

BACKGROUND PAPER

Longevity

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Note

The author was commissioned by the Nuffield Council on Bioethics to write this paper in order to inform the Council's discussions about possible future work on this topic. The paper is intended to provide an overview of key clinical, ethical, social, legal and policy issues, but is not intended to offer any conclusions or recommendations regarding future policy and practice. Any views expressed in the paper are the author's own and not those of the Nuffield Council on Bioethics.

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Background paper

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Executive summary

Subject and approach

For the first time, interventions to slow physical ageing are within reach. This background paper examines a possible increase in longevity and its potential ethical implications. The current situation is presented as follows:

- Several interventions have successfully slowed ageing, prevented or postponed ageassociated diseases, and prolonged the life span of animals in laboratory settings.
- Biogerontologists are confident that their knowledge and methods can be applied to humans. They present these methods as a new paradigm for medicine.
- Clinical trials of some interventions are already underway.
- The primary goal would be to prevent age-associated diseases by slowing ageing, but as a corollary, longevity is likely to increase as well.

The background paper describes the possible increase of longevity achieved by slowing biological ageing as a 'second longevity revolution'. The 'first longevity revolution' refers to the increase of longevity since the middle of the 19th Century. One of the results of these revolutions in longevity is the phenomenon of 'population ageing', and its associated implications. It is important that biogerontology and its application to medicine is analysed and evaluated in this broader context.

Terminology

Average life span: indicates the calculated average life time of an organism of a particular population.

Maximum life span: the longest life span of such an organism that has been observed.

Age: can simply refer to the chronological age; may also constitute part of an entity's life course.

Ageing: is not a single or simple process but a combination of many different physiological, psychological, and cultural processes.

Population ageing and its challenges

The increase in life expectancy humans have achieved over the last 100 years is higher than in the previous 50 centuries.

• The number of older age groups has risen to historically unprecedented heights in many societies.

Population ageing is a global phenomenon.

Two major challenges of population ageing are an increase in the old-age dependency ratio, and a projected rise in spending for healthcare and nursing care.

Geriatrics and gerontology. The multidisciplinarity of gerontology

A proper theoretical understanding of old age and ageing requires a multidisciplinary approach, including:

- **Geriatrics**, which can be defined as "the study of the medical aspects of old age and the application of knowledge related to the biological, behavioural, and social aspects of aging to prevention, diagnosis, treatment, and care of older persons".
- **Gerontology**, the theoretical study of old age or "the study of ageing from the broadest perspective". This includes: psychological gerontology, social gerontology, and biogerontology.

Each gerontological field pursues specific practical goals. These goals are closely related to the challenges of population ageing. Examples are: successful ageing, active ageing, and healthy ageing.

Biogerontology: institutions, basic conceptions, interventions, and goals

Biogerontological research: infrastructure, investment and funding

The infrastructure and funding of biological ageing research in the US is well ahead of that in Europe. Funding increases in biogerontology are seen as key to further advances in this area of research being realised. Levels of investment also appear to be increasing in the private sector.

Boundary work

Biogerontologists who describe themselves as part of the scientific mainstream have sharply criticised proponents of current 'anti-ageing-medicine'. They also have denied that radical life extension will be possible in the near future. The most well-known proponent of such a radical vision may be Aubrey de Grey, who propagates a so-called 'Strategy for Engineered Negligible Senescence' (SENS).

Basic concepts of biogerontology: Rattan's three principles

The biogerontologist Suresh Rattan summarises the current knowledge base of biogerontology in three concise principles:

- The "mechanistic principle" provides a fundamental definition: biological ageing is the accumulation of molecular damage in cells and tissue over time, while cellular repair mechanisms lose their potential.
 - This raises the question as to whether ageing itself should be considered a disease. The position that separates ageing from disease now seems to be a minority view in biogerontology.

- The "non-genetic principle", which does not deny that there may be a genetic component of longevity and ageing, but rejects the idea that biological ageing is genetically programmed.
- The "evolutionary life history principle": according to this principle, the length of the typical life span of a species is the result of an evolutionary adaptation in which a balance between reproduction and physiological repair mechanism is achieved.

Interventions

The molecular and genetic aspects of biological ageing indicate the mechanisms that could be targeted by new interventions based on current biogerontological knowledge.

- Caloric restriction
- · Genetic mutations
- Different pharmaceutical drugs
- Stem cells
- A combination of interventions.

