

**NUFFIELD
COUNCIL ON
BIOETHICS**

Background paper on the future of ageing

**Exploring the ethical implications of the emerging role of
science and technology in helping people live well in old
age**

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Terms of Reference for the working group

1. To explore the ethical implications of the emerging role of biomedical science and technology in helping people live as well as possible in old age, with a particular focus on:
 - a. the way that ageing is conceptualised, and the implications for policy and research;
 - b. The aims of biomedical research and technological innovation in seeking to respond to the opportunities, challenges and implications of the age shift in the population, and the way that these aims, and any alternatives to them, are prioritised;
 - c. the role of diverse older people themselves in driving the research / innovation agenda, and in identifying the needs to which research seeks to respond;
 - d. ethical challenges specific to the conduct of research in this field, including recruitment criteria, selection of meaningful endpoints, and measures of effectiveness;
 - e. issues of equity, within diverse parts of the older population, and between generations;
 - f. issues of personal, familial, professional, societal, and state responsibility; and
 - g. the implications of all these factors for both research and wider social policy.
2. To draft a report and make recommendations relating to policy and practice

I Introduction

The 'grand challenge' of meeting the needs of an ageing population

1. In most countries, people are living longer and healthier lives than ever, but are still spending a significant number of years in poor health towards the end of their lives.¹ Increases in lifespan have not been matched by equivalent increases in healthy lifespan ('healthspan'), and there is a growing period of disability and ill health at the end of life.² Common conditions experienced by older people include cardiovascular disease, cancer, dementia, arthritis, and general frailty, all of which can have a major impact on people's quality of life.
2. Given that the number of older people is predicted to increase markedly over the next 25 years, addressing age-related health conditions and enabling people to 'live well' in old age is widely regarded as a pressing societal, as well as individual, challenge. 'Healthy ageing' is a priority policy area both for the World Health Organization, which has launched a 'Decade of Health Ageing' from 2020-2030,³ and for governments around the globe. The UK's 'Ageing Society Grand Challenge' (one of four themes in the Government's 2017 *Industrial strategy*⁴) aims to "harness the power of innovation to help meet the needs of an ageing society" with a "mission [to] ensure that people can enjoy at least five extra healthy, independent years of life by 2035, while narrowing the gap between the experience of the richest and poorest."⁵ It is suggested that "success in this mission will help people remain independent for longer, continue to participate through work and within their communities, and stay connected to others to counter the epidemic of loneliness." Targets for research funding as part of this Grand Challenge include:
 - *From data to early diagnosis and precision medicine* – combining research data and evidence from the NHS to create new products and services that diagnose disease earlier, including using artificial intelligence approaches to early diagnosis;

¹ Office for National Statistics (2021) Health state life expectancies, UK: 2017 to 2019; James SL, Abate D, Abate KH *et al.* (2018) Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017 *The Lancet* **392**(10159): 1789-858.

² The Royal Society and the Academy of Medical Sciences (2020) *Healthy ageing: conference report*, available at: <https://royalsociety.org/-/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>, at page 4; Office for National Statistics (2021) Health state life expectancies, UK: 2017 to 2019.

³ WHO (2020) *Decade of healthy ageing 2020-2030*, available at: <https://www.who.int/ageing/decade-of-healthy-ageing>. The initiative was formally adopted by the UN General Assembly (14 December 2020) *The decade of healthy ageing: a new UN-wide initiative*, available at: <https://www.who.int/news/item/14-12-2020-decade-of-healthy-ageing-a-new-un-wide-initiative>.

⁴ HM Government (2017) *Industrial strategy: building a Britain fit for the future*, available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/730048/industrial-strategy-white-paper-web-ready-a4-version.pdf.

⁵ Department for Business, Energy & Industrial Strategy (2019) *The Grand Challenge missions*, available at: <https://www.gov.uk/government/publications/industrial-strategy-the-grand-challenges/missions>.

- *Healthy ageing* – developing products and services that help people to remain independent, productive, and active into older age, from new care technologies and housing models to innovative saving apps for retirement; and
 - *Leading edge healthcare* – accelerating the development of new medicines and treatments, including digital health products and technologies.⁶
3. While technology – from developments in biomedical science to digital and other innovation – clearly has a part to play in the ‘grand challenge’ of meeting the needs of an ageing society, commentators have highlighted the dangers of focusing only on such technological innovations. Age UK, for example, has argued that technology is not an interventional ‘silver bullet’: “investment is needed in public health, housing, communities, transport, and welfare, alongside investment in the NHS and social care to help older people live well for longer. Technology can support strategies but should not be seen as a solution in itself.”⁷
 4. Similar points have been made by others, with many organisations working in the sector signing up to *A consensus on healthy ageing* launched in 2019 by Public Health England and the Centre for Ageing Better.⁸ This consensus statement highlights the importance of:
 1. Putting prevention first and ensuring timely access to services and support when needed.
 2. Removing barriers and creating more opportunities for older adults to contribute to society.
 3. Ensuring good homes and communities to help people remain healthy, active and independent in later life.
 4. Narrowing inequalities in years of life lived in good health between richer and poorer people, between different population groups and between different areas of the country – focussing efforts on those most at risk.
 5. Challenging ageist and negative language, culture and practices wherever they occur, in both policy and practice.

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⁶ Department for Business, Energy & Industrial Strategy (2019) *The Grand Challenges*, available at: <https://www.gov.uk/government/publications/industrial-strategy-the-grand-challenges/industrial-strategy-the-grand-challenges>; Gov.uk (2019) *Industrial Strategy Challenge Fund: for research and innovation*, available at: <https://www.gov.uk/government/collections/industrial-strategy-challenge-fund-joint-research-and-innovation#healthy-ageing>; and UKRI (2020) *Ageing society*, available at: <https://www.ukri.org/our-work/delivering-economic-impact/industrial-strategy-challenge-fund/ageing-society/>.

⁷ Age UK (2019) *Written evidence to House of Lords Select Committee on Science and Technology - Ageing: science, technology, and healthy living*, at page 1.

⁸ Public Health England and the Centre for Ageing Better (2019) *A consensus on healthy ageing*, available at: <https://www.gov.uk/government/publications/healthy-ageing-consensus-statement/a-consensus-on-healthy-ageing>.

The latest *State of Ageing* report by the Centre for Ageing Better similarly highlights the central role of housing, work and community connection, as well as good health, in supporting people in living well in later life.⁹

The role of the Nuffield Council

5. In 2018, the Nuffield Council published a Briefing Note, *The search for a treatment for ageing*, that explored the role of geroscience in researching interventions that delay biological ageing and reduce the risk of age-related conditions.¹⁰ Geroscience, also called biogerontology, is a field of research exploring the biological processes that underlie ageing. Researchers working in this field believe that intervening in these processes could be a more efficient way of increasing healthspan than tackling each condition individually. Some commentators describe the aims of geroscience as developing a ‘cure’ for ageing, with claims that the human life-span could be dramatically extended.¹¹ Others focus on the scope for better understanding of the biological processes underlying ageing to lead to a healthier and more independent old age, and a compressed period of physical decline before death – while recognising that a phase of declining health leading up to death will remain inevitable for most people.¹² This expansion of healthspan might, or might not, also be accompanied by a further extended lifespan.¹³
6. The Council’s Briefing Note (on which this background note draws) summarises a number of practical and ethical challenges for geroscience researchers – and notes that some in the field are calling for an ethical framework specifically for geroscience research.¹⁴ It is certainly the case that the conduct of research in this field raises a number of ethical and regulatory challenges (see paragraph 49). However, rather than considering these in isolation, it is suggested that they should be explored in the context of the much broader question as to the role that geroscience, along with other forms of technological innovation, can ethically play in helping people ‘age well’. This approach has at least two significant implications for the Council’s inquiry:

⁹ The Centre for Ageing Better (2020) *State of ageing in 2020*, available at: <https://www.ageing-better.org.uk/summary-state-ageing-2020>.

¹⁰ Nuffield Council on Bioethics (2018) *The search for a treatment for ageing*, available at: <https://www.nuffieldbioethics.org/assets/pdfs/The-search-for-a-treatment-for-ageing.pdf>.

¹¹ See, for example, de Grey A (2007) *Ending aging: the rejuvenation breakthroughs that could reverse human aging in our lifetime* (St. Martin’s Publishing Group). See also: the discussion of the potential future role of ‘longevity medicine’ in: Zhavoronkov A, Bischof E, and Lee K-F (2021) Artificial intelligence in longevity medicine *Nature Aging* **1(1)**: 5-7.

¹² Cosco TD, Stephan BCM, and Brayne C (2013) Deathless models of aging and the importance of acknowledging the dying process *CMAJ : Canadian Medical Association journal = journal de l’Association medicale canadienne* **185(9)**: 751-2.

¹³ See, for example, Dame Linda Partridge’s presentation to the February 2020 [Healthy ageing](#) conference hosted by the Royal Society and the Academy of Medical Sciences: “We want to keep people healthier for longer before they die. The aim is not to make people live longer – that’s happening already – the problem is this period of ill health at the end of life”, at page 6.

¹⁴ See also: the calls for a ‘framework’ for this area of research in the panel discussion at the end of the two day conference on Healthy Ageing, hosted by the Royal Society and Academy of Medical Sciences in February 2020: Royal Society and Academy of Medical Sciences (2020) *Healthy ageing*, available at: <https://royalsociety.org/-/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>.

- First, it brings within the project's remit a much broader spectrum of technological innovations that seek to enhance quality of life in older age. This would include innovations in preventative healthcare, from wearable biosensor technologies that can monitor aspects of people's health in real time,¹⁵ to developments that facilitate earlier diagnosis and effective intervention in conditions that particularly affect health in older age, such as the scope for greater use of biomarkers as a diagnostic tool in the initial stages of various forms of dementia.¹⁶ It would also include the role of technology in supporting independent living and quality of life in older age. This could be in the form of assistive technologies (developed either for direct use by older people themselves, or primarily to support carers), and also through facilitating subjective well-being in other ways that are not necessarily associated with biological losses: for example digital technologies that enable close contact with distant family members, which is of value regardless of any impaired mobility.
 - Second, and most importantly, it sets scrutiny of the role of geroscience and innovations in age-related technologies firmly in a wider policy context. Just as many factors other than the provision of health services influence people's health throughout their lives, many wider social and economic factors, including intergenerational considerations, will affect how people are able to live well in old age. Crucial questions also arise as to what 'living well' involves (including the likely diversity of answers) – an issue to which we return in the next section. Any consideration of the possible benefits (and pitfalls) of biomedical and technological developments must at the same time be mindful of this larger picture.
7. There is considerable current interest in the policy implications of the UK Government's Healthy Ageing Grand Challenge and in parallel developments in research and policy – including in the form of a substantial inquiry by the House of Lords Select Committee on Science and Technology on *Ageing: science, technology and healthy living*. This Committee published its final report in January 2021, calling robustly for much more concerted action by Government if the aims of the Grand Challenge are to be met:

“Improving healthy life expectancy is a vital and worthy ambition, but there has been a lack of leadership and planning for the Ageing Society Grand Challenge mission, resulting in minimal progress. The Government should act now to revitalise the mission and utilise

¹⁵ Kim J, Campbell AS, de Ávila BE *et al.* (2019) Wearable biosensors for healthcare monitoring *Nature Biotechnology* **37**: 389-404.

¹⁶ See, for example, Rice L, and Bisdas S (2017) The diagnostic value of FDG and amyloid PET in Alzheimer's disease-A systematic review *Eur J Radiol* **94**(16-24); and Voytyuk I, De Strooper B, and Chávez-Gutiérrez L (2018) Modulation of γ - and β -secretases as early prevention against Alzheimer's disease *Biological psychiatry* **83**(4): 320-7. An earlier Nuffield Council report also highlighted the challenges of 'early' (as opposed to 'timely') diagnosis at a point when effective interventions are not yet available: Nuffield Council on Bioethics (2009) *Dementia: ethical issues*, available at: <https://www.nuffieldbioethics.org/assets/pdfs/Dementia-report-for-web.pdf>.

