthy ageing humans in their 90s and 100s, and discoveries of interventions to increase healthy lifespan in animal models.

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1. National Institute on Ageing. *Geroscience: the intersection of basic aging biology, chronic disease, and health*. <https://www.nia.nih.gov/research/dab/geroscience-intersection-basic-aging-biology-chronic-disease-and-health> (accessed 7 February 2024).
  2. The Health Foundation. REAL Centre. Raymand A *et al.* 2021. *Our Ageing Population: how ageing affects health and care need in England*. <https://reader.health.org.uk/our-ageing-population> (accessed 11 February 2024).
  3. National Institute for Health and Care Research. *Multi-morbidity predicted to increase in the UK over the next 20 years*. <https://evidence.nihr.ac.uk/alert/multi-morbidity-predicted-to-increase-in-the-uk-over-the-next-20-years/> (accessed 10 February 2024).
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The field of geroscience offers significant potential for promoting healthy ageing. To realise these promises, we must ensure that scientific endeavours are: (1) bolstered by a collaborative and interdisciplinary research and innovation ecosystem focussed on the ageing process as a whole, that can spur change and catalyse progress; (2) fuelled by ambitious and long-term funding to attract talent and foster innovation; (3) enabled by an agile and innovative regulatory framework for drug design and clinical trials, streamlining the path from laboratory discovery to patient treatment; and (4) accompanied by shifts in policy to fully translate the UK's scientific strengths into people's lives.

### The UK's population is getting older and sicker

As with most other advanced economies, the UK's population is ageing. By 2066 it is projected that there will be around 5.1 million people over the age of 85 living in the UK, an increase of around 3.5 million from 2016<sup>4</sup>. In contrast, the population of working-age is likely to remain relatively static. Despite improvements in life expectancy, healthy life expectancy has not kept pace – meaning that there is an increasing period of ill health at the end of people's lives. Between 2000 and 2019, it is estimated that the average proportion of life spent in poor health has increased from 10.3 years to 11.3 years<sup>5</sup>. This is because advancing age is the main driver of frailty and multimorbidity (which can be defined as the presence of two or more long-term health conditions), with ageing-related diseases such as cancers, musculoskeletal disorders, neurological conditions and sense organ diseases all increasing in incidence with age<sup>6</sup>. Due to the projected rise in the number of older adults over the coming decades, we expect to see a corresponding surge in the occurrence of multimorbidity and frailty across the UK population.

There are significant inequalities in terms of both life expectancy and healthy life expectancy based on location and socioeconomic status. Inequalities are substantial across all four nations – with a nearly 22-year healthy life expectancy gap between people living in the most and least deprived regions of Scotland, for example<sup>7</sup>.

This situation is of utmost concern in some rural and coastal areas where the concentration of deprivation and older age is driving an even greater proportion of disease and disability than in other parts of the country.

The consequences of living with multiple health conditions can be profound. Individuals suffering from several conditions experience poorer quality of life, loss of independence and greater risk of premature death. As the number of people with multimorbidity grows, so will the pressures on many aspects of the economy, including labour markets, economic outputs, pensions, government tax revenue and public service spending. More than two-fifths of national health spending in the UK is devoted to people over 65 (who currently represent over 19% of the total population)<sup>8</sup>, a figure that is only likely to increase. Unless action is taken to support healthy ageing, it is predicted that NHS spending will need to grow by 3.1% a year and social care funding by 4.3% a year in the next 10 – 15 years to meet the needs of the UK's ageing population<sup>9</sup>. This is clearly an unsustainable fiscal burning platform.

### Living healthier for longer

Traditionally, medical research has focussed on the diagnosis and treatment of ageing-related diseases on an individual basis – meaning that patients with multimorbidity are often cared for by doctors in different specialities and likely to be taking multiple drugs to control their illnesses (which poses risks including adverse drug interactions and increased healthcare costs). The geroscience approach represents a paradigm shift in that it explores the possibility of targeting the biological mechanisms of the ageing process itself in order to prevent or delay the onset and progression of multiple ageing-related conditions at the same time<sup>10</sup>. Of note, lifestyle interventions such as diet and physical exercise are recognised as prevention strategies capable of targeting multiple ageing-related conditions, and AgeTech (a subset of the health technology industry which uses technology to support health ageing) is also rapidly developing. However, this briefing does not specifically address these interventions.