Paradigm for medicine: the longevity dividend

- Some biogerontologists argue that their approach represents a superior strategy of tackling age-associated diseases by addressing their common cause.
- They promise a "longevity dividend", provided that society invests in research and development.
- This 'dividend' would be generated in the form of a healthier old age and an increase in life expectancy by seven years, both within decades.

Practical goals of biogerontology: preparing a 'second longevity revolution'

- Ageing could be slowed, arrested or even reversed by biogerontological interventions.
- This would prevent or postpone age-associated diseases.
- Life span will also be extended. An extension of the former trend characterising the first longevity revolution might be considered as 'moderate life extension'. A 'radical life extension' would include any substantial increase beyond the current maximum life span.
- What matters is not only the amount of time but also the phase of life that would be extended: the developmental span, the health span, or the senescent span. The obvious goal is to extend the health span at the expense of the senescent span, which corresponds to the widely acclaimed goal of a 'compression of morbidity'.

Ethical aspects: individual perspective

- Arguments for increased longevity based on utility point to reduced suffering from ageassociated diseases and to the experience of pleasure over a longer period of time.
- Others have argued that the experience of physical ageing is valuable, even if it
 involves suffering. It is either an irreplaceable way to experience human finitude or
 considered to be a part of the human life course and a fully human life.
- Some philosophers have defended the thesis that only mortality gives meaning to human life, and a shapeless and limitless life would also lack meaning and purpose.

- Conversely, other philosophers have argued that death negates the meaning and value of human lives.
- Opponents have argued that radically extended life spans would either lead to boredom or a loss of identity.
- Some authors have equated preventing or treating ageing with saving lives.

Ethical aspects: social perspective

- The scenario of a compression of morbidity achieved by slower ageing is the scenario of a 'longevity dividend': healthier and more active lives.
- Others have dismissed the economic arguments of longer and more productive lives.
 Instead, a further increase of older age groups would reduce the dynamics and productivity of a society.
- Another common objection concerns projections of population growth. This is called the 'Malthusian objection'.
- Treating ageing with biogerontological intervention would lead to an increase in the 'biomedicalisation of ageing'. In sum, biomedicalisation prevents people from finding better ways to accept and integrate old age as a part of their life course, and consequently from a conception of a good or flourishing life in old age.
- The social gerontologist John Vincent argues that basic biogerontological concepts stem from an ageist culture, which will be reinforced once these concepts become more influential.
- If old age as a part of life loses its value, age discrimination and neglecting the problems of older people could result.
- Access to interventions that slow ageing could be limited according to the ability to pay, especially when it comes to 'radical life extension'. Existing health inequalities linked to social determinants could be increased.

Conclusion: Open questions, guidance, and public awareness

- An interdisciplinary dialogue between biogerontology, other gerontological disciplines, geriatrics, and other relevant disciplines needs to be fostered.
- Part of this interdisciplinary dialogue needs to estimate the impact of new interventions into ageing on health inequalities.
- The problem of global justice has to be addressed.
- Options for ethical and legal guidance need to be discussed.
- Public awareness of biogerontology, its conceptions, goals, and potential benefits and risks is low and needs to be increased.

Introduction

- 1 For the first time in human history, interventions to slow physical ageing are close at hand, based on broad scientific knowledge and animal experiments. Clinical trials of some interventions are already underway. Biogerontologists are confident that soon it will be possible to apply their knowledge to humans. The goals would be to prevent age-associated diseases by slowing ageing, and to prolong the human life span. These promises appear to be convincing to public funding agencies and private investors, and the infrastructure of research facilities seems to be expanding. This picture justifies the necessity and timeliness of an ethical analysis of and critical reflection on the "second longevity revolution", which could soon lie ahead of us (the first revolution being the phenomenon of population ageing).
- 2 This second revolution, together with the results of the one still in progress, will shape the future of ageing and old age. It is therefore crucial to consider a potential increase in longevity achieved by means of biogerontological methods in the context of demographic change and population ageing. These developments have also led to a flourishing in social, psychological, and cultural studies on ageing and old age. So far, bioethical literature has primarily examined the issue in connection with the project of radical life extension and the fundamental questions associated with such an outlook (e.g., whether there is a limit to the human life span beyond which living is no longer desirable). What has not been considered in a sufficient way, however, are the contexts of demographic change and an interdisciplinary perspective on ageing and old age.
- 3 After these contexts are described, an overview of ethical positions regarding a second longevity revolution will be provided. This overview is based on a distinction between different sets of goals from a moderate extension of human longevity to a radical one. The structure of the ethical discussion will proceed from an individual perspective to a social one. First, the question will be examined in which sense an increased longevity would be desirable or not from an individual perspective. Then the social consequences will be analysed. Finally, some neglected questions and the need for further discussions will be outlined.