*opportunities in science, technology and public health to ensure it is achieved.*¹⁷

In line with the Nuffield Council's remit to explore the ethical questions raised by developments in science and technology, this project will draw on existing work by the House of Lords and others, as valuable context to its own specific focus on the ethical issues raised.

¹⁷ Science and Technology Committee (Lords) (2021) *Ageing: science, technology and healthy living*, available at: <https://committees.parliament.uk/work/1/ageing-science-technology-and-healthy-living/>.

II Framing the question: what is the challenge being addressed?

Societal, individual, and public health perspectives

8. A crucial question in exploring the role that biomedical and technological innovation could play in helping people age well is how we frame the 'problem' that these technologies are seeking to help 'solve'. Statistics and projections on demographic ageing that illustrate the increasing proportion of the population represented by older people tend to present the challenge as one of managing a 'burden': how to meet the costs of supporting ever-greater numbers of older people in the context of a declining number of people in the workforce (conceptualised as the 'dependency ratio' between numbers of older people and those of working age).¹⁸ In turn, this tends to encourage an emphasis on technology as a 'cheap substitute' solution to inadequate numbers of working-age people willing and able to provide care, coupled with financial constraints on the public purse.¹⁹
9. A very different way, however, of framing the question is that of asking how to make the most appropriate use of technology to support wellbeing in old age – including recognising when technology may not be the best solution, or can only offer part of the solution. The use of robots in care, for example, highlights these different approaches very vividly. There are likely to be a number of tasks that robots, and other forms of assistive devices, can perform as well, or potentially better than a human being, and over time they may prove to be a cost-effective as well as acceptable means of assistance. However, what they are unlikely to be able to provide is genuine emotional connection with another human being – and where that connection is an important element of what is being provided, the robot will not be a meaningful substitute. COVID-19, in particular, has shone a bright light on the fundamental importance of human contact and compassion in meaningful care – and on the many challenges faced by an underfunded and undervalued social care system.²⁰
10. James Banks, in his keynote speech to the Health Ageing conference in February 2020, similarly argued for the need to distinguish between societal and individual perspectives: "To understand ageing, population and the individual perspectives must each be considered separately. The issues societies have with ageing arise from the population having a higher proportion of older people. These are distinct from the issues individuals have with ageing, which relate to how to live their lives

¹⁸ See, for example, Eurostat (2020) *Population structure and ageing*, available at:

https://ec.europa.eu/eurostat/statistics-explained/index.php/Population_structure_and_ageing.

¹⁹ See, for example, some of the discussion in BBC Future (5 November 2020) *The technologies that could transform ageing*, available at: <https://www.bbc.com/future/article/20201104-the-technologies-that-could-transform-ageing>.

²⁰ See, for example, Clarke R (2020) Care in crisis, *The Lancet* **396(10262)**: 1550-1; and The BMJ Opinion blog (6 November 2020) *We all have a right to dignity in public health emergencies*, available at: <https://blogs.bmj.com/bmj/2020/11/06/we-all-have-a-right-to-dignity-in-public-health-emergencies/>.

given that they will be living much longer than previous generations.”²¹ As Banks implies, it is also very important to look beyond the need for care (a common focus, particularly in response to the demographic changes) to include many other factors that are a part of living a life we value as we age – critically including older people’s ability to continue to contribute to society through means such as paid work, volunteering, family support and knowledge-sharing. Moreover, this recognition that older people continue to contribute in important ways to the economy itself undermines traditional conceptions of ‘dependency ratios’ between those in work and those needing support: it has been argued that a more accurate (and positive) way of monitoring those ratios is between those in need of active support, and those able to contribute, regardless of age.²²

11. A further relevant distinction raised in a recent scoping review of conceptual approaches to technology for healthy ageing is that of the extent to which technology contributes to a society that supports older people better (the public health angle), as opposed to questions of whether particular technological developments are acceptable, or of value, to individual older members of society.²³ The public health angle identified here, capturing the extent to which wider society as a whole works for older people, brings a quite different societal perspective from that concerned with the affordability and feasibility of providing support for increasing numbers of older people.
12. Significant ‘big picture’ ethical questions arise in connection with all three of these approaches to the possible role of science and technology in responding to the needs of an ageing population (i.e. quite apart from ethical challenges specific to particular technologies). These include:
 - Whose voices are being heard in framing both research questions and related social policy? To what extent is the research agenda open to influence by older people, able to bring their own perspectives and experience on what is good, and what is more challenging, in their lives? In other words, who is deciding what it is to ‘live well’ in old age, and hence the ultimate target for innovators and researchers? And how can we account for ways in which these perspectives may change, as those who are currently middle-aged or younger reach their old age?²⁴
 - What consideration is being given to the structural inequities that affect health throughout people’s lives, and are associated with significant differences in life expectancy and quality of life in older age?²⁵ For example,

²¹ The Royal Society and the Academy of Medical Sciences (2020) *Healthy ageing: conference report*, available at: <https://royalsociety.org/-/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>, at page 8.

²² Dixon A (2020) *The age of ageing better?* (London: Green Tree), at pages 21-2.

²³ Kim H, Kelly S, Lafortune L *et al.* (2020) A scoping review of the conceptual differentiation of technology for healthy aging *The Gerontologist*: gnaa051.

²⁴ See, for example, the discussion in Dixon A (2020) *The age of ageing better?* (London: Green Tree), at pages 18-9.

²⁵ Bennett HQ, Kingston A, Spiers G *et al.* (2021) Healthy ageing for all? Comparisons of socioeconomic inequalities in health expectancies over two decades in the Cognitive Function and Ageing Studies I and II *International Journal of Epidemiology*; Centre for Ageing Better

to what extent do ageing research agendas reflect the needs of those who are already disadvantaged, rather than those who have always been well placed to exert influence or have their interests considered? And to what extent do those research agendas respond to the great diversity within the older population? – with respect to factors including ethnicity, culture, gender, sexual diversity, class, financial security, mental and physical health, and mental capacity?

- To what extent does public policy see older people as part of society, rather than as a separate, often marginalised group with its own needs ('integration vs segregation')? For example, to what extent are access issues considered in mainstream housing or town planning policy, as opposed to being seen as 'niche' issues for specialist developments?²⁶ How much are older people's perspectives included in digital developments?
- How can the many competing interests in this field be fairly managed? The financial and workforce challenges alluded to above are an essential part of the policy context, despite the importance of avoiding framing the primary issue in terms of societal burden. The question of how benefits, burdens and costs should best be distributed at a societal level between younger and older generations potentially sets the interests of those generations in competition – while also recognising both the crucial way in which generations are inter-connected through families, and the particular vulnerability of older people who no longer have any close family to support them. Similarly, competing interests may arise in individual terms too: the needs and interests of older people and their families may not always coincide, particularly where substantial caring is involved.

What do we mean by old age?

13. A further aspect of clarifying the issues that the project will address is that of terminology, and in identifying that part of the population with which we are concerned. 'Ageing' takes place throughout the life course, from birth onwards. However, as a result both of increasing life expectancies and wider social changes, our perception of our life course, and especially of what constitutes later life, is changing. Today, the phase of 'old age' is, on average, not only much longer than in previous centuries (potentially reaching from, for example, state

(2020) *The State of Ageing: Coronavirus 'to set people in mid-life on a path to poverty and ill-health' with inequalities widening*, available at: <https://www.ageing-better.org.uk/news/state-ageing-coronavirus-set-people-mid-life-path-poverty-and-ill-health-inequalities-widening>; and Rimmer A (2020) Covid-19: tackling health inequalities is more urgent than ever, says new alliance *BMJ* **371**.

²⁶ See, for example, The Guardian (5 June 2019) *Why aren't new homes fully accessible for older and disabled people?*, available at: <https://www.theguardian.com/society/2019/jun/05/new-homes-accessible-older-disabled-people>; and Marston HR, Shore L and White PJ (2020) How does a (smart) age-friendly ecosystem look in a post-pandemic society? *International Journal of Environmental Research and Public Health* **17(21)**: 8276. Striking parallels arise with some of the arguments around appropriate public health/public policy responses to COVID-19 – as in the [Barrington Declaration](#) with its focus on 'protecting the vulnerable' (in practice by isolating them from society) so that the rest of the population could get on with their ordinary lives.

pension age to over 100 years), but it also usually covers a very heterogeneous period of life. Moreover, many people leave paid employment well before reaching state pension age, whether voluntarily, or as a result of ill-health or unemployment, thus entering a state of retirement, strongly associated with old age, in their 50s and early 60s.

14. In the earlier and middle part of this extended period of later life, some people may live very active, healthy and engaged lives – and may be better off in various ways than other parts of the population. This will not, however, be true for certain groups of people in their 60s and 70s (or younger, particularly for those living with certain conditions or disabilities) – often as a result of the health and social inequalities touched on above.²⁷ The mid-80s seem to constitute a critical point in the life course frequently associated with declining health and increasing impairment and dependency. Gerontological research has developed various theoretical models to describe these differences, such as the distinction between the third age (the so-called “young old”) and the fourth age (the “old old”).²⁸ However, these models show a tendency to create new stereotypes, and therefore need further critical examination and discussion.²⁹
15. In her review of the philosophical aspects of old age as expressed in literature, Helen Small endorses the suggestion that old age should be defined as “the later years of a long life, when there is an inevitable and irreversible deterioration in the organism as a consequence of its age”.³⁰ This approach avoids categorisation by chronological age alone but focuses instead on the impact that the biological ageing process has on our bodies – and through this on all aspects of our lives. It is potentially much narrower than including all those over state pension age (even as that shifts upwards), but is sensitive to the fact that ‘old age’ in this sense will be reached at different times by different people (and indeed potentially well before state pension age, for example for those with certain learning disabilities, as well as those forced early out of paid work through chronic ill health). Nevertheless, it still covers a very heterogeneous group – not only with respect to chronological age, but also with respect to the extent of the impact of that physical decline on people’s day-to-day lives; disabilities and chronic conditions that are unconnected with age; mental capacity (including learning disabilities irrespective of age, as well as the impacts of dementia); ethnicity; gender; education; and socio-economic situation.

²⁷ For an account of some of the challenges of attempting a clear definition of ‘old’ or ‘older’ age by reference to chronological age, see M Lovatt (25 January 2021) *What do we mean by ‘self-identified’ older adult*, available at: <https://reimaginingthefutureinolderage.stir.ac.uk/2021/01/25/what-do-we-mean-by-self-identified-older-adult/>.

²⁸ Gilleard, C and Higgs, P (2014) “Third and fourth ages” in *The Wiley Blackwell encyclopedia of health, illness, behavior, and society*, at pages 2442-8.

²⁹ Wahl H-W, and Ehni H-J (2020) Advanced old age as a developmental dilemma: an in-depth comparison of established fourth age conceptualizations *Journal of Aging Studies* **55**: 100896.

³⁰ Small H (2007) *The long life* (Oxford: OUP), at page 3.

What is it to 'live well' in old age?

16. This is clearly an enormous question – and one with which the working group will need to engage from early on in the project (potentially through engagement activities as well as literature review³¹), recognising that it is a philosophical and spiritual question, as well as a social and anthropological one. The WHO's 2015 [World report on ageing and health](#) emphasises that older age involves many features, both positive and negative, in addition to physical deterioration:

"Beyond these biological losses, older age frequently involves other significant changes. These include shifts in roles and social positions, and the need to deal with the loss of close relationships. In response, older adults tend to select fewer and more meaningful goals and activities, optimize their existing abilities through practice and the use of new technologies, and compensate for the losses of some abilities by finding other ways to accomplish tasks. Goals, motivational priorities and preferences also appear to change, with some suggesting that older age may even be the stimulus for a shift from materialistic perspectives to more transcendent ones. Although some of these changes may be driven by adaptations to loss, others reflect ongoing psychological development in older age that may be associated with 'the development of new roles, viewpoints and many interrelated social contexts'. These psychosocial changes may explain why in many settings older age can be a period of heightened subjective well-being."³²

17. The importance of recognising that "healthy ageing, for policy purposes, is more about functioning and wellbeing than disease" was reiterated in the Royal Society *Healthy Ageing* conference proceedings.³³ It is similarly important to recognise that good health itself is not the only factor in a 'good' old age – not least for those who have always had to contend with chronic conditions and disabilities. This has led to concerns that a focus on the language of 'successful' or 'healthy' ageing may itself be problematic, not least because of the implication that those who do not 'succeed' in ageing well are personally responsible, or have 'failed'.³⁴ Critics of this terminology have drawn on the work of Amartya Sen, Martha Nussbaum and others to promote instead a 'capabilities approach'³⁵ to ageing:

³¹ Longitudinal studies such as the English Longitudinal Study of Ageing will be particularly important in seeking to understand the impact of many different factors on people's experiences of ageing, available at: <https://www.elsa-project.ac.uk/>. See also: The Hastings Center (2018) *What makes a good life in late life? Citizenship and justice in aging societies*, available at: <https://www.thehastingscenter.org/publications-resources/special-reports-2/what-makes-a-good-life-in-late-life-citizenship-and-justice-in-aging-societies/> for a series of linked articles on this issue in the Hastings Center Report.