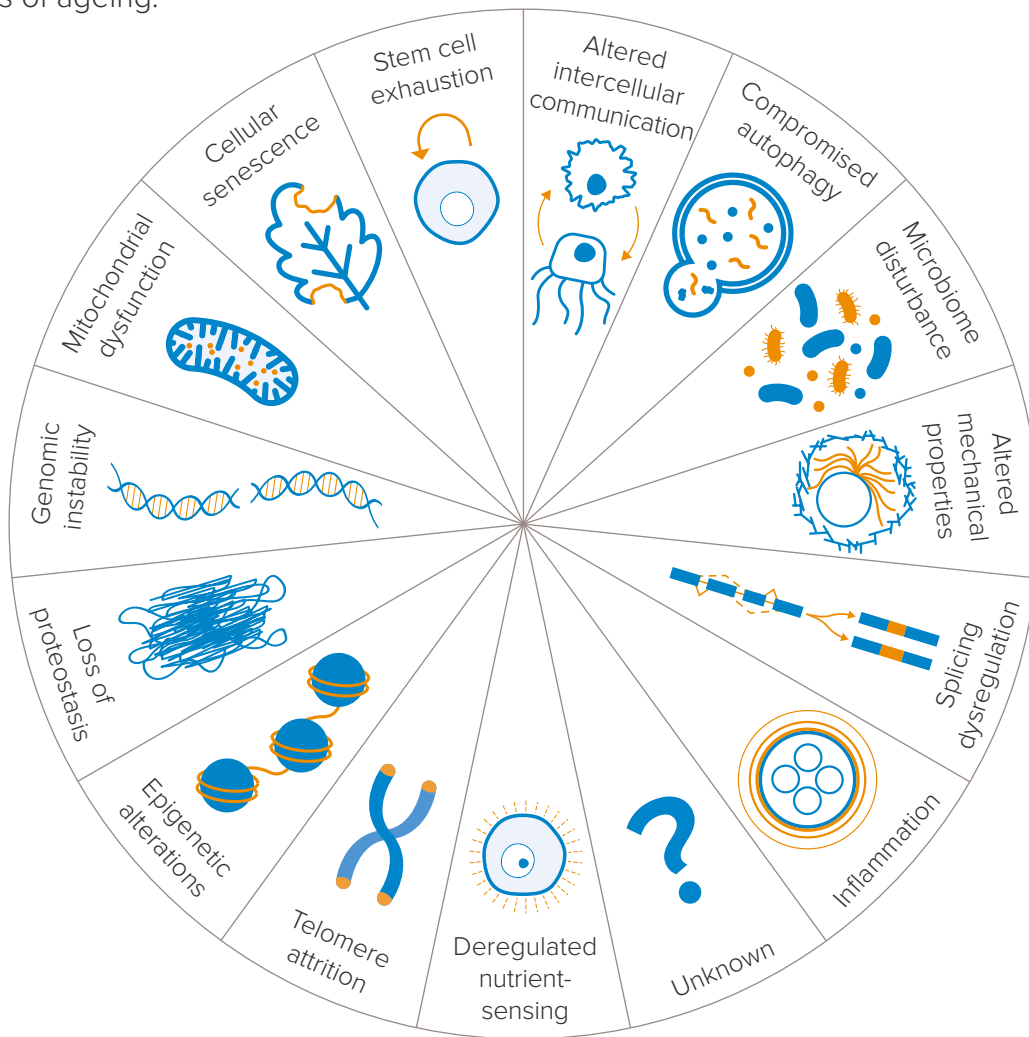
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- Chief Medical Officer. Chief Medical Officer's Annual Report. 2023. *Health in an ageing society*. <https://assets.publishing.service.gov.uk/media/65562ff2d03a8d00d07faa6/chief-medical-officers-annual-report-2023-web-accessible.pdf> (accessed 15 January 2024).
  - World Health Organization. *Health expectancy and healthy life expectancy*. <https://www.who.int/data/gho/data/themes/topics/indicator-groups/indicator-group-details/GHO/life-expectancy-and-healthy-life-expectancy>. (accessed 1 February 2024).
  - Guo J *et al.* 2022 Ageing and ageing-related diseases: from molecular mechanisms to interventions and treatments. *Signal Transduction and Targeted Therapy* **7**. (doi:10.1038/s41392-022-01251-0).
  - The Health Foundation. *Health life expectancy and healthy life expectancy at birth by deprivation*. <https://www.health.org.uk/evidence-hub/health-inequalities/life-expectancy-and-healthy-life-expectancy-at-birth-by-deprivation>. (accessed 20 February 2024).
  - Centre for Ageing Better. *Summary: the state of ageing 2022*. <https://ageing-better.org.uk/summary-state-ageing-2022>. (accessed 12 February 2024).
  - The Health Foundation. REAL Centre. Rocks S *et al.* 2021. *Health and social care funding projections 2021*. [https://www.health.org.uk/sites/default/files/upload/publications/2021/REALCentreFundingProjections\\_WEB.pdf](https://www.health.org.uk/sites/default/files/upload/publications/2021/REALCentreFundingProjections_WEB.pdf) (accessed 17 January 2024).
  - Lebrasseur MK *et al.* 2021 Identifying biomarkers for biological age: geroscience and the ICFSR task force. *The Journal of Frailty and Aging* **10**. (doi: 10.14283/jfa.2021.5).