Terminology: basic conceptions related to longevity and ageing

Longevity, life expectancy, average and maximum life span, life course: age and ageing.

4 The Oxford English Dictionary defines 'longevity' as "long life" or "long duration of existence". The term is also sometimes equated with life expectancy; the period of time for which something is expected to exist. The first meaning of longevity – the concept of a 'long life' – refers to life considered in its length and unity; that is a 'life span'. The 'average life span' indicates the calculated average life time of an organism of a particular population. 'Maximum life span' is the longest life span of such an organism that has been observed. The longest human life span to date is 122.4 years reached by the French woman Jeanne Calment who died in 1997.² In the second meaning of

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Check Hayden E (2015) Anti-ageing pill pushed as bona fide drug *Nature* **522(7556)**: 265-6.
Coles LS (2004) Aging: the reality demography of human supercentenarians *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* **59(6)**: B579-B86.

longevity, the aspect of continuity over time is highlighted; the perspective of a 'life course' consists of specific moments and periods over the life time of something that can be measured. The longevity of either an object or an organism is measured as its age. Therefore, the concept of longevity is inseparable from the concepts of age and ageing.

- 'Age' can simply refer to the chronological age of something to indicate a specific point in time in its life span. Further, 'age' can also be seen in the context of the 'life course' of an entity and the changes it may undergo over time. In this case, 'phases of life' may be distinguished as a part of the life course characterised by particular features: for example in the human life course juvenile age is characterised by growth, among other things. A traditional perspective of the phases of a human life is depicted in the socalled 'Alterstreppe' (staircase of ageing) which describes human life as an ascent on a staircase until middle age (around 50), followed by a descent until death. Contemporary sociologists deny this perspective of a uniform decline beginning with middle age to old age, which conventionally begins at 65 according to many statistical tables. This is sometimes criticised since it refers to an arbitrary fixation of pension age, which may in the future change due to gains in life expectancy at 65. This fixation masks the diversity of people in one age group and also ignores the differences regarding the health and life expectancy of 65 year olds of former generations and those alive today. Alternative understandings of 'age' count a particular time until death in an average life span as 'old age'.3
- In either case, it is now common to distinguish a third age (the 'young old') from a fourth age (the 'old old' or 'oldest old'). While people in their third age today are healthier than this age group has been in the past, it is often suggested that people in their fourth age still struggle with age-associated health problems, such as frailty and morbidity.4 The processes that bring about the changes leading to the advanced phases of life across the life course can be summarised by the general term 'ageing'. These changes may be seen under different aspects. Firstly, these changes may be physiological or biological, as they concern the constitution of the body. Secondly, changes may be psychological because they refer to the character and maturity of a person. Finally, 'ageing' also implies changes in the role and relationship towards others in society. 'Ageing' is thus not a single or simple process but a combination of many different physiological, psychological, and cultural processes. These processes are closely linked to the phases of the life course and their diverse meanings. This contributes to a highly complex meaning of 'longevity' and the different stages of age, including the respective ageing processes during the course of a long life. Further, the complex meaning of 'longevity' is not only descriptive but also has important ethical elements.

Sanderson WC, and Scherbov S (2007) A new perspective on population aging *Demographic Research* 16: 27-58.

⁴ Fulop T, Larbi A, Witkowski JM *et al.* (2010) Aging, frailty and age-related diseases *Biogerontology* **11(5)**: 547-63; Baltes PB, and Smith J (2003) New frontiers in the future of aging: from successful aging of the young old to the dilemmas of the fourth age *Gerontology* **49**: 123-35.