³² WHO (2015) *World report on ageing and health*, available at: <https://apps.who.int/iris/handle/10665/186463>, at page 25.

³³ The Royal Society and the Academy of Medical Sciences (2020) *Healthy ageing: conference report*, available at: <https://royalsociety.org/-/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>, at page 10.

³⁴ See, for example, Pfaller L, and Schweda M (2019) Excluded from the good life? An ethical approach to conceptions of active ageing *2019* 7: 10.

³⁵ Stanford Encyclopedia of Philosophy (2016) *The capability approach*, available at: <https://plato.stanford.edu/entries/capability-approach/>.

“The capability approach provides an environmentally, socially and ethically oriented framework for research, policy, and intervention in ageing and health by taking into account the influence of the social and material environment and the diverse values of older people. Sen’s theoretical focus is on people’s ‘capabilities’ or the extent to which they are able to function in ways that they value. The capability approach recognises differences in social standing and material circumstances that influence these capabilities, and accounts for social and cultural diversity in values. Sen’s capability approach provides a theoretical framework for research leading to social rather than individual change.”³⁶

18. Other commentators have used the language of ‘health assets’ in opposition to a focus on the physical ‘deficits’ that increasing age may bring, with assets defined both as an individual’s internal or external strengths, and as any accessible resources that enhance their ability to optimise health. A systematic review published in 2017 of such assets found that higher scores of self-rated health, psychological well-being and life satisfaction were associated with better health in older age. Important support mechanisms included social networks, contact with family and friends, and engagement in leisure and social activities, while education and financial resources represented key economic health assets for older adults.³⁷ Both the capability approach and the idea of ‘health assets’ highlight the crucial importance of recognising the diversity of what it is that older people value in their lives, how this may be affected by culture and religion (not least by attitudes to the shape of one’s life course and beliefs about the meaning of death), and how cultural expectations of ageing are changing across time.
19. In initial scoping this project has used the language of ‘living well’ in old age with the aim of encompassing these wider social, as well as individual, factors influencing our experiences and perspectives as we age. It will be helpful to discuss within the working group whether this is the most appropriate terminology to capture this breadth of concern.

Recognising the relevance of ageism

20. The description of ageing by WHO, and its inclusion of highly positive elements of old age, brings to the fore the key relevance for this project of ageism and ageist assumptions – not only in terms of how older individuals themselves may experience discrimination, but critically in the way that the challenges of ageing are characterised and policy implemented.³⁸ The way that the issues associated with ageing are defined (in an often dehumanising manner) in turn inevitably

³⁶ International Network for Critical Gerontology (8 December 2016) *A capabilities approach to healthy ageing: Towards more inclusive identities for older people*, available at: <https://criticalgerontology.com/capabilities-approach-healthy-ageing/>.

³⁷ Hornby-Turner YC, Peel NM, and Hubbard RE (2017) Health assets in older age: a systematic review *BMJ open* **7(5)**: e013226. See also: Bloomberg M, Dugravot A, Dumurgier J *et al.* (2021) Sex differences and the role of education in cognitive ageing: analysis of two UK-based prospective cohort studies *The Lancet Public Health* **6(2)**: e106-e115; and NIACE (2011) *Older people, learning and education: what do we know?*, available at: <http://stephenmcnair.uk/wp-content/uploads/2015/07/2011-Older-Learners-Key-Facts.pdf>.

³⁸ See, for example, Harper S (2020) The COVID-19 pandemic and older adults: institutionalised ageism or pragmatic policy? *Journal of Population Ageing* **13(4)**: 419-25.

influences what solutions are then sought. The '#valuable not vulnerable' campaign being run by Greater Manchester Ageing Hub, for example, provides many illustrations of how both language and images matter in developing services that see possibility in people, and support their strengths, rather than treating them as 'broken'.³⁹ The value to society of the enormous contribution made by older people in voluntary activity – both through formal volunteering and through unpaid family childcare⁴⁰ – has been highlighted in the first COVID 'lockdown' in the UK, when regulations prevented such activity. Reflecting the importance of imagery in combatting assumptions about old age, the Centre for Ageing Better has recently run a competition to design age-positive icons representing ageing and older people, in order to replace the familiar stereotypes of sticks and hunched backs.⁴¹ The winning entry shows a dancing couple using a stick as a dancing cane.⁴²

21. Such social stereotypes and cultural imagery shape how we perceive, experience, and evaluate ageing, and how we behave towards older people. However, it is crucial to acknowledge that ageism comes in many different shapes: from outright negative, deficit-oriented and degrading stereotypes, to the paternalistic 'compassionate ageism' implicit in much of the public discussion of COVID-19. Overly positive models of 'successful', 'active', 'productive' and 'healthy' ageing can also be problematic: in recognising and valuing active old age, it is important to recognise the risks of devaluing the lives of those who are no longer able to be active in these ways. There is thus a potential tension between the emphasis on increasing healthspan, thereby reducing ill-health and its impacts for as long as possible in older age – and in recognising and maximising the scope for high quality of life in a final period of declining health before death. The value placed on the first should not implicitly undermine the importance of the second. Rather than replace one biased stereotype by another, the aim should be to develop a more differentiated understanding of ageing and old age, including both its positive and negative aspects, and being sensitive to social diversity.

³⁹ See: <https://twitter.com/GMAgeingHub> and https://twitter.com/hashtag/valuablenotvulnerable?src=hashtag_click.

⁴⁰ Estimated to be worth £7.7bn in 2016/2017: Iparraguirre J (2017) *The economic contribution of older people in the United Kingdom*: https://www.ageuk.org.uk/globalassets/age-uk/documents/reports-and-publications/reports-and-briefings/active-communities/the_economic_contribution_of_older_people_update_to_2017.pdf.

⁴¹ The Centre for Ageing Better (2020) *Age-positive icons competition launched*, available at: <https://www.ageing-better.org.uk/news/age-proud-icons>.

⁴² The Centre for Ageing Better (2020) *Dancing couple design wins age-positive icon competition*, available at: <https://www.ageing-better.org.uk/news/dancing-couple-design-wins-age-positive-icon-competition>.

III The role of science and technology: a brief overview

Framing considerations

22. This section provides a brief overview of recent developments, first in assistive technologies and other innovations, and then in the field of geroscience. In exploring the opportunities and benefits these biomedical and technological developments may offer, it will also be important to be alert to their capacity to shape and change both individual and societal views of old age: for example in perceived associations and distinctions between ageing and disease, and in the associated medicalisation of ageing and old age.
23. While these considerations may appear to arise most strongly in connection with geroscience research, related issues arise in the context of products aimed at the older market, whether or not they are specifically badged as 'assistive technologies'. For example, Joseph Coughlin, the director of the MitAgeLab, has robustly argued that a common failure by developers to engage meaningfully with older people as consumers means that many products purportedly designed to meet older people's needs are not taken up:

"There's an expectations gap between what older consumers want from a product and what most of these products deliver, and it's no frivolous matter. If you need a hearing aid but no one can make one that you think is worth buying, that will have serious ramifications for your quality of life, and may lead to social isolation and physical danger down the road... Why do products built for older people so often seem so uninspiring—big, beige, and boring?"⁴³

Coughlin goes on to argue that this disjunction between the development of products and the needs / wishes of older people is not simply a consumer concern: rather, that the way in which products 'for' older people are presented serves to reinforce and perpetuate negative and passive perceptions of old age and older people.

Assistive technologies and other innovations

24. There has been longstanding interest in the role that technology can play in supporting older people to live independently, from the use of self-operated pendant alarm systems that enable people to call for help (for example after a fall), to a wide range of practical devices that make daily living tasks, from cooking to putting on socks, easier or safer to perform.⁴⁴ In addition to such daily living and safety functions, technological devices may be used to support exercise and rehabilitation; provide cognitive support (such as medication reminders and other kinds of memory joggers); and enhance mobility. More recent developments in

⁴³ MIT Technology Review (21 August 2019) "Old age" is made up - and this concept is hurting everyone, available at: <https://www.technologyreview.com/2019/08/21/75537/old-age-is-made-up-and-this-concept-is-hurting-everyone/>.

⁴⁴ For a 2014 review of 'technology today' and likely future developments, see: Centre for Policy on Ageing (2014) *The potential impact of new technologies*, available at: <http://www.cpa.org.uk/information/reviews/CPA-Rapid-Review-The-potential-impact-of-new-technology.pdf>.

AI, alongside transformations in digital connectivity, have offered scope for many of these technologies to play a much more fundamental and potentially intrusive role in people's lives, facilitating remote interactions of many kinds, real-time monitoring for health and safety purposes, and scope for robotic assistance. The evidence base for the effectiveness of such developments in supporting people in living independently for longer, however, is still relatively weak.⁴⁵ Moreover, concerns have been expressed about the temptation to use novel technologies inappropriately in cases where much more low-tech and preventative solutions may not only be cheaper, but may also promote longer-term independence.⁴⁶

25. Issues of access, affordability and confidence in the use of non-specialist digital technologies (for example video-calling with its scope to keep older people connected with more distant family members) have been highlighted by organisations such as AgeUK, and are likely to remain limiting factors for many older people.⁴⁷ Other ethical issues arising in connection with more specialist technologies include the extent to which they meet the needs and preferences of older people themselves, as opposed to those of paid and family carers (while recognising the separate and legitimate interests of the latter); the associated risks of other forms of support being de-prioritised; and questions of control and privacy. More generally, any system that involves 'black box' machine learning or the application of algorithms raises concerns about the starting assumptions that underpin how such devices 'learn', and associated risks of reinforcing existing stereotypes or failing to account for important aspects of people's lives.⁴⁸

Increasingly 'smart' homes

26. 'Smart home' technologies potentially bring together many of the technologies described above, involving a diverse range of functions, from well-established household safety devices, to much more sophisticated (and potentially intrusive) systems that combine safety and (tele)health monitoring. The latter could involve a complex range of sensors, for example monitoring a person's bed and chair occupancy to pick up unexpected patterns of movement or inactivity, food consumption, and pulse and heart rate. A 'live feed' of data then links into automated decision-making – for example triggering a home visit by a GP or the delivery of a prescription.⁴⁹ Other features of smart homes may include various forms of cognitive assistance and prompts, for example medication reminders,

⁴⁵ Howard R, Gathercole R, Bradley R *et al.* (2021) The effectiveness and cost-effectiveness of assistive technology and telecare for independent living in dementia: a randomised controlled trial *Age and Ageing*.

⁴⁶ See, for example, Peter Gore's explanation of the LifeCurve, and the importance of prevention and rehabilitation, before moving to technologies that compensate for lost abilities, available at: <https://www.youtube.com/watch?v=iem0uhgksbg>.

⁴⁷ Age UK (2018) *Digital inclusion evidence review*, available at: https://www.ageuk.org.uk/globalassets/age-uk/documents/reports-and-publications/age_uk_digital_inclusion_evidence_review_2018.pdf.