Much geroscience research is focussed on 14 interdependent cellular and molecular mechanisms that underpin the ageing process – the ‘hallmarks of ageing’ (Figure 1)<sup>11</sup>. While ageing hallmarks are not themselves diseases, they are each involved in the ageing of different body systems and contribute to the development of ageing-related diseases, multimorbidity and frailty<sup>12</sup>. For example: genomic instability and epigenetic alterations often contribute to the development of certain cancers;

failed proteostasis is implicated in neurodegenerative diseases such as Alzheimer’s Disease, Amyotrophic Lateral Sclerosis and Parkinson’s Disease; and cellular senescence can result in tumour development, chronic inflammation, immune deficit and stem cell exhaustion<sup>13, 14, 15</sup>. Importantly, it is now becoming clear that the hallmarks are amenable to modulation, paving the way for clinical geroscience trials, an opportunity seized by a number of biotech companies with strong roots in academic research<sup>16</sup>.

FIGURE 1

The hallmarks of ageing.



11. Lopez-Otin C *et al.* 2014 *Hallmarks of aging: an expanding universe*. *Cell* 19. (doi: 10.1016/j.cell.2022.11.001).
12. Chief Medical Officer. Chief Medical Officer’s Annual Report. 2023. *Health in an ageing society*. <https://assets.publishing.service.gov.uk/media/65562ff2d03a8d000d07faa6/chief-medical-officers-annual-report-2023-web-accessible.pdf> (accessed 15 January 2024).
13. Fraser CH *et al.* 2021 Biological mechanisms of aging predict age-related disease co-occurrence in patients. *Aging Cell* 21. (doi: 10.1111/acel.13524).
14. Kurtishi A *et al.* 2019 Cellular proteostasis in neurodegeneration. *Molecular Neurobiology* 56. (doi: 10.1007/s12035-018-1334-z).
15. Huang W *et al.* 2022 Cellular senescence: the good, the bad and the unknown. *Nature Reviews Nephrology* 18. (doi: 10.1038/s41581-0022-00601-z).
16. Chief Medical Officer. Chief Medical Officer’s Annual Report. 2023. *Health in an ageing society*. <https://assets.publishing.service.gov.uk/media/65562ff2d03a8d000d07faa6/chief-medical-officers-annual-report-2023-web-accessible.pdf> (accessed 15 January 2024).

# Areas of consideration

There are several areas where more effort is required to ensure that the UK and its citizens reap the benefits of geroscience:

1. For UK geroscience to thrive, it needs to be supported by a collaborative and interdisciplinary research and innovation ecosystem focussed on the ageing process as a whole, capable of driving change and catalysing progress. This entails nurturing academic and clinical talent in the field and encouraging greater permeability between scientific disciplines and stakeholders along the innovation pipeline (including funders and regulators) to support translational geroscience and strengthen global collaboration capabilities.
2. The UK's capacity to discover and deliver game changing therapeutics to treat and prevent ageing-related diseases hinges on an ambitious and long-term funding commitment. This includes increasing research and development spending in understanding the biological processes of ageing while also fostering a conducive economic environment for investors, biotech and pharmaceutical companies to operate effectively.
3. Ensuring the translation of geroscience discoveries into clinical practice requires an agile and innovative regulatory environment for drug design and clinical trials to streamline the pathway from bench to bedside. Required adaptations include exploring novel trial designs, approving trials targeting multiple conditions, using mixed trial endpoints including biomarkers and ensuring inclusion of older people with multimorbidity into clinical trials.
4. Maximising the health and independence of older adults should be acknowledged as a paramount scientific priority integral to our broader political, societal and cultural approach to ageing. Scientific advances will yield public benefits only when accompanied by a societal shift across multiple policy domains, ensuring the full realisation of their potential.