The longevity revolution and population ageing or demographic change

Population ageing

- 7 Longevity as it pertains to healthy and flourishing lives has been and remains a basic value according to many different cultural and religious perspectives. The philosopher Thomas Hobbes famously wrote that in the state of nature human life is "solitary, nasty brutish, and short." For Hobbes, longer and safer lives thus become a major reason to join the social contract and leave the state of nature. His contemporaries and cofounders of modern philosophy René Descartes and Francis Bacon saw an increase in longevity as a major goal of the science and medicine they envisioned. This vision had started to become a reality by the middle of the 19th Century (first experienced by women from the aristocracy in industrialising countries), and life expectancy has continued to rise ever since, on average three months per year.
- Increasing life expectancy is now becoming a global phenomenon. As a result of these increases and a simultaneous decline in birth rates, the number of people in older age groups has risen to historically unprecedented heights in many societies. This has been described as 'population ageing', or 'demographic change'. In order to emphasise how profound the changes brought about by this process are, the gerontologist Robert N. Butler referred to it as "the longevity revolution"8. Just how radical these changes are can be seen in the simple fact that the increase in life expectancy humans have achieved over the last 100 years is higher than in the previous 5,000 years. While in many societies old age had been an exceptional phenomenon only experienced by two or three percent of the population, 9 it is now common for most people in industrialised societies and is becoming more and more common across the globe. 10 Considering the great value placed on longevity, as outlined above, it is clear that the high, and still rising, life expectancies and the resulting 'longevity revolution' are major achievements of contemporary civilisation. On this basis, Butler points to the beneficial aspects of the longevity revolution and population ageing. However, he is also aware of the widely perceived challenges.

Challenges of population ageing

9 Currently, the over 80s' age group in the 'fourth age' is the fastest growing age group across the globe. While life expectancy continues to rise, with the highest gains being for the age groups at 65 and over, birth rates in many industrialised countries have

Hobbes T, and Malcolm N (2012) Leviathan (Oxford: Clarendon Press) XIII, 9.

Bacon F, and Weinberger J (1989) *New Atlantis ; and, The great instauration*, Rev. ed. Edition: Harlan Davidson), Descartes R, and Maclean I (2006) *A discourse on the method of correctly conducting one's reason and seeking truth in the sciences* (Oxford: Oxford University Press).

Hollingsworth TH (1965) The demography of the British peerage *Population Studies* **18**: 56-7, Riley JC (2001) *Rising life expectancy* (Cambridge: Cambridge University Press).

⁸ Butler RN (2008) *The longevity revolution*, 1st Edition (New York: PublicAffairs).

⁹ Butler RN (2008) *The longevity revolution*, 1st Edition (New York: PublicAffairs).

McDaniel SA, and Zimmer Z (2013) *Global ageing in the twenty-first century* (Farnham, Surrey: Ashgate).

dropped below the replacement rate of 2.1.¹¹ Both factors are leading to the double phenomenon of ageing at the top (the increase of older age groups), and ageing at the bottom (the decrease of younger ones). The future development of this demographic situation is hard to foresee given that the future trend of life expectancy is contested and birth rates might rise again. Migration is another factor contributing to difficulty in making predictions. At the same time, 'demographic change' generates some well-known and widely discussed challenges.¹² A major issue is the rising old-age dependency ratio, which demonstrates that a smaller workforce will eventually have to support a growing number of older people. This may, in turn, lead to an insecurity of pensions.

10 Public concerns are often related to rising costs of healthcare and nursing homes. As early as 1971, Abel Omran coined the term of a "transition of disease" from infectious to chronic illnesses, which primarily affects older people. Because this transition requires new priorities in healthcare and medical research, the healthcare system has to be adapted according to the specific health and nursing care needs of older people. This presents a challenge to low and middle income countries in particular because they are simply less well prepared and financially equipped for such changes. These challenges and the higher social importance and visibility of old age and ageing have made their impact on the sciences and the social sciences of old age. The 'longevity revolution' and demographic change have contributed to the foundation of the discipline of geriatrics dedicated to the health needs of older people. They have also generated the prolific, interdisciplinary scientific field of study concerned with ageing and old age: gerontology.

The academic field: geriatrics and gerontology

Studying and dealing with the 'longevity revolution' and 'population ageing'

11 Geriatrics ("geron" Greek for "old man" and "iatreia" Greek for "art of healing") can be defined as "the study of the medical aspects of old age and the application of knowledge related to the biological, behavioural, and social aspects of aging to prevention, diagnosis, treatment, and care of older persons". The second part of this definition points to the knowledge gained in another academic discipline, that of gerontology ("logos" Greek for "speech, reason, study"): the theoretical study of old age or "the study of aging from the broadest perspective". Both terms were coined in the early 20th Century, while "geriatric" knowledge on specific maladies of older people dates back to the founding fathers of Western medicine, Hippocrates and Galen. But the institutional academic structures of geriatric medicine took shape in the form of wards, societies and associations as late as the 1930s. The same is true for gerontology, which first emerges as a science at this time with the corresponding

See, for example, the discussion in Christensen K, Doblhammer G, Rau R, and Vaupel JW (2009) Ageing populations: the challenges ahead *The Lancet* **374(9696)**: 1196-208.