⁴⁸ For a helpful overview, see: UK Parliament POST (2021) *AI and healthcare*, available at: <https://post.parliament.uk/research-briefings/post-pn-0637/>.

⁴⁹ Royal Society and Academy of Medical Sciences (2020) *Healthy ageing*, available at: <https://royalsociety.org/-/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>, at page 39.

lost key locators, and assistance with video and phone calls.⁵⁰ A rather different approach, however, has been taken in the design of a 'multi-generational kitchen' that aims both to provide a space four generations want to spend time in – and meet the needs of all four generations in terms of functionality.⁵¹

Developments in the use of robots

27. The prospect of robots providing acceptable forms of assistance for older people has been the target of considerable interest for some time among both researchers and policymakers.⁵² Innovation in this field has focused on a broad range of potential uses and emphases, many of which overlap with the functions provided by smart homes, noted above, but presented in a more anthropomorphic form:

- **Supporting physical needs and acting as a 'robot butler'** – for example by bringing objects on request; providing reminders; supporting mobility (for example by helping the user get up from their chair); regularly patrolling/clearing the floor in order to prevent or detect falls; and making emergency calls. Examples include the Hobbit⁵³ and Care-o-Bot robots.⁵⁴ The latest version of the Care-o-Bot (Care-o-Bot 4) has been designed to engage with the users at an emotional level, and claims to "create empathy".⁵⁵ Unlike the Hobbit, it is considered to be focused primarily on the user rather than on carers, for example through being able to distinguish the user from other people and give priority to their requests.⁵⁶
- **Supporting social needs** – from providing access to entertainment (e.g. reading the newspaper out loud, playing games and making phone calls) to acting as a virtual pet. Examples include the Japanese Paro⁵⁷ and

⁵⁰ See, for example, Demiris G and Hensel BK (2008) Technologies for an aging society: a systematic review of "smart home" applications *Methods of Information in Medicine* **47(1)**: 33-40; and Cook DJ, Crandall AS, Thomas BL *et al.* (2013) CASAS: A smart home in a box *Computer (Long Beach Calif)* **46(7)**: 62-9.

⁵¹ National Innovation Centre Ageing (5 February 2021) *Ready, steady cook... the multigenerational 4GenKi*, available at: <https://www.uknica.co.uk/ready-steady-cook-the-multigenerational-4genki/>.

⁵² For useful overviews, see: Ethikrat, Deutscher (2020) *Robotics for good care*: <https://www.ethikrat.org/fileadmin/Publikationen/Stellungnahmen/englisch/opinion-robotics-for-good-care.pdf>); and Fosch-Villaronga E, Lutz C, and Tamò-Larrieux A (2020) Gathering expert opinions for social robots' ethical, legal, and societal concerns: findings from four international workshops *International Journal of Social Robotics* **12(2)**: 441-58.

⁵³ HOBBIT (2020) *HOBBIT - the mutual care robot*, available at: <http://hobbit.acin.tuwien.ac.at/>; Fischinger D, Einramhof P, Papoutsakis K *et al.* (2016) Hobbit, a care robot supporting independent living at home: first prototype and lessons learned *Robotics and Autonomous Systems* **75**: 60-78

⁵⁴ Fraunhofer IPA (2020) *Care-O-bot 4*, available at: <https://www.care-o-bot.de/en/care-o-bot-4.html>.

⁵⁵ Kittmann R, Fröhlich T, Schäfer J *et al.* (2015) Let me introduce myself: I am Care-O-bot 4, a gentleman robot, in *Mensch und Computer 2015 – Proceedings* (Berlin: De Gruyter Oldenbourg).

⁵⁶ Sorell T and Draper H (2014) Robot carers, ethics, and older people *Ethics and Information Technology* **16**: 183-95.

⁵⁷ PARO (2014) *PARO therapeutic robot*, available at: <http://www.parorobots.com/index.asp>.

PaPeRo⁵⁸ robots. Paro, a fur-covered robot that looks like a seal, is designed as a social companion without any assisting functionality, and is programmed to exhibit a range of animal-like behaviours, such as responding to being petted. Studies with care home residents suggest that Paro can be calming and help improve loneliness,⁵⁹ although it has been emphasised that this should not mean it can be regarded as a full substitute for animal, or indeed human, companionship.⁶⁰ PaPeRo, by contrast, is a social assistive robot and its primary function is that of communicating with and entertaining users. PaPeRo can hear and recognise people's voices, using voice recognition to give answers based on the words it hears. Its responses are designed to mimic human behaviour through, for example, turning towards the user as they approach, and nodding when they talk.⁶¹

- **Providing help with cognitive impairment** – for example using speech to remind users of appointments, or the need to have a drink; initiating video calls; and providing a range of cognitive exercises. An example is CompanionAble, a collaborative research project funded by the European Union's 7th Framework Programme, which aimed to combine intelligent home systems and robotics.⁶² In trials, CompanionAble has been found to be valued and useful – although the highest scores were given by carers rather than users themselves.⁶³
- **Telepresence systems** – systems that aim to support independent living by facilitating remote communications between the user and third parties, integrating information and communication technologies on to a robotic platform. The GiraffPlus system, for example, uses a network of sensors to monitor both activity around the house and the user's physiological data such as blood pressure, and shares this information with family members, carers and health professionals. It can also facilitate virtual visits through a Skype-like interface. A small trial with potential users in their own homes found that, while considering the trial

⁵⁸ Robot Center (2020) *PaPeRo Robot NEC*, available at: <https://www.robotcenter.co.uk/products/papero-robot-nec>. See also: Geva N, Uzefovsky F, and Levy-Tzedek S (2020) Touching the social robot PARO reduces pain perception and salivary oxytocin levels *Sci Rep* **10**(1): 9814, where it is suggested that Paro has a role in pain relief, in similar ways to the impact of touch with humans or pets.

⁵⁹ Misselhorn C, Pompe U and Stapleton M (2013) Ethical considerations regarding the use of social robots in the fourth age *GeroPsych: The Journal of Gerontopsychology and Geriatric Psychiatry* **26**(2): 121-33.

⁶⁰ Sorell T and Draper H (2014) Robot carers, ethics, and older people *Ethics and Information Technology* **16**: 183-95.

⁶¹ It is claimed that this makes communication with PaPeRo "almost like talking with a family member or friend": NEC Corporation (2020) *Shin Ishiguro*, available at: https://www.nec.com/en/global/innovators/s_ishiguro/01.html.

⁶² European Commission (2009) *Companion robots will improve elderly people's quality of life in smart homes*, available at: <https://cordis.europa.eu/article/id/113110-companion-robots-will-improve-elderly-peoples-quality-of-life-in-smart-homes/pl>.

⁶³ Schroeter C, Mueller S, Volkhardt M *et al.* (2013). Realization and user evaluation of a companion robot for people with mild cognitive impairments. In 2013 IEEE International Conference on Robotics and Automation, pp. 1153-9.

a positive experience, some participants were worried about “surveillance by unknown people”.⁶⁴

The role of geroscience: intervening in the hallmarks of ageing

28. The field of geroscience research has identified a number of ‘hallmarks of ageing’: linked factors that contribute to biological ageing in different organisms, and which may potentially provide avenues for drug-based interventions to promote healthy ageing in humans.⁶⁵ As noted in the Introduction, the underlying tenet of this field of research is that such interventions may be much more effective in postponing, ameliorating or even preventing the diseases associated with biological ageing, than tackling each of them separately as is currently the case.⁶⁶ Nine such hallmarks were identified and categorised in 2013.⁶⁷

- **Genomic instability:** The body constantly monitors physical or chemical damage to the genome and rapidly repairs lesions in DNA. However, these repair mechanisms can be imperfect and are compromised with advancing age, leading to mutations in the genome that in turn can lead to disease. Genetic damage, including mutations, thus accumulates with age. Deficiencies in DNA repair mechanisms have been found to cause accelerated ageing in mice and also underlie several human progeroid (premature ageing) syndromes. Research with transgenic mice suggests that the artificial enhancement of DNA repair mechanisms can delay ageing.
- **Telomere attrition:** Telomeres, the tips of chromosomes, are vital for cell division and repair. Telomere shortening can cause growing cells to stop dividing and to enter an inflammatory senescent state (see cell senescence below). Telomeres in many cells in the body become shorter with age. The enzyme telomerase lengthens telomeres and has been suggested as a target for anti-ageing interventions.⁶⁸
- **Epigenetic alterations:** Ageing is accompanied by epigenetic changes (the way in which genes and genomes undergo functional changes that are not associated with changes in DNA sequence).⁶⁹ Better understanding and

⁶⁴ Coradeschi S, Cesta A, Cortellessa G *et al.* (2014) GiraffPlus: a system for monitoring activities and physiological parameters and promoting social interaction for elderly *Human-Computer Systems Interaction: Backgrounds and Applications* **3**: 261-71.

⁶⁵ López-Otín C, Blasco MA, Partridge L *et al.* (2013) The hallmarks of aging *Cell* **153(6)**: 1194-217.

⁶⁶ Kaeberlein M, Rabinovitch PS, Martin GM (2015) Healthy aging: the ultimate preventative medicine *Science* **350(6265)**: 1191-3.

⁶⁷ López-Otín C, Blasco MA, Partridge L *et al.* (2013) The hallmarks of aging *Cell* **153(6)**: 1194-217. This overview section also draws on Kaeberlein M, Rabinovitch PS, Martin GM (2015) Healthy aging: the ultimate preventative medicine *Science* **350(6265)**: 1191-3; Royal Society and Academy of Medical Sciences (2020) *Healthy ageing*, available at: <https://royalsociety.org/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>; and Nuffield Council on Bioethics (2018) *The search for a treatment for ageing*, available at: <https://www.nuffieldbioethics.org/assets/pdfs/The-search-for-a-treatment-for-ageing.pdf>.

⁶⁸ See also: Chakravarti D, LaBella KA, and DePinho RA (2021) Telomeres: history, health, and hallmarks of aging *Cell* **184(2)**: 306-22.

⁶⁹ Nuffield Council on Bioethics (2 May 2019) *What’s the big deal about epigenetics?*, available at: <https://www.nuffieldbioethics.org/blog/whats-the-big-deal-about-epigenetics>.

manipulation of the epigenome is thought to hold promise for extending healthy lifespan.

- **Loss of proteostasis:** Proteostasis is the process that regulates proteins within the cell, removing any that are damaged, in order to maintain the health of both the cell and the organism itself. Autophagy – the way in which cells break down and recycle potentially toxic cellular material such as damaged proteins – plays an important part in proteostasis, but works much less effectively as we age. Unfolded, misfolded or aggregated proteins contribute to the development of some age-related conditions, such as Alzheimer’s disease, Parkinson’s disease and cataracts. Genetic modifications have been shown to improve proteostasis and delay ageing in mammals.⁷⁰
- **Deregulated nutrient-sensing:** The ability of cells in the body to respond to nutrients such as glucose or amino acid becomes less effective with age, predisposing people to develop diabetes and suffer tissue loss. Dietary restriction without malnutrition has been shown to prevent this decline and extend healthy lifespan in a range of animals. In humans, it has been shown to reduce risk factors for diabetes, cardiovascular disease, and cancer, and to slow biological ageing. Similar effects are seen when the activity of metabolic pathways that detect nutrients (such as the mTOR enzyme) are reduced by drugs or by gene mutations. This inhibition of the mTOR pathway in turn upregulates (enhances) protective pathways including the process of autophagy.⁷¹
- **Mitochondrial dysfunction:** Mitochondria are essential for cell function, encompassing all energy (ATP) producing processes within the cell. Damage to the mitochondria, and a failure to replace damaged mitochondria (by autophagy, termed mitophagy), is thought to be a major contributor to ageing and age-related diseases, although understanding the mechanisms remains a major challenge.
- **Cellular senescence:** Damaged cells either die or become senescent cells, which remain in the body and give out inflammatory chemicals. Studies in mice have shown that removing senescent cells delays age-related diseases and extends lifespan. Clinical trials are already underway in humans to determine the benefits of removing senescent cells or blocking their pro-ageing secretions.⁷²
- **Stem cell exhaustion:** Stem cell function decreases with age, reducing the ability to replace tissues. Injecting stem cells into animals has been shown to enhance the repair of age-related damage in organs such as the brain, and to increase lifespan.