## AREA OF CONSIDERATION 1:

### A COLLABORATIVE AND INTERDISCIPLINARY ECOSYSTEM

The UK's geroscience capabilities are impressive, yet reviews have found the current research effort to be fragmented, often focussed on single aspects of ageing and neglecting crucial areas like frailty research<sup>17</sup>. From a fundamental science perspective, understanding the complex interactions between ageing mechanisms and the dynamics within different cell types and tissues at different ages remains a challenge. Another challenge is the scarcity of clinician scientists specialising in geroscience. Despite their crucial role across various health research domains, there is a notable lack of incentives to encourage professionals to pursue careers in this area, hindering the development of expertise and innovation needed to address the complexities of ageing-related healthcare effectively.

To address these gaps, the UK needs to attract academic talent and create interdisciplinary research and innovation networks capable of integrating expertise across disciplines. Such networks would facilitate a more comprehensive understanding of ageing biology and strategies to enhance healthy lifespan to improve ageing research outcomes. Science of ageing networks should aim to foster collaboration not only among various disciplines but also between academia and a wide array of stakeholders, including biotech and pharmaceutical companies, the NHS, funders and policymakers. By doing so, these networks could effectively promote the translation of research findings into interventions and public health benefits.

There have been network initiatives in the field, including UK SPINE and the UK Ageing Network (UKAN). No longer active, UK SPINE was based on a collaboration between six research partners focussed on furthering understanding of ageing biology and creating tools, reagents and assays necessary for drug discovery. UK SPINE also provided a network linking external stakeholders with the core network, bringing expertise in while also offering avenues to lobby for ageing research. UKAN is jointly funded by the Biotechnology and Biological Sciences Research Council (BBSRC) and the Medical Research Council (MRC). The consortium brings together 11 UK ageing research networks to facilitate knowledge exchange, forge new collaborations and drive innovative research across all academic disciplines. UKAN also aims to facilitate collaboration outside of academia to ensure proper resourcing of ageing research and rapid implementation of findings into policy and practice. Similar to UK SPINE, UKAN lacks a long-term outlook, with funding only running until February 2025.

Despite the existence of a few consortia, the UK is far from having an embedded authority comparable to that of the National Institute on Ageing in the United States (Box 1).

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17. Boucher E *et al.* 2023 Prevalence and outcomes of frailty in unplanned hospital admissions: a systematic review and meta-analysis of hospital-wide and general (internal) medicine cohorts. *eClinicalMedicine* **59**. (doi: 10.1016/j.eclinm.2023.101947).

## National Institute on Ageing (NIA).

The NIA, part of the United States' National Institutes of Health, spearheads efforts to improve the health and well-being of older adults through research. With a robust investment in scientific initiatives and innovation, the NIA conducts groundbreaking research and maintains an active communications and outreach program, disseminating knowledge to both the research community and the public.

### **Key takeaways from the NIA that could be leveraged by the UK include:**

- **Bold investment in research:** The NIA's substantial funding for research on ageing has catalysed groundbreaking discoveries in understanding the ageing process, treating ageing-related diseases and promoting healthy ageing.
- **Interdisciplinary approach:** By fostering research across diverse fields such as biology, psychology, sociology and public health, the NIA encourages a holistic understanding of ageing, laying the groundwork for effective interventions.
- **Research to impact:** Actively translating research findings into actionable policies, programs and interventions, the NIA ensures that scientific breakthroughs directly benefit older adults.
- **Collaborative partnerships:** The NIA collaborates with other government agencies, academic institutions, industry partners and international organisations, driving collective progress in ageing research.
- **Engaging and educating the public:** Through public engagement activities, the NIA promotes awareness of healthy ageing practices and increases public support for ageing research initiatives.

## AREA OF CONSIDERATION 2: AN AMBITIOUS AND LONG-TERM FUNDING COMMITMENT

A large proportion of hospital inpatients are older adults, with those aged 65 and above making up 70% of hospital days in the UK and those aged 75 and above, with frailty accounting for 20% of all bed days across England<sup>18</sup>. Additionally, there are currently more than 2.6 million working-age people who are out of the labour market due to long-term sickness<sup>19</sup>. The estimated total economic cost attributed to lost output among working-age individuals due to ill health is approximately £150 billion annually<sup>20</sup>.