Achenbaum WA (1995) Crossing frontiers (Cambridge: Cambridge University Press).

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Lutz W, and K CS (2010) Dimensions of global population projections: what do we know about future population trends and structures? *Philosophical Transactions of the Royal Society of London Series B, Biological Sciences* **365(1554)**: 2779-91, United N (2007) *World population ageing 2007* (New York: United Nations, Dept. of Economic and Social Affairs, Population Division).

Omran AR (2005) The epidemiologic transition: a theory of the epidemiology of population change *Milbank Quarterly* **83(4)**: 731-57.

Achenbaum WA (1995) Crossing frontiers (Cambridge: Cambridge University Press), at page 14.

academic and institutional structures. For instance, the German society for the study of ageing was founded in 1938, and re-emerged in 1966 as the German Society of Gerontology. The Gerontological Society of America was founded in 1945¹⁷ and the International Association of Gerontology and Geriatrics (IGG) in 1950. The International Association of Gerontology and Geriatrics (IGG) in 1950.

The multidisciplinarity of gerontology: gerontological disciplines and their practical goals

- 12 A proper theoretical understanding of the different physiological, psychological, and social aspects of old age and ageing requires a combination of different scientific methods and perspectives. This necessity is reflected by the multidisciplinarity of gerontology and gerontological societies (e.g. the membership of the Gerontological Society of America includes medical doctors, biologists, sociologists, and psychologists). Gerontology can thus be divided into psychological gerontology, social gerontology, and biogerontology. Each of the gerontological disciplines contributes both to the theoretical picture of old age and ageing, and pursues specific practical goals. These goals are closely related to demographic change and population ageing, as well as policies developed to meet corresponding challenges.
- 13 Psychological gerontology examines attitudes towards ageing and develops approaches supporting personal well-being in the third and fourth ages of life. 'Successful ageing' is a key term for a practical goal in this respect, and refers to keeping the risk of disease and disability low, maintaining cognitive function, and participating actively in social life. Another influential example is the so-called SOCThesis (S: Selection, O: Optimization, C: Compensation) put forward by the German gerontologist Paul B. Baltes. This thesis summarises a strategy of how to deal with age-related changes and potential losses in order to enhance subjective well-being. Baltes suggests selecting activities according to abilities, to optimise those activities, and to try to compensate for activities one is no longer able to perform. 20
- 14 Social gerontology describes the changes societies undergo in population ageing and the new situation and diversity of older age groups in this process. Longitudinal studies that follow people over long periods of time have contributed to an increase in knowledge about the specific features of demographic change and population ageing. Famous examples of such studies are the ongoing Baltimore Longitudinal Study of Aging (BLSA), which began in 1958; the Cognitive Function and Ageing Studies (CFAS) in the UK, which first started in 1989; and the Berlin Study of Ageing (BASE), which began in 1990 and is now continued in BASE II.

DGGG-online.de (2015) English: overview, available at: http://www.dggg-online.de/englisch.php.

International Association of Gerontology and Geriatrics (2015) *Past presidents*, available at: http://www.iagg.info/sub02 01 Past Presidents.php.

Rowe and Kahn have written the classical text on this issue and recently summarized and updated the discussions around their concept: Rowe JW, and Kahn RL (2015) Successful Aging 2.0: Conceptual Expansions for the 21st Century *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences* See also: Bowling A, and Dieppe P (2005) What is successful ageing and who should define it? *BMJ: British Medical Journal* **331(7531)**: 1548-51.

Freund AM, and Baltes PB (1998) Selection, optimization, and compensation as strategies of life management: correlations with subjective indicators of successful aging *Psychology and Aging* **13(4)**: 531-43.

The Gerontological Society of America (2015) *History*, available at: https://www.geron.org/about-us/history.