⁷⁰ Zhang C, and Cuervo AM (2008) Restoration of chaperone-mediated autophagy in aging liver improves cellular maintenance and hepatic function *Nature medicine* **14**(9): 959-65.

⁷¹ See also: Martel J, Chang S-H, Wu C-Y *et al.* (2021) Recent advances in the field of caloric restriction mimetics and anti-aging molecules *Ageing Research Reviews* **66**: 101240.

⁷² See also: Prašnikar E, Borišek J, and Perdih A (2021) Senescent cells as promising targets to tackle age-related diseases *Ageing Research Reviews* **66**: 101251.

- **Altered intercellular communication:** A decline in cell signalling occurs with ageing, affecting the body's tissue, and leading to age-related diseases. Alterations in cell communication include 'inflammaging': a long-lasting low-level inflammation that develops with older age. Inflammaging is caused by several factors including increased obesity (fat tissue is pro-inflammatory) and a build up of pro-inflammatory senescent cells. Inflammaging can cause damage to tissues such as blood vessels, and contribute to the breakdown of tissues such as muscle and bone. Genetic, nutritional and pharmacological interventions are being explored for restoring defective intercellular communication. There is a further link to the gut microbiome: altering the gut microbiome can activate the innate immune system which causes inflammation and in turn affects other systems in the body.

Pharmacological interventions associated with the hallmarks

29. Pharmacological interventions being explored in connection with one or more of these hallmarks include:

- **Metformin:** an effective diabetes drug used for over 50 years, which works partly by enhancing the activity of an enzyme (AMP kinase) that is involved in the metabolic processes and nutrient sensing essential for health. The responsiveness of this enzyme has been found to decline with ageing, suggesting that metformin may have beneficial effects on the ageing process.⁷³ The Targeting Aging with Metformin (TAME) Trial plans to run a series of six-year clinical trials at 14 leading research institutions across the US, aiming to engage over 3,000 individuals between the ages of 65-79 once launched (currently at the fund-raising stage).⁷⁴ TAME aims to measure whether metformin can delay the onset of any one of a number of age-related conditions including stroke, heart failure, dementia and cancer – thus using a composite, rather than single disease, endpoint. It could potentially be very significant in that the pre-approval of the research protocol by the FDA thus allowed for the equivalent of "ageing" to be used as the primary target of interest (see paragraph 49).⁷⁵
- **Rapamycin:** a drug currently used to prevent organ transplant rejection, which inhibits the mTOR pathway involved in nutrient sensing, and has been found to extend lifespan in animals.⁷⁶ In anti-ageing studies the drug is used at concentrations much lower than those used in transplant patients, and the effects of rapamycin on frailty in people aged 60 and over with heart disease

⁷³ Salminen A and Kaamiranta K (2012) AMP-activated protein kinase (AMPK) controls the aging process via an integrated signaling network *Ageing Research Reviews* **11**: 230-41.

⁷⁴ AFAR (2020) *The TAME trial: Targeting the biology of aging. Ushering a new era of interventions*, available at: <https://www.afar.org/tame-trial>.

⁷⁵ Olshansky SJ (2019) The longevity dividend – a brief update *Public Policy & Aging Report* **29(4)**: 116-8.

⁷⁶ Ehninger D, Neff F, and Xie K (2014) Longevity, aging and rapamycin *Cell Mol Life Sci* **71(22)**: 4325-46.

have been explored in a small clinical trial in the US.⁷⁷ Given the potential side-effects associated with rapamycin, there is however considerable interest in developing similar safer drugs, known as ‘rapalogues’.⁷⁸ For example, a similar drug, RAD001, has been shown in a small trial to boost the immune system (in terms of vaccination responses) of healthy volunteers aged 65 years or over by inhibiting the TORC1 multiprotein complex within which mTOR functions.⁷⁹ Two other TORC1 inhibitors, sirolimus and RTB101, are being explored by the company resTORbio with a stage 1b/2a clinical trial in patients with Parkinson’s.⁸⁰

- **Resveratrol and other sirtuin activators:** A group of enzymes called sirtuins have a role in inhibiting cellular processes that affect ageing, including mitochondrial dysfunction and epigenetic alterations.⁸¹ Chemicals that increase sirtuins thus have potential as anti-ageing treatments. Resveratrol, for example, a naturally occurring chemical found in red wine, is known to activate sirtuins, in particular sirtuin 1 (SIRT1), and affect the ageing process in animals.⁸² The resveratrol anti-ageing supplement market is already big business globally, but only small amounts of resveratrol are absorbed into the body when administered in humans and the long-term health effects are unproven.⁸³ Synthetically-produced sirtuin activators show more promise, and some have been found to improve the health and extend the lifespan of mice.⁸⁴ The pharmaceutical industry has invested heavily in the development of synthetic sirtuin activators, but they have not yet been translated into drugs for human use.⁸⁵
- **Senolytics and senostatics:** Several research groups and companies are working on developing drugs, collectively called senolytics, that will selectively kill senescent cells. Others are working on blocking their pro-

⁷⁷ ClinicalTrials.gov (2016) Exercise and low-dose rapamycin in older adults with CAD: cardiac rehabilitation and rapamycin in elderly trial (CARE), available at: <https://clinicaltrials.gov/ct2/show/NCT01649960>.

⁷⁸ de Magalhães JP, Stevens M and Thornton D (2017) The business of anti-ageing science, *Trends in Biotechnology* **35**(11).

⁷⁹ Mannick JB, Del Giudice G, Lattanzi M *et al.* (2014) mTOR inhibition improves immune function in the elderly *Sci Transl Med* **6**(268): 268ra179.

⁸⁰ The Royal Society and the Academy of Medical Sciences (2020) *Healthy ageing: conference report*, available at: <https://royalsociety.org/-/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>, at page 13.

⁸¹ Bonkowski MS and Sinclair DA (2016) Slowing ageing by design: the rise of NAD⁺ and sirtuin-activating compounds *Nature Reviews Molecular Cell Biology* **17**: 679-90; and Li J, Bonkowski MS, Moniot S *et al.* (2017) A conserved NAD(+) binding pocket that regulates protein-protein interactions during aging *Science* **355**(6331): 1312-7.

⁸² Borra MT, Smith BC, and Denu JM (2005) Mechanism of human SIRT1 activation by resveratrol *J Biol Chem* **280**(17): 17187-95; and Kaeberlein M, McDonagh T, Heltweg B *et al.* (2005) Substrate-specific activation of sirtuins by resveratrol *J Biol Chem* **280**(17): 17038-45.

⁸³ Walle T (2011) Bioavailability of resveratrol *Annals of the New York Academy of Sciences* **1215**: 9-15.

⁸⁴ Minor RK, Baur JA, Gomes AP *et al.* (2011) SRT1720 improves survival and healthspan of obese mice *Sci Rep* **1**: 70; and Mitchell SJ, Martin-Montalvo A, Mercken EM *et al.* (2014) The SIRT1 activator SRT1720 extends lifespan and improves health of mice fed a standard diet *Cell Rep* **6**(5): 836-43.

⁸⁵ Nature News Blog (13 March 2013) *GSK absorbs controversial 'longevity' company*, available at: <http://blogs.nature.com/news/2013/03/gsk-absorbs-controversial-longevity-company.html>.

inflammatory activity with drugs called senostatics. Several senolytics have been found to extend lifespan and treat age-related diseases in mice, and the first trial in humans with idiopathic pulmonary fibrosis was reported in 2019.⁸⁶ Other examples described by the company UNITY Biotechnology at the *Health Ageing* conference in February 2020, for example, include a Phase 2 trial of the drug UBX0101 in patients with moderate-to-severe osteoarthritis of the knee, and non-clinical toxicology studies in the use of the drug UBX1325 for age-related eye conditions by targeting senescence in retinal cells.⁸⁷ Studies with senostatics have only taken place in mice so far, but have also been shown to treat age-related diseases such as osteoporosis.

- **Increasing telomerase activity:** The plant-based supplement TA-65, said to increase telomerase activity, is available to buy worldwide as an anti-ageing aid. Industry studies suggest TA-65 has beneficial effects on the health span of mice,⁸⁸ and the US-based manufacturer was reported in 2016 to be conducting clinical trials on healthy adults.⁸⁹ However, the reliability and independence of these studies have been questioned, and there are concerns that stimulating telomerase activity could increase the risk of cancer.⁹⁰ Another way of activating telomerase – gene therapy – has been shown to increase lifespan and healthspan in mice without causing cancer.⁹¹ At least one biotechnology company is hoping to develop telomerase gene therapy for use in humans.⁹²
- **Stem cell therapy:** The effects of stem cell therapy on age-related conditions such as frailty and Alzheimer's disease are being explored in

⁸⁶ Chang J, Wang Y, Shao L *et al.* (2016) Clearance of senescent cells by ABT263 rejuvenates aged hematopoietic stem cells in mice *Nature Medicine* **22(1)**: 78-83; Yosef R, Pilpel N, Tokarsky-Amiel R *et al.* (2016) Directed elimination of senescent cells by inhibition of BCL-W and BCL-XL *Nature Communications* **7**: 11190; ClinicalTrials.gov (2017) *Senescence in chronic kidney disease*, available at: <https://clinicaltrials.gov/ct2/show/NCT02848131>; Kirkland JL, Tchkonja T, Zhu Y *et al.* (2017) The clinical potential of senolytic drugs *J Am Geriatr Soc* **65(10)**: 2297-301; and Justice JN, Nambiar AM, Tchkonja T *et al.* (2019) Senolytics in idiopathic pulmonary fibrosis: results from a first-in-human, open-label, pilot study *EBioMedicine* **40**: 554-63.

⁸⁷ The Royal Society and the Academy of Medical Sciences (2020) *Healthy ageing: conference report*, available at: <https://royalsociety.org/-/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>, at page 12.

⁸⁸ Bernardes de Jesus B, Schneeberger K, Vera E *et al.* (2011) The telomerase activator TA-65 elongates short telomeres and increases health span of adult/old mice without increasing cancer incidence *Aging Cell* **10(4)**: 604-21; and Harley CB, Liu W, Blasco M *et al.* (2011) A natural product telomerase activator as part of a health maintenance program *Rejuvenation Res* **14(1)**: 45-56.

⁸⁹ ClinicalTrials.gov (2016) Effect of TA-65MD on healthy volunteers (TA-65MD) (entry not updated since 2016).

⁹⁰ Kaerberlein M, Rabinovitch PS, Martin GM (2015) Healthy aging: the ultimate preventative medicine *Science* **350(6265)**: 1191-3.

⁹¹ Bernardes de Jesus B, Vera E, Schneeberger K *et al.* (2012) Telomerase gene therapy in adult and old mice delays aging and increases longevity without increasing cancer *EMBO Molecular Medicine* **4(8)**: 691-704.

⁹² See: www.bioviva-science.com.

early-stage clinical trials in the US.⁹³ Unproven and unlicensed stem cell treatments, as well as blood plasma infusions, for a range of 'rejuvenation' purposes are also being offered by private clinics across the world.⁹⁴ There is a possible future role for gene therapy to edit muscle stem cells in older patients with sarcopenia (progressive loss of skeletal muscle).⁹⁵

- **The use of statins:** statins have been found to be very effective in improving the way that neutrophils (white blood cells that form an important part of the innate immune system) migrate through tissue to reach bacteria. This both increases their effectiveness in clearing bacteria from the body, and reduces the physical damage and associated inflammation caused to the tissues. In one study, use of high dose statins for seven days led to a sharp decrease in the numbers of older patients with pneumonia dying within the next six months.⁹⁶

30. Other important areas of research highlighted in the February 2020 *Health Ageing* conference include:

- Scope for modulating the gut microbiome, given its crucial role in digestion, appetite, mood, metabolism, control of the immune system, and people's response to most drugs and foods.⁹⁷ There is a correlation between higher levels of microbe diversity and lower levels of disease – and this diversity decreases as we age. In studies in fish, implanting the microbiome of a young fish into an old fish has been shown to increase lifespan and maintain motor function. The same has been shown in mice.
- Increasing understanding of the role that genetic factors play in ageing, and how these might translate into interventions. Research with mice that have been modified by knocking out genes associated with ageing, suggests that this can lead not only to longer, but also to healthier, lifespans – for example with increased immunity and motor function, and lower levels of osteoporosis. In humans, genetic analysis across populations has found an association between levels of natural mutations in the FOXO3a gene (a gene related to those studied in mice) and longer life.