Implementing interventions informed by geroscience to improve the ratio of the healthy to unhealthy population could result in significant economic advantages such as decreasing NHS and social care costs and stimulating inward investment into the UK. Recent research indicates that even a one-year increase in healthy life expectancy among the UK's working population could generate an annual boost of around £60 billion in aggregate lifetime earnings<sup>21</sup>. In the United States, a study evaluating the economic value of geroscience-informed interventions has shown that targeting ageing offers potentially larger economic gains than focussing on individual diseases. A slowdown in ageing that increases life expectancy by one year would be worth \$38 trillion, and by 10 years, \$367 trillion<sup>22</sup>.

There are currently several initiatives making steps in the right direction. For example, the BBSRC 'healthy ageing across the life course' programme funds research aimed at improving our understanding of maintenance of health throughout life and the UK Research and Innovation cross-council 'healthy ageing' challenge is investing up to £98 million to support the delivery of market innovation within the healthy ageing domain. The successor to that programme is the UKRI 'securing better health, ageing and wellbeing' theme. This theme will enable working across disciplines, leveraging new and existing investment and activity to address challenges around ageing, multiple long-term conditions, mental health and health inequalities<sup>23</sup>.

With over 180 established biotech entities worldwide focussed specifically on developing new geroscience-based drugs and an estimated global market value of \$64 billion, geroscience is a worthwhile investment (Box 2)<sup>24</sup>. The UK holds a prominent position in academic geroscience research, ranking as the fourth largest producer of research papers in this field. Additionally, the country is competitive commercially, with 7% of all geroscience companies based in the UK. Several of these show promising potential to introduce new drugs to clinic in the medium term<sup>25</sup>. This comparative advantage not only fosters domestic growth but also opens up significant export opportunities to vast markets, leveraging the predictability of ageing trends in large parts of the world.

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18. Chief Medical Officer. Chief Medical Officer's Annual Report. 2023. *Health in an ageing society*. <https://assets.publishing.service.gov.uk/media/65562ff2d03a8d000d07faa6/chief-medical-officers-annual-report-2023-web-accessible.pdf> (accessed 15 January 2024).

19. The Health Foundation. *What we know about the UK's working-age health challenge*. <https://www.health.org.uk/publications/long-reads/what-we-know-about-the-uk-s-working-age-health-challenge> (accessed 20 January 2024).

20. Oxera. 2023. The economic cost of ill-health among the working-age population. [https://www.oxera.com/wp-content/uploads/2023/01/230116\\_The-Economic-Cost-of-Ill-Health-Among-the-Working-Age-Population.pdf](https://www.oxera.com/wp-content/uploads/2023/01/230116_The-Economic-Cost-of-Ill-Health-Among-the-Working-Age-Population.pdf) (accessed 2 February 2024).

21. Royal Society of Arts. *Building a healthy economy*. <https://www.thersa.org/blog/2022/04/building-a-healthy-economy> (accessed 11 February 2024).

22. Scott AJ *et al.* 2021 The economic value of targeting aging. *Nature Aging* **1**. (doi: 10.1030/s43587).

23. UKRI. *Securing better health, ageing and wellbeing*. <https://www.ukri.org/what-we-do/browse-our-areas-of-investment-and-support/securing-better-health-ageing-and-well-being/>. (accessed 2 March 2024).

24. Chief Medical Officer. Chief Medical Officer's Annual Report. 2023. *Health in an ageing society*. <https://assets.publishing.service.gov.uk/media/65562ff2d03a8d000d07faa6/chief-medical-officers-annual-report-2023-web-accessible.pdf> (accessed 15 January 2024).

25. Chief Medical Officer. Chief Medical Officer's Annual Report. 2023. *Health in an ageing society*. <https://assets.publishing.service.gov.uk/media/65562ff2d03a8d000d07faa6/chief-medical-officers-annual-report-2023-web-accessible.pdf> (accessed 15 January 2024).



Despite this, the UK's spending on ageing research represents a tiny fraction of that of comparable economies. Moreover, a significant portion of research funding purportedly dedicated to ageing is, in reality, directed towards single disease investigations, misrepresenting the true focus on ageing biology by funders. The total cost of ageing amounts to approximately £63 billion a year, of which some researchers estimate we spend only 0.049% on research seeking to improve ageing – by comparison,

it was suggested that 10% of spending on heart disease goes into research<sup>26</sup>. Until a spending shift happens, we will continue to focus our efforts on addressing the consequences, rather than the root causes, of ageing ill-health. A 10-fold increase to 0.49%, or approximately £300 million a year, should allow for some progress to be made. This is equivalent in proportion to what is happening in the United States where the NIA is funded to \$4.4 billion annually<sup>27</sup>.