15 Closely connected to studies such as these, which focus on improving the understanding of the situation and diversity of older age groups, is the fight against stereotypes associated with old age and age discrimination. Robert N. Butler coined the term 'ageism', which is analogous to racism and sexism, in that it refers to similar attitudes and practices, but is directed toward older people. For many social gerontologists, fighting ageism is another major objective of their academic endeavours. Some other important practical goals to meet the challenges of population ageing are developed across different disciplines of gerontology, including "active ageing" and "healthy ageing". Thus, an important emphasis in all of these goals of ageing research and related policies lies in the fight against age-associated diseases. The biological branch of gerontology (biogerontology) claims a key role in this fight based on important advances in its field. A possible 'second longevity revolution' could be brought about by biogerontology completing and continuing the first revolution. Understanding this possible development requires some basic knowledge of biogerontology, its institutions, and its current progress towards slowing human ageing.

Current biogerontology: institutions, 'boundary work', basic conceptions, and interventions

The current institutionalisation of biogerontological research: infrastructure, investment, and funding

16 The infrastructure and funding of biological ageing research in the US is currently well ahead of that in Europe. The US National Institute for Aging (NIA) which spends a significant amount of its budget on biological ageing research – around 173,291 million USD in its latest budget request – was created in 1975. 24 Comparable structures and funding efforts are still nascent in most other countries and in Europe. There is no counterpart to the NIA in Europe, but the increasing importance of the field is acknowledged. Correspondingly, there is an emerging landscape of biogerontological research facilities and increasing public funding. In the UK, two centres in London (UCL) and Newcastle unite prominent biogerontologists, such as Tom Kirkwood, Linda Partridge, David Gems, among others. The Academy of Medical Sciences²⁵ and the Royal Society²⁶ have also published reports on, and overviews of, the new biology of ageing and its potential application in medicine, which escapes public attention in most other countries. In Germany, however, a Max Planck Institute for the Biology of Ageing was recently founded in Cologne, and on this occasion a report was published on the

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Butler RN (1969) Age-ism: another form of bigotry *The Gerontologist* **9(4, Part 1)**: 243-6.

European Commission (2015) Innovation for active & healthy ageing, available at:

https://ec.europa.eu/research/innovation-union/pdf/active-healthy-ageing/ageing_summit_report.pdf.
Carstensen LL, Rosenberger ME, Smith K, and Modrek S (2015) Optimizing health in aging societies

Public Policy & Aging Report 25(2): 38-42.
 NIH National Institute on Aging (2015) Fiscal year 2016 budget, available at: https://www.nia.nih.gov/about/budget/2015/fiscal-year-2016-budget.

The Academy of Medical Sciences (2009) *Rejuvenating ageing research*, available at: https://www.acmedsci.ac.uk/viewFile/publicationDownloads/ageingwe.pdf.

Partridge L, Thornton J, and Bates G (2011) The new science of ageing *Philosophical Transactions of the Royal Society of London Series B, Biological Sciences* **366(1561)**: 6-8.

- "future of ageing".²⁷ The infrastructure and funding in other European countries is similar, or indeed less developed, compared to the situation in the UK and Germany.²⁸
- 17 Levels of investment in biogerontology also appear to be increasing in the private sector. 29 Google's foundation of Calico in 2013, a biotechnological company developing methods to tackle ageing, garnered a lot of attention. Further, the strong push for interventions to slow ageing is highlighted by the recent report that the CEO of an antiageing company herself underwent gene therapy to prevent age-associated diseases. 30 Other companies and wealthy individuals with a connection to Silicon Valley are contributing to a much more radical vision of the second longevity revolution. The most well-known proponent of such a radical vision may be Aubrey de Grey, who propagates a so-called "Strategy for Engineered Negligible Senescence" (SENS), a combination of different methods to halt or reverse ageing processes, and is the president of the charity of the same name (SENS Foundation). He is also edits the biogerontological journal *Rejuvenation Research* and has received a lot of media attention as a result of his conviction that people who will experience arrested ageing have already been born. (de Grey and Rae, 2007) (de Grey and Rae, 2007)