⁹³ ClinicalTrials.gov (2017) Allogeneic human mesenchymal stem cells (hMSC) in patients with aging frailty via intravenous delivery (CRATUS); ClinicalTrials.gov (2017) Allogeneic human mesenchymal stem cell infusion versus placebo in patients with Alzheimer's disease.

⁹⁴ International Society for Stem Cell Research (28 August 2017) *ISSCR responds to FDA announcement of enforcement direction for stem cell treatments*, available at: <https://www.isscr.org/isscr-news/isscr-responds-to-fda-announcement-of-enforcement-direction-for-stem-cell-treatments>.

⁹⁵ The Royal Society and the Academy of Medical Sciences (2020) *Healthy ageing: conference report*, available at: <https://royalsociety.org/-/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>, at page 16.

⁹⁶ The Royal Society and the Academy of Medical Sciences (2020) *Healthy ageing: conference report*, available at: <https://royalsociety.org/-/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>, at page 14.

⁹⁷ Claesson MJ, Jeffery IB, Conde S *et al.* (2012) Gut microbiota composition correlates with diet and health in the elderly *Nature* **488(7410)**: 178-84.

- Improved understanding of the role that diet plays in biological ageing – data from the TwinsUK study, for example, show the importance of environmental factors such as diet, given that the gut microbiome is unique to individuals.⁹⁸ It was argued that the findings from the TwinsUK study show that genes are not as crucial to the ageing process as had previously been thought. Physical activity (see below) is another non-genetic factor that influences healthy ageing, with studies in older adults who have remained physically very active showing that many features considered to be “normal ageing” such as loss of muscle and bone, were not seen in these adults.⁹⁹

Non-pharmacological approaches

31. As the emphasis on diet and the gut microbiome noted above implies, increased understanding of the hallmarks of ageing, and their relevance to age-related conditions, has implications for non-pharmacological interventions, in particular with relation to exercise and to diet. ‘Social prescribing’ offers opportunities for such interventions to be promoted through the health service, as well as being part of wider public health policy.¹⁰⁰ On the other hand, concerns have been expressed that conceptualising these fundamental aspects of healthy life (along with others such as social connectedness) as something to be ‘prescribed’ by a health professional risks not only over-medicalising our lives, but also failing to address some of the underpinning causes of unhealthy lifestyles.¹⁰¹ While the role in healthy ageing of diet and exercise is touched upon in this section, other interventions that might be thought of as ‘non-pharmacological’, in particular supporting meaningful activity and social connection, are covered under the section on wider social policy picture (paragraphs 41–43).

Exercise

32. There is a large body of evidence showing that the health benefits of exercise are consistent with healthy life in old age. A theory has been proposed that there is a “dose” dependent effect of exercise on ageing healthily. In essence, the claim is that one must have the right balance of type, duration, intensity, and frequency of exercise. Too much long-term and extreme exercise is associated with an increased risk of cardiovascular disease and possibly impaired immune function. The nature of the effect on the immune system of lifetime exercise “dose”, and its relationship with ageing, is however contentious. Exercise may also offer an

⁹⁸ See, for example, Liu X, Liu X, Shi Q *et al.* (2021) Association of telomere length and telomerase methylation with n-3 fatty acids in preschool children with obesity *BMC Pediatrics* **21(1)**: 24.

⁹⁹ Pollock RD, Carter S, Velloso CP *et al.* (2015) An investigation into the relationship between age and physiological function in highly active older adults *J Physiol* **593**: 657-80.

¹⁰⁰ See, for example, NHS England (no date) *Social prescribing*, available at: <https://www.england.nhs.uk/personalisedcare/social-prescribing/>; and The King’s Fund (2020) *What is social prescribing?*, available at: <https://www.kingsfund.org.uk/publications/social-prescribing>.

¹⁰¹ See, for example, Dixon A (2020) *The age of ageing better?* (London: Green Tree), at page 243.

indirect anti-immunosenescence effect through, for example, better anti-viral control mediated by redox balance and less inflammatory activity.¹⁰²

33. Others have focused on the importance of preserving skeletal muscle mass and strength in older age. Improving muscle weakness through strength exercises has been linked to decrease risk of osteoarthritis of the knee, for example,¹⁰³ while exercise that increases muscle mass can improve the effects of sarcopenia.¹⁰⁴ Exercise can also help combat the deterioration of the balance system that occurs with age: including balance training in exercise programs for older individuals is recommended both to improve strength and reduce the risk of falls.¹⁰⁵ There have been calls for physical exercise guidelines to make more specific reference to the benefits of resistance exercise and higher-intensity aerobic training for older people, alongside encouraging older adults to undertake aerobic-based physical activity and household tasks.¹⁰⁶ In their latest guidance, the UK Department of Health¹⁰⁷ and the WHO¹⁰⁸ both recommend that exercise programs for older individuals should include three key components: aerobic exercise, strength and balance.
34. In order for older people to gain the optimal effects of exercise, there is increasing awareness of the need for more specific exercise programs to be developed. This need has been reinforced in the light of the impact of COVID-19 on older people (including the physical effects of self-isolation), with the Physiological Society and Centre for Ageing Better joining together to call for the development of tailored exercise or physical activity goals for older people.¹⁰⁹ In the US, for example, it is estimated that only 3.5–10% of older adults are meeting the recommended level of physical activity, with reported barriers to participating in regular exercise including a lack of confidence in one's ability to exercise, lack of interest, environmental factors such as lack of convenient access to resources, and poor health.¹¹⁰ There is also increased understanding of how lower education and

¹⁰² Turner JE (2016) Is immunosenescence influenced by our lifetime “dose” of exercise? *Biogerontology* **17**: 581-602.

¹⁰³ Dargent-Molina P, Favier F, Grandjean H *et al.* (1996) Fall-related factors and risk of hip fracture: the EPIDOS prospective study *Lancet* **348(9021)**: 145-9.

¹⁰⁴ Lopez P, Pinto RS, Radaelli R *et al.* (2018) Benefits of resistance training in physically frail elderly: a systematic review *Aging clinical and experimental research* **30(8)**: 889-99.

¹⁰⁵ Chodzko-Zajko WJ, Proctor D, Singh MF *et al.* (2009) Physical activity for older adults *Medicine & Science in Sports & Exercise* **41(7)**: 1510-30.

¹⁰⁶ Witard OC, McGlory C, Hamilton DL, and Phillips SM (2016) Growing older with health and vitality: a nexus of physical activity, exercise and nutrition *Biogerontology* **7**: 529-46.

¹⁰⁷ Department of Health and Social Care UK (2019) *Physical activity guidelines: UK Chief Medical Officers' report*, available at: <https://www.gov.uk/government/publications/physical-activity-guidelines-uk-chief-medical-officers-report>.

¹⁰⁸ World Health Organization (2010) *Global recommendations on physical activity for health*, available at: http://www.who.int/dietphysicalactivity/factsheet_recommendations/en/.

¹⁰⁹ The Physiological Society and Centre for Ageing Better (2020) *A national COVID-19 resilience programme: improving the health and wellbeing of older people during the pandemic*, available at: <https://www.physoc.org/policy/public-health-and-ageing/covid19resilience/>.

¹¹⁰ Dondzila CJ, Swartz AM, Keenan KG *et al.* (2014) Geospatial relationships between awareness and utilization of community exercise resources and physical activity levels in older adults *Journal of aging research* **2014**(; Addy CL, Wilson DK, Kirtland KA *et al.* (2004) Associations of perceived social and physical environmental supports with physical activity and walking

older age, independent of health factors, are contributing to lower participation in health and fitness exercise.¹¹¹ The development of community-based fitness resources including better availability of exercise options, a network of peers, guidance on exercise programmes and equipment, and health support resources can provide older individuals with the opportunity to engage in exercise and help minimise barriers to physical activity.¹¹² However, attention must also be given to addressing the personal factors that play a role in reduced uptake of exercise in older age such as lack of confidence and motivation.

Diet

35. Dietary restriction is probably the most studied intervention for delaying ageing with a majority of studies documenting significant increases in both lifespan and healthspan when dietary restriction is applied in laboratory models. Limited studies indicate important health benefits in people who practise dietary restriction. However, difficulties in translating this approach to the population level has elicited a search for alternative dietary modifications such as low-protein diets, as well as the pharmacological approaches described above.
36. Increased understanding of the role in ageing played by the microbiome, and the extent to which this is influenced by environmental factors (see paragraph 30) highlights the scope for a personalised, rather than generic, approach to nutrition in supporting healthy ageing. Innovative new apps are being developed to increase the application of personalised nutrition: for example, the Zoe app recently created by King's College London which makes it possible for individuals to record their food intake and their vital signs.¹¹³ Using AI technology this will indicate to the user which foods improve their long-term health, and which foods they should avoid.

The role of preventative approaches to healthy ageing

37. At policy level, considerable emphasis has been placed on the important role of preventative approaches to good health throughout the life-course in supporting better health in old age.¹¹⁴ A major report, *Transforming the future of ageing*, published in 2019 by Science Advice for Policy by European Academies (SAPEA – part of the European Commission's Scientific Advice Mechanism) sets out two key strategies to respond to “current and future opportunities and challenges posed by ageing”:

behavior *American journal of public health* **94(3)**: 440-3; and Tucker JM, Welk GJ, and Beyler NK (2011) Physical activity in US adults: compliance with the physical activity guidelines for Americans *American journal of preventive medicine* **40(4)**: 454-61.

¹¹¹ Rydwick E, Welmer AK, K  reholt I *et al.* (2013) Adherence to physical exercise recommendations in people over 65--the SNAC-Kungsholmen study *Eur J Public Health* **23(5)**: 799-804.

¹¹² Mathews AE, Laditka SB, Laditka JN *et al.* (2010) Older adults' perceived physical activity enablers and barriers: a multicultural perspective **18(2)**: 119.

¹¹³ Zoe (2021) *Understand how your body responds to food*, available at: <https://joinzoe.com/>

¹¹⁴ See, for example, Centre for Ageing Better (2021) *Preventing the preventable: healthy ageing webinars*, available at: <https://www.ageing-better.org.uk/events/preventing-preventable-webinar>.

- promoting healthy lifestyles over the life course, as well as detecting and modifying early and mid-life risk factors of impaired function and chronic diseases, in order to delay age-related disability; and
- providing more appropriate health and social care for the aged EU population by offering integrated and holistic care in all-age community and health care facilities.¹¹⁵

38. Drawing on evidence from longitudinal studies on physical and social exposures during gestation, childhood, adolescence, and adult life that may have long-term effects on the ageing process, the report concludes that:

- innovative health promotion and early and midlife preventive strategies may enable younger generations to enjoy healthy ageing in the future;
- lifelong health promotion and disease prevention play crucial roles;
- all-age communities enable older people to feel secure and to go about their daily life comfortably;
- favouring ageing in the home is a high priority;
- technology will both impact individual and population ageing and revolutionise healthcare delivery – but however technology advances, an adequate number of skilled health care professionals will be essential; and
- education will play a major role in transforming ageing into an opportunity for all.