## BOX 2

### Emerging therapeutic targets for treating the diseases of ageing.

- Rapamycin (a selective inhibitor of the mechanistic target of rapamycin (mTOR)) was the first therapeutic shown to extend lifespan in mammals and enhance responses to flu vaccination in older people. Biotech company Tornado Therapeutics is developing a portfolio of next generation rapalogs (rapamycin derivatives) that includes multiple compounds that are potent TORC1-specific inhibitors. These compounds are predicted to have superior safety and/or efficacy to currently first generation rapalogs.
- Biotech companies are repurposing drugs and creating new molecules targeting the cellular senescence hallmark, with clinical trials in humans showing positive health outcomes. For example, the cancer drug Dasatinib is being repurposed in combination with Quercetin to induce cell death in senescent cells, and companies like Deciduous Therapeutics are using AI to identify novel molecules that can activate an immune surveillance mechanism to selectively remove senescent cells.
- The Biotech company Altos targets epigenetics hallmarks to decipher the pathways of cellular rejuvenation programming to safely rejuvenate cells to reverse ageing-related diseases and injuries.
- Longeveron is a clinical-stage biotechnology company acting on the cell exhaustion hallmark to develop cellular therapies for ageing-related conditions. Their lead investigational product is derived from culture-expanded medicinal signalling cells that are sourced from bone marrow of young healthy donors.
- Many companies are using AI to identify new target molecules and pathways. This is exemplified by the work of BioAge, which targets the altered intercellular communication hallmark using a combination of longitudinal data sources, multi-level omics and AI to map pathways for adverse ageing phenotypes. The company recently identified a drug target which is in phase 2 trials for obesity and other metabolic diseases.
- A number of biotech startups are exploring plasma and its derivatives to tackle ageing-related disease. The company Elevian, for example, is working on therapies to elevate the activity of growth differentiation factor 11 (GDF11) – a protein in blood plasma that it believes decreases with age in mice.
- SENISCA, an award-winning biotech from the University of Exeter, focusses on the process of cellular ageing via the development of RNA senotherapeutics which specifically target the causative molecular mechanisms that drive senescence. The company is leveraging its founders' discovery of a novel hallmark of ageing, dysregulated RNA splicing, to develop novel senotherapeutics.

26. Professor Lynne Cox, University of Oxford.

27. National Institute on Aging. *Budget and paylines update: 2023 coming into focus*. <https://www.nia.nih.gov/research/blog/2023/01/budget-and-pay-lines-update-2023-coming-focus> (accessed 21 February 2024).



### AREA OF CONSIDERATION 3: AN AGILE AND INNOVATIVE REGULATORY FRAMEWORK

The current drug development model is not fit for understanding, treating and preventing ageing-related diseases. In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) is responsible for approving clinical trials involving medicinal products and for granting authorisation before drugs can be marketed. For a drug to be authorised for use, it must demonstrate efficacy against a particular condition (or indication) in clinical trials in humans. It is important to note that regulators currently do not recognise ageing itself as a disease indication. Once authorised, drugs can only be prescribed for their designated indication(s), which is not a model suited to testing the ability of single drugs to target underlying ageing processes and multimorbidity<sup>28</sup>. Trials must also explicitly outline the outcome that is being measured, referred to as the endpoint. For instance, a cancer drug trial might have a five-year survival endpoint. Geroscience trials aiming to demonstrate a healthspan extension endpoint would be both lengthy and prohibitively expensive<sup>29</sup>. A compounding challenge is that, until recently, older people were often excluded from clinical trials, and it remains rare to see patients with multimorbidity included<sup>30</sup>. Consequently, most drugs are tested on the healthy, working-age population. This is challenging given that older and multimorbid patients are the target population for gerotherapeutics.

Without regulatory approval, insurers are reluctant to cover the costs of gerotherapeutic treatments, which disincentivises pharmaceutical companies from pursuing geroscience-guided approaches<sup>31</sup>. In light of this, it is imperative to conduct well-designed geroscience clinical trials aimed at demonstrating that repurposing existing or developing novel gerotherapeutics can significantly delay a cluster of ageing-related diseases, thereby translating the UK's strengths in ageing research into tangible clinical benefits. Regulatory flexibility is particularly required on two fronts: including the most appropriate target population and measuring key clinically relevant endpoints.