39. As the SAPEA conclusions indicate, while preventative approaches to health are often understood in terms of individual responsibility, they are critically underpinned by action at societal level. Many ‘choices’ around diet and exercise, for example, are both facilitated and constrained by the environment in which we live,¹¹⁶ while the impact of other factors such as education, work opportunities, and the built environment are even more clearly determined by factors outside individual control. The relationship between many of these factors and mental health may be particularly important for life expectancy, with the lifespan of people with severe mental health disorders estimated as being on average 15-20 years shorter than that of the general population.¹¹⁷ The majority of these deaths are due to chronic health conditions such as cardiovascular disease, diabetes and respiratory disease, with suicide being another important cause of death in people with severe mental health disorders.¹¹⁸ Lifestyle and health risk behaviours such as obesity, poor diet, smoking and lack of exercise are associated with mental health disorders and can contribute to chronic health illnesses. However, there is also some evidence to suggest people with severe

¹¹⁵ SAPEA (2019) *Transforming the future of ageing*, available at: <https://www.sapea.info/wp-content/uploads/tfa-report.pdf>, at page 12. On 27 January 2021, the EU Commission published a Green Paper based on this report: see https://ec.europa.eu/info/files/green-paper-ageing-fostering-solidarity-and-responsibility-between-generations_en.

¹¹⁶ For a fuller discussion, see Nuffield Council on Bioethics (2007) *Public health: ethical issues*, available at: <https://www.nuffieldbioethics.org/publications/public-health>.

¹¹⁷ Chesney E, Goodwin GM, and Fazel S (2014) Risks of all-cause and suicide mortality in mental disorders: a meta-review *World psychiatry* **13**(2): 153-60.

¹¹⁸ Osborn DP, Levy G, Nazareth I *et al.* (2007) Relative risk of cardiovascular and cancer mortality in people with severe mental illness from the United Kingdom's General Practice Research Database *Archives of General Psychiatry* **64**: 242-9.

mental health illness are more likely to receive lower quality health and social care than the general population.¹¹⁹ It is also clear that people with mental illness are often at a disadvantage compared to the general population owing to unemployment, isolation and exclusion, as well as socioeconomic status, all of which are associated with poor health and premature mortality.

40. A common theme in both the SAPEA report and the UK's Ageing Society Grand Challenge (see paragraph 2) is the role that advances in healthcare technologies may play in preventative healthcare, through enabling earlier detection and modification of age-related conditions (assuming that earlier diagnosis can be accompanied by access to effective treatments). Examples of current developments in this field include:

- Developments in brain imaging to detect cognitive decline earlier – for example the use of diffusion tensor imaging (DTI) to detect changes associated with degeneration in white matter.¹²⁰ Diffusion kurtosis imaging (DKI) is being used in combination with machine learning to measure changes in brain structures that may serve as biomarkers of the transition from normal ageing to the earliest stages of neurodegenerative disease.¹²¹
- The use of machine learning algorithms to screen patients' electronic data in order to identify early warning signals and prompt earlier diagnosis.¹²² Machine learning might similarly be used to recognise changes in motor function, through assessing performance against simple drawing and writing tasks,¹²³ and in speech.¹²⁴
- Increased focus on biomarker identification to detect age-related diseases – for example the detection of elevated levels of Alzheimer's disease-related biomarker (A β 42) in saliva,¹²⁵ and DNA methylation of epigenetic biomarkers to identify individuals during the pre-diabetic stage, which increase the possibility of early prevention of type 2 diabetes.¹²⁶ Elevated levels of neurofilament light chain (NfL), which is

¹¹⁹ Lawrence D, and Kisely S (2010) Inequalities in healthcare provision for people with severe mental illness *J Psychopharmacol* **24(4 Suppl)**: 61-8.

¹²⁰ Li X-Y, Tang Z-C, Sun Y et al (2016) White matter degeneration in subjective cognitive decline: a diffusion tensor imaging study *Oncotarget* **7(34)**: 54405-14.

¹²¹ Benitez A, Jensen JH, Helpert JA et al. (2018) Modeling white matter tract integrity in aging with diffusional kurtosis imaging.

¹²² Myszczyńska MA, Ojames PN, Lacoste AMB et al. (2020) Applications of machine learning to diagnosis and treatment of neurodegenerative diseases, *Nature Reviews Neurology* **16**: 440–56.

¹²³ Kotsavasiloglou C, Kostikis N, Hristu-Varsakelis D, and Arnaoutoglou M (2017) Machine learning-based classification of simple drawing movements in Parkinson's disease, *Biomedical Signal Processing and Control* **31**: 174-80.

¹²⁴ Association of Computational Linguistics (2014) *Workshop on Computational Linguistics and Clinical Psychology from Linguistic Signal to Clinical Reality*, available at: <https://www.aclweb.org/anthology/W14-3200.pdf>.

¹²⁵ Lee M, Guo JP, Kennedy K et al. (2017) A method for diagnosing alzheimer's disease based on salivary amyloid- β protein 42 levels *J Alzheimers Dis* **55(3)**: 1175-82.

¹²⁶ Salameh Y, Bejaoui Y, and El Hajj N (2020) DNA Methylation Biomarkers in Aging and Age-Related Diseases *Frontiers in Genetics* **11(171)**: .

emerging as a promising biomarker for the progression of a number of neurological conditions, have also been associated more generally with mortality in old age (in centenarians and nonagenarians).¹²⁷

- The development of artificial ‘deep neural networks’ (DNNs) that can be trained to detect changes in albumin, alkaline phosphatase, urea and erythrocytes (identified as the five most important biomarkers for ageing) and thus predict the ‘biological age’ of individuals from a blood sample.¹²⁸

41. In addition to developments linked with the diagnosis and treatment of specific conditions, as described above, it has also been argued that AI techniques such as deep learning (DL) have an important role to play in a much more integrated approach to ‘longevity medicine’, with deep ageing clocks enabling clinicians to “be able to more precisely assess and monitor individual health risks and tailor appropriate interventions or changes in lifestyle for a specific person”.¹²⁹

The wider social policy picture

42. As noted in the introduction, the implications of the technological developments described in this section, and their scope to contribute to living well in old age, need to be explored in the context of the many other factors influencing both health and well-being. This would include:

- Implications for self-esteem and sense of place, associated with a changing role in society and the attitudes of others to us as we age. Choices around retirement, scope for continuing to work flexibly into older age where this is desired, and opportunities to contribute through voluntary work all affect meaning and purpose in life. Meaningful activity through volunteering has been identified as an important way in which to increase purpose in life, with additional associated significant health benefits.¹³⁰
- The role of meaningful relationships through family and community contact and the detrimental effect of social isolation and loneliness¹³¹ – highlighted in particular through the experiences of older people under the restrictions introduced to combat the COVID-19 pandemic. Research is needed to understand what social interventions are most effective in

¹²⁷ Kaeser SA, Lehallier B, Tigard M *et al.* (2021) A neuronal blood marker is associated with mortality in old age *Nature Aging* **1(2)**: 218-25.

¹²⁸ Putin E, Mamoshina P, Zhavoronkov A *et al.* ((2016) Deep biomarkers of human aging: application of deep neural networks to biomarker development, *Ageing (Albany NY)* **8(5)**: 1021-30.

¹²⁹ Zhavoronkov A, Bischof E, and Lee K-F (2021) Artificial intelligence in longevity medicine *Nature Aging* **1(1)**: 5-7.

¹³⁰ The Royal Society and the Academy of Medical Sciences (2020) *Healthy ageing: conference report*, available at: <https://royalsociety.org/-/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>, at page 42.

¹³¹ See for example Davies K, Maharani A, Chandola T *et al.* (2021) The longitudinal relationship between loneliness, social isolation, and frailty in older adults in England: a prospective analysis *The Lancet Healthy Longevity* **2(2)**: e70-e7.

addressing social connectedness, and why.¹³² This is particularly important given the scope for cultural diversity both in needs and in effective responses.

- The role of housing – not in the sense of ‘smart’ housing, but in minimally-decent housing that can be kept warm, and accessible housing that reduces risks of falls.¹³³
- Physical infrastructure in a person’s home region, such as accessible and regular public transport systems and local shops.¹³⁴
- The importance of an adequate income.¹³⁵
- Access to the digital infrastructure which is rapidly affecting how not only healthcare but many other services are provided and accessed.¹³⁶
- The provision of culturally and individually appropriate forms of social care and support, and the value placed on a trained and adequately rewarded social care workforce (a particular issue in the light of shortage of care-workers in the UK, and current reliance on workers from other countries).¹³⁷

43. The importance of these wider social, physical and environmental factors in enabling people to live well in old age raises significant questions for policymakers, not least in terms of the relative priority (and funding) to be given to technological approaches, given the inevitable opportunity costs of funding both research and policy development with limited budgets. The complex web of factors that influence wellbeing in later life also demonstrate the need for cross-

¹³² O’Rourke HM, Collins L, and Sidani S (2018) Interventions to address social connectedness and loneliness for older adults: a scoping review *BMC Geriatrics* **18**(1): 214.

¹³³ See, for example, Centre for Ageing Better (2020) *The need for healthy homes*, available at: <https://www.ageing-better.org.uk/blogs/need-healthy-homes>; and Government Office for Science (2015) *What developments in the built environment will support the adaptation and ‘future proofing’ of homes and local neighbourhoods so that people can age well in place over the life course, stay safe and maintain independent lives?*, available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/445583/gs-15-11-future-ageing-homes-neighbourhoods-er21.pdf.

¹³⁴ Government Office for Science (2015) *What developments in the built environment will support the adaptation and ‘future proofing’ of homes and local neighbourhoods so that people can age well in place over the life course, stay safe and maintain independent lives?*, available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/445583/gs-15-11-future-ageing-homes-neighbourhoods-er21.pdf. See also: the WHO Age friendly cities initiative: https://www.who.int/health-topics/urban-health/creating-age-friendly-cities-and-communities#tab=tab_1.

¹³⁵ See, for example, AGE Platform Europe (no date) *Adequate income & social inclusion*, available at: <https://www.age-platform.eu/policy-work/adequate-income-social-inclusion>; and Centre for Ageing Better (27 Jan 2021) *We need to tackle wealth inequalities to improve our nation’s health*, available at: <https://www.ageing-better.org.uk/blogs/we-need-tackle-wealth-inequalities-improve-our-nations-health>.

¹³⁶ See, for example, Good Things Foundation (no date) *Digital inclusion*, available at: <https://www.goodthingsfoundation.org/areas-of-work/digital-inclusion>.

¹³⁷ For a strong critique of the funding of social care in the UK, including the need for a better career structure and higher pay for social care workers, see: House of Lords Economic Affairs Committee (2019) *Social care funding: time to end a national scandal*: <https://publications.parliament.uk/pa/ld201719/ldselect/ldeconaf/392/392.pdf>.

departmental collaboration and co-operation at governmental level, incentives for which have tended to be lacking in the past.¹³⁸

¹³⁸ See, for example, The Royal Society and the Academy of Medical Sciences (2020) *Healthy ageing: conference report*, available at: <https://royalsociety.org/-/media/events/2020/02/tof-healthy-ageing/Healthy-Ageing-Conference-Report-2020.pdf>, at page 10.

IV Ethical issues to be explored

44. This background paper has aimed to provide an overview of some of the key areas of biomedical and technological development that might play a role, at both individual and societal level, in supporting increasing numbers of older people to 'live well' in their old age. At points, it has also alluded to ethical issues that arise in connection with particular developments, as well as seeking to place these developments in the wider context of the many other aspects of social policy that influence wellbeing in later life. This final section brings together a number of these ethical questions.