#### Target population for geroscience clinical trials

The regulatory environment should ensure that older people and people with multimorbidity are included more frequently in clinical trials. There are certain challenges associated with their participation, many of which are related to retention concerns and clinical requirements associated with the 'one drug-one disease' approach. However, there are no sufficient ethical or scientific justifications strong enough for excluding this patient group, especially when the tested drugs are intended for their use. Regulatory interventions from other disciplines or countries could inspire innovative approaches by the UK regulator. These include regulatory interventions for trials of drugs for paediatric use<sup>32</sup>, and the design of geroscience trials like the Targeting Ageing with Metformin (TAME) trial in the United States (Box 3). Given that the life expectancy and healthspan of the wealthiest currently exceeds that of the poorest, it is also imperative that geroscience clinical trials ensure representation from a diversity of social, economic and ethnic backgrounds.

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28. House of Lords Science and Technology Select Committee. 2021. *Ageing: science, technology and health living*. <https://committees.parliament.uk/publications/4286/documents/79148/default/> (accessed 2 February 2024).

29. Chief Medical Officer. Chief Medical Officer's Annual Report. 2023. *Health in an ageing society*. <https://assets.publishing.service.gov.uk/media/65562ff2d03a8d000d07faa6/chief-medical-officers-annual-report-2023-web-accessible.pdf> (accessed 15 January 2024).

30. House of Lords Science and Technology Select Committee. 2021. *Ageing: science, technology and health living*. <https://committees.parliament.uk/publications/4286/documents/79148/default/> (accessed 17 February 2024).

31. Kulkarni S *et al.* 2022 Geroscience-guided repurposing of FDA-approved drugs to target aging: a proposed process and prioritization. *Aging Cell* **21**. (doi: 10.1111/acel.13596).

32. Chief Medical Officer. Chief Medical Officer's Annual Report. 2023. *Health in an ageing society*. <https://assets.publishing.service.gov.uk/media/65562ff2d03a8d000d07faa6/chief-medical-officers-annual-report-2023-web-accessible.pdf> (accessed 15 January 2024).

## Endpoints for geroscience clinical trials

The regulatory environment should support geroscience clinical trials focussed on outcomes capable of capturing the wide-ranging effects of tested gerotherapeutics and their ability to prevent and treat multimorbidity. Given financial and time constraints making lifespan extension an unrealistic endpoint, most studies rely on composite outcomes to monitor the development of diseases<sup>33</sup>. Some studies attempt to gain approval for trials that target multiple conditions relying on novel endpoints, such as the time taken to develop a second ageing-related disease after the onset of the first<sup>34</sup>.

A promising option is to use ageing biomarkers (which are measurable features capable of predicting the rate of ageing)<sup>35</sup> to stratify the individual risk, develop prevention strategies and monitor treatment response<sup>36</sup>. For example, epigenetic biomarkers leveraging DNA methylation, known as ‘epigenetic clocks’, have been developed to indicate the pace of individual ageing, and a trial has already demonstrated the susceptibility of this biomarker to modification through drugs targeting ageing processes<sup>37</sup>. Using biomarkers instead of clinical outcomes could also substantially reduce the size and the duration of clinical trials<sup>38</sup>. While the search for ageing biomarkers has intensified in recent years, currently there is no consensus on how biomarkers of ageing should be validated before their translation to the clinic<sup>39</sup>.

### BOX 3

#### Targeting Ageing with Metformin (TAME).

The Food and Drug Administration-approved TAME trial marks an important milestone in medical research. Unlike traditional clinical trials focussed on single diseases, TAME aims to extend longevity and delay the onset of various ageing-related diseases, such as stroke, cancer and dementia, as well as decline in mobility and cognitive function. Using metformin, a commonly prescribed and very safe medication for type 2 diabetes, the trial seeks to validate the hypothesis that targeting one or several ageing hallmark(s) may impact health outcomes and influence the development and severity of chronic diseases.

With a duration of six years and 3,000 participants aged 65 to 80, TAME will be conducted across 14 research institutes in the United States. By focussing on mixed endpoints like the time to the onset of major ageing-related conditions or death, this study not only holds promises for healthier ageing but also suggests potential shifts in medical approaches, encouraging further investment in geroscience research and potentially influencing future drug development strategies and regulatory approvals. If successful, the trial could also provide proof of concept that ageing can be treated as a standalone medical condition.