The aims of research in this field – and scope for conflicts of interest

45. As noted in Part II of this paper, the way that the challenges associated with ageing are framed – in particular whether the primary question is seen as being how to 'manage the burden' of old age as implied by some commentators – fundamentally affects the aims of any associated research and innovation. The way the issues are framed is itself heavily value-laden, in terms of implicit attitudes to the value of old age and older people, and to their place within mainstream society. Framing this inquiry in terms of how biomedical science and technological innovation can support people in 'living well' in old age – while recognising the resource challenges of changing demographics – in itself takes a particular ethical stance about these questions. It also requires significant work to clarify conceptions and criteria about 'ageing well' (asking 'what are the valuable and desirable aspects and dimensions of old age?') in order to provide the basis for evaluating scientific and technological interventions against this aim.
46. Important questions arise with respect to how the voices, needs and perspectives of older people themselves, and of diverse groups within this heterogeneous cohort, influence the aims and conduct of research in these fields (see below, paragraph 48). In the field of geroscience research, there appears to be a degree of tension regarding the extent to which current research priorities should primarily be concerned with maximising 'healthspan' ('adding life to years' as emphasised in the WHO's [Decade of Healthy Ageing](#)); or about increasing, perhaps significantly, the total length of our (healthy) lives. While it may be possible for research to target both aims, the values and concerns that underlie each research aim are quite distinct. Increasing longevity *per se* values 'more' life as a good in itself, raising challenging questions about how long we really want to live, and how strenuous efforts should be to achieve this, particularly given the trade-offs in terms of opportunity costs for investment in other areas of research. Focusing on maximising healthspan, in contrast, values the goods that a physically and mentally healthier old age can bring, regardless of its length.
47. The commercial interests involved in this area of research are also significant, with considerable amounts of private funding being invested in the hope of "monumental" outcomes for companies if they achieve a successful breakthrough

in anti-ageing interventions.¹³⁹ This commercial element identifies a further independent aim of such research: that of making money for private investors. The amount of money at stake raises linked concerns regarding the role that hype may play in generating demand for anti-ageing projects on the market, whether or not these have a good evidence base for their claims (see paragraph 29, for example with respect to stem cell therapies and ‘young blood’). The role of hype is also important because of the prospect that even pharmaceutical interventions that ‘work’ in maximising healthy life may not make a difference for people who are already relatively healthy and have an active life.¹⁴⁰ It will therefore be important to explore the extent to which any developments offer benefits that cannot be achieved through existing and well-established public health approaches.

Questions of equity

48. Given the starting point of considerable inequities in health and life chances, referred to throughout this paper, questions of equity are likely to be a key focus for this project, from issues of research selection and prioritisation to the crucial question of access to the outcomes of research:

- Socio-economic inequalities strongly influence life expectancy and general physical and mental health from the earliest years of childhood, and these inequalities may deepen with age. How should this recognition influence research priorities and wider policy aims in connection with supporting higher levels of wellbeing in old age?
- Such inequalities disproportionately affect Black, Asian, and minority ethnic people, indicating how structural racism intersects with socio-economic disadvantage to affect health and wellbeing.¹⁴¹ How can research agendas seek to engage with these multiple forms of disadvantage?
- Given these vast differences in life expectancy, both within and between countries, can a focus on research that aims to increase total life expectancy, as opposed to improving health in later life, be ethically justified? The often maverick private funding of research in this area is likely to be highly significant in exploring the ways in which research priorities in

¹³⁹ See the overview of ‘investment in ageing research’ in Nuffield Council on Bioethics (2018) *The search for a treatment for ageing*, available at:

<https://www.nuffieldbioethics.org/assets/pdfs/The-search-for-a-treatment-for-ageing.pdf>. See also companies such as <https://nuchido.com/> advertising products “that address the underlying biological complexity that is required for healing and repair to succeed”.

¹⁴⁰ Glossmann HH, and Lutz OMD (2019) Metformin and aging: a review *Gerontology* **65(6)**: 581-90; and Furrer R, and Handschin C (2020) Lifestyle vs. pharmacological interventions for healthy aging *Aging* **12(1)**: 5-7.

¹⁴¹ See, for example, The Centre for Ageing Better (19 August 2020) *Ethnic inequalities among over 50s revealed in new research*, available at: <https://www.ageing-better.org.uk/news/ethnic-inequalities-among-over-50s-revealed-new-research>; and The Conversation (27 October 2020) *Racism is the key to understanding ethnic inequalities in COVID-19 – despite what UK government says*, available at: <https://theconversation.com/racism-is-the-key-to-understanding-ethnic-inequalities-in-covid-19-despite-what-uk-government-says-148838>. See also: The Lancet Healthy Longevity (2021) Compounding inequalities: racism, ageism, and health *The Lancet Healthy Longevity* **2(3)**: e112.

this field are set, and in which researchers working on fundamental ageing in order to mitigate chronic conditions become aligned to those who are seeking extreme long lives through individualised approaches.

- In the case of research / innovation into technological means to support ageing well, how inclusively have these needs been identified? Are technological developments addressing the needs of the most excluded / marginalised, or are they primarily focused on the needs of the minority who are already relatively well supported in later life? And/or are they more focused on the needs of others, such as paid or unpaid carers, rather than on the needs and preferences of older people themselves? Both these aspects of equity bring in issues explored in recent Nuffield Council projects, concerning how the supposed beneficiaries of research and development can be meaningfully involved in identifying needs, setting research priorities, and shaping the conduct of the research.¹⁴²
- Genomic research seeking to understand genetic aspects of long healthy life (as, for example, in research with extremely long-lived families in Sardinia, Greece and Japan),¹⁴³ and research into epigenetic factors influencing biological ageing, raise particular issues of equity. Close attention needs to be given to the implications of such research and the benefits/harms that might come out of approaches based on such research evidence, in particular with relation to the way in which broader societal responsibilities with respect to equity in health are understood (see also below, paragraphs 50–51).

Specific research challenges

49. Biomedical research in ageing and, in particular, research focused on preventative interventions much earlier in the life course, generate a number of ethical and regulatory challenges. These include:

- Time scales and appropriate endpoints for studies, given the slow manifestation of ageing. The issue of research timescales that are both meaningful and feasible highlights the need for acceptable proxy endpoints for studies, with some promise offered by developments in biomarkers (see paragraph 40).
- Challenge with composite endpoints: traditional regulatory approaches look for endpoints based on the impact of the trial intervention on a single disease, creating difficulties for interventions that seek to modify processes underlying a number of different diseases. This has led to calls for 'ageing' itself to be classified as a disease – if only for regulatory purposes. It has been noted with respect to the planned TAME study on the effects of

¹⁴² See: Nuffield Council (2015) *Children and clinical research: ethical issues*, available at: <https://www.nuffieldbioethics.org/publications/children-and-clinical-research/>; and Nuffield Council (2020) *Research in global health emergencies: ethical issues*, available at: <https://www.nuffieldbioethics.org/publications/research-in-global-health-emergencies/>.

¹⁴³ See, for example, US National Library of Medicine, Medline Plus (2020) *Is longevity determined by genetics?*, available at: <https://medlineplus.gov/genetics/understanding/traits/longevity/>.

metformin, for example, that: “instead of following a traditional structure given to FDA approved trials (that look for a single disease endpoint) TAME has a composite primary endpoint – of stroke, heart failure, dementia, myocardial infarction, cancer, and death. Rather than attempting to cure one endpoint, it will look to delay the onset of any endpoint, extending the years in which subjects remain in good health – their healthspan.”¹⁴⁴

- Appropriate recruitment criteria: partly because of these regulatory challenges, trials that are currently being conducted have mainly recruited older people with co-morbidities. Yet reversing cellular damage is quite different from protecting against it. These recruitment challenges exist on top of well-established concerns about lack of diversity in research participation with respect to gender and ethnicity.
- Evidence of effectiveness of the proposed interventions: the standard challenges of translating from animal to human models are exacerbated by the fact that humans do not behave like laboratory animals: “humans are not big worms or huge mice”.¹⁴⁵ This highlights the importance of research in biological ageing being complemented and supported by research concerned with the social, cultural and behavioural aspects of ageing.¹⁴⁶ Moreover, the laboratory animals used in many studies are themselves young: it has been noted, for example that preclinical vaccine studies are usually carried out in young animals, even though many vaccines are targeted at older age groups, whose immune systems are not as effective as those of young people.¹⁴⁷
- Risks that research seeking to delay the onset of age-related disorders may lead, not to compression of morbidity, but to longer periods of ill health as part of an extended lifespan: “Will our medicated centenarians lead fulfilling lives with eventual sudden collapse, or will they suffer from proportionally protracted durations of chronic disease?”¹⁴⁸ Such concerns link with wider challenges associated with the risks of polypharmacy and the increasing medicalisation of old age.¹⁴⁹

Where do responsibilities (and choices) lie?

50. As noted in paragraph 48 in the specific context of genetic research, the increasing focus on more medicalised and/or high-tech solutions to the challenges and opportunities associated with ageing also potentially raises more

¹⁴⁴ Fight aging (2019) *TAME trial for the effects of metformin in humans to proceed this year*, available at: <https://www.fightaging.org/archives/2019/09/tame-trial-for-the-effects-of-metformin-in-humans-to-proceed-this-year/>.

¹⁴⁵ de Magalhães JP, Stevens M, and Thornton D (2017) The business of anti-ageing science *Trends in Biotechnology* **35(11)(11)**: 1062-73.

¹⁴⁶ See, for example, the Dunedin Study: <https://dunedinstudy.otago.ac.nz/>.

¹⁴⁷ Kaeberlein M, Rabinovitch PS, Martin GM (2015) Healthy aging: the ultimate preventative medicine *Science* **350(6265)**: 1191-3.

¹⁴⁸ Kaeberlein M, Rabinovitch PS, Martin GM (2015) Healthy aging: the ultimate preventative medicine *Science* **350(6265)**: 1191-3.

¹⁴⁹ Dagli RJ, and Sharma A (2014) Polypharmacy: a global risk factor for elderly people *J Int Oral Health* **6(6)**: i-ii.

general issues of personal versus social responsibility, and personal choice. What will be the (actual or perceived) pressures on individuals to take particular medicines once they are available, and will the availability of such treatments affect the priority given to more holistic support for those who are very old and frail? What are the implications of ever-earlier diagnosis, increased medicalisation across the lifespan and the resulting role of polypharmacy as people enter old age? Similar issues are already being discussed in terms of the risks of older people losing human contact through the provision of more automated forms of social care (see paragraphs 9 and 22). The demographic pressures with which society as a whole need to grapple (with their implications both for public finance and the size of the workforce) are likely to add to risks of individual choices and preferences being eroded, if technological solutions become default options.

Implications for society as a whole: intergenerational solidarity and justice

51. Finally, in any examination of these issues, the implications for wider society must be taken carefully into account in considering how any interventions might be implemented – whether these take the form of technological innovations or new medicines, developments in the provision of social services, or indeed wider changes in the structure of society. This wider question, of how responding to the challenges of old age might affect other parts of society, raises important questions of intergenerational equity and solidarity.¹⁵⁰ It also highlights the importance of whole-society public engagement (as distinct from engagement specifically with older people) in considering the implications of any novel interventions or proposed shifts in social policy. At the same time, any consideration of how interests may compete between generations needs also to take into account how generations connect through families, with both advantage and disadvantage being passed on through the generations. Factors to consider include:

- The implications for all parts of society of significant demographic changes, including, for example: increased involvement (compared with today's baseline) in the workforce by older people; changing demands on, and/or expectations of, the welfare state; and the environmental impacts / sustainability challenges both of increasing population size and of different ways of living in old age.¹⁵¹
- The implications for all parts of society for the way in which technology is used, and resources consumed, in responding to these challenges, recognising the sustainability challenges of increasing medicalisation and reliance on technologies.¹⁵²

¹⁵⁰ See, for example, House of Lords Select Committee on Intergenerational Fairness and Provision (2019) *Tackling intergenerational unfairness*: <https://publications.parliament.uk/pa/ld201719/ldselect/ldintfair/329/329.pdf>.

¹⁵¹ See, for example, the 2018 Planetary Health Meeting: <https://www.ed.ac.uk/global-health/planetary-health/planetary-health-meeting-2018>.

¹⁵² The BMJ Opinion Blog (30 December 2019) *Innovation should support societal responsibility for health*, available at: <https://blogs.bmj.com/bmj/2019/12/30/innovation-support-societal-responsibility-health/>; [https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568\(20\)30072-6/fulltext](https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(20)30072-6/fulltext).

- Questions of personal, familial, professional, societal and state responsibility, and the extent to which any increased medicalisation of old age may affect perceptions and/or policies of where responsibility for supporting older people lies (through, for example, expecting individuals and/or their families to assume more responsibility for their own health in old age, or in affecting the current distinctions between 'health' and 'social' care).
- The economic implications, particularly in terms of any tensions between what people desire / prefer, and the costs (which may arise across different time frames along with known and potential benefits / harms).