33. Rolland Y *et al.* 2023 Challenges in developing geroscience trials. *Nature Communications* **14**. (doi: 10.1038/s41467-023-39786-7).

34. House of Lords Science and Technology Select Committee. 2021. *Ageing: science, technology and health living*. <https://committees.parliament.uk/publications/4286/documents/79148/default/> (accessed 17 February 2024).

35. Hartmann A *et al.* 2021 Ranking biomarkers of aging by citation profiling and effort scoring. *Frontiers in genetics* **12**. (doi: doi.org/10.3389/fgene.2021.686320).

36. Rolland Y *et al.* 2023 Challenges in developing geroscience trials. *Nature Communications* **14**. (doi: 10.1038/s41467-023-39786-7).

37. Chief Medical Officer. Chief Medical Officer's Annual Report. 2023. *Health in an ageing society*. <https://assets.publishing.service.gov.uk/media/65562ff2d03a8d000d07faa6/chief-medical-officers-annual-report-2023-web-accessible.pdf> (accessed 15 January 2024).

38. Cummings S, Kritchevsky S. 2022 Endpoints for geroscience clinical trials: health outcomes, biomarkers, and biologic age. *GeroScience* **44**. (doi: 10.1007/s11357-022-00671-8).

39. Moqri M *et al.* 2024 Validation of biomarkers of aging. *Nature Medicine* **30**. (doi: 10.1038/s41591-023-02784-9).

## AREA OF CONSIDERATION 4:

### A SOCIETAL SHIFT ACROSS MULTIPLE POLICY DOMAINS

Scientific advances aimed at optimising the health and independence of older adults will deliver public benefits only alongside a societal shift across multiple policy domains. The following bullet points briefly outline key areas requiring government intervention. While not exhaustive, they highlight the imperative of a coordinated approach to foster a positive societal shift in our approach to ageing.

#### Regional health policy to address health inequalities

- Allocating resources to regions with higher concentrations of older adults to ensure equitable access to healthcare services.
- Implementing targeted health promotion initiatives aimed at older populations, addressing prevalent health issues like chronic diseases and mental health concerns.

#### NHS operational policy

- Developing strategies to incentivise medical professionals to specialise in geriatric medicine.
- Adapting NHS resource allocation to accommodate demographic shifts, particularly in rural and coastal areas experiencing significant migration of older residents.

#### Planning policy to support mobility needs

- Integrating ageing-friendly infrastructure and transportation options into urban planning initiatives to facilitate mobility and independence for older individuals.
- Ensuring accessibility standards are met in public spaces, housing and transportation networks to accommodate the needs of an ageing population.

#### Employment and pensions policy

- Implementing measures to encourage older adults to remain active in the workforce, such as flexible working arrangements and training programs tailored to their needs.
- Reviewing pension policies to ensure adequacy and sustainability, considering factors like increasing life expectancy and changing employment patterns.

#### Innovation enterprise and trade policy

- Fostering innovation in products and services targeted at older consumers, encouraging entrepreneurship and investment in sectors such as assistive technology and healthcare.
- Supporting businesses in accessing international markets by facilitating trade agreements and providing export incentives, thereby maximising the growth and export potential of ageing-related industries.

# Conclusion

The UK's demographic landscape is rapidly shifting as its ageing population continues to grow at an unprecedented rate. While life expectancy has been increasing, healthy life expectancy has not increased at the same rate. As a consequence, ageing-related morbidity is dramatically expanding. This situation is particularly concerning in regions where high levels of deprivation and an older demographic converge, further exacerbating health issues. Caring for an ageing population brings several challenges for the social and healthcare system, including increasing pressures on the NHS and various sectors of the economy.

By attempting to address the root causes, rather than the consequences, of ageing ill-health, geroscience offers promising potential to optimise the health and independence of older adults. Implementing geroscience-informed interventions in the UK would offer benefits such as compressing illness towards the end of life, reducing strain on the NHS, boosting workforce productivity, attracting investment and addressing inequalities in healthy life expectancy.

This policy briefing highlights the need for coordinated action across four key areas to unlock the full potential of geroscience. Firstly, it calls for a collaborative and interdisciplinary research and innovation ecosystem focussed on the ageing process as a whole. Secondly, it stresses the need for ambitious and sustained funding. Thirdly, it underlines the importance of an adaptable regulatory framework that prioritises inclusion of older people with multimorbidity into clinical trials and enables the use of mixed trial endpoints. Finally, it emphasises alignment across different policy domains to translate scientific advancements into tangible benefits for the UK population.

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