Boundary work

- 18 Biogerontologists have often distanced themselves from both utopian outlooks of radical life extension and the existing associations of 'anti-ageing-medicine'. However, often such visions of radical life extension have obtained most public attention and awards from organisations with corresponding interests. The World Transhumanist Association, for example, has acclaimed Aubrey de Grey's radical vision of "Ending ageing", and awarded him the 'H. G. Wells Award for Outstanding Transhumanist Contributions of the Year'. Radical life extension and abolishing ageing is also discussed in bioethical debates on human enhancement (i.e. the improvement of human nature with technological methods). John Harris, for example, has called immortality "the holy grail of enhancement" and Nick Bostrom has written an allegory pledging to abolish ageing.
- 19 In principle this goal to combat ageing is shared by proponents of the field of 'anti-aging medicine' who sometimes claim that interventions into ageing processes already exist. However the scientific evidence for the safety and effectiveness of such interventions is still missing. Biogerontologists who described themselves as part of the scientific mainstream have criticised proponents of current anti-ageing-medicine sharply and

²⁷ Gruss P (2007) *Die Zukunft des Alterns* (München: Beck).

MIT Technology Review (14 October 2015) *A tale of do-it-yourself gene therapy*, available at: http://www.technologyreview.com/news/542371/a-tale-of-do-it-yourself-gene-therapy/.

de Grey ADNJ, and Rae M (2007) *Ending aging: the rejuvenation breakthroughs that could reverse human aging in our lifetime*, 1st Edition (New York: St. Martin's Press).

Khavinson V, and Rattan SI (2011) Biogerontological research in Europe: special issue *Biogerontology* **12(1)**: 1

For a summary of earlier activities, see: Hall SS (2003) *Merchants of immortality* (Boston: Houghton Mifflin).

The Observer (11 January 2015) Live for ever: scientists say they'll soon extend life 'well beyond 120', available at: http://www.theguardian.com/science/2015/jan/11/-sp-live-forever-extend-life-calico-google-longevity.

Harris J (2007) *Enhancing evolution* (Princeton and Oxford: Princeton University Press).

³⁴ Bostrom N (2005) The fable of the dragon tyrant *Journal of Medical Ethics* **31(5)**: 273-7.

denied that radical life extension will be possible anytime soon.³⁵ The bioethicist Robert Binstock sees this as an example of "boundary work" of biogerontology to gain legitimacy by demarcating its own goals and outlook from allegedly dubious endeavours.³⁶ This clarifies what prominent biogerontologists claim to be the current state of their field: at present, there is no safe and effective anti-ageing medicine, and there is no prospect of abolishing ageing altogether anytime in the near future. But biogerontological knowledge has recently made some substantial gains in terms of a commonly-shared general theory. On this basis, biological ageing can be manipulated in animals. Many biogerontologists believe that, due to similar mechanisms of biological ageing across species, human ageing could be modified with the same methods. This requires a closer look at the basic conceptions of biogerontological knowledge, the methods that could be used to alter human ageing, and the goals that could be achieved this way.

Basic conceptions of biogerontology: three principles by Rattan

- 20 David Gems, a professor of biogerontology at the Institute of Healthy Ageing, recently claimed that "ageing is a problem that is going to be solved", 37 a reference to the title of one of the classic books of biogerontology: "An unsolved problem in biology" written in 1952 by Peter Medawar. Gems' confidence runs counter not only to Medawar's puzzle but also to the bewilderment experienced by Zhores Medvedev who 25 years ago distinguished around 300 different theories of ageing in his attempt to classify them. In contrast to these 300 theories that attempt to explain different mechanisms of biological ageing, it seems that there is now a widely accepted basis of biogerontological knowledge. This includes molecular and genetic explanations of biological ageing, and an evolutionary framework for both. The biogerontologist Suresh Rattan summarises this knowledge base in three concise principles: the mechanistic principle, the non-genetic principle, and the evolutionary life course principle.
- 21 The 'mechanistic principle' provides a fundamental definition: biological ageing is the accumulation of molecular damage in cells and tissue over time, while cellular repair mechanisms lose their potential. This leads to a loss of function in cells, tissue, and organs and to an increased vulnerability to disease, injury, and death. Examples include damaged DNA, proteins that are synthesised the wrong way and the cross-linking of protein molecules leading, for instance, to plaques in neurons or to the stiffening of arteries. Many biogerontologists believe that there is a causal connection between such damaged molecules and age-associated diseases. ⁴¹

Olshansky SJ, Hayflick L, and Carnes BA (2002) Position statement on human aging *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* **57(8)**: B292-B7, Warner H, Anderson J, Austad S *et al.* (2005) Science fact and the SENS agenda *EMBO reports* **6(11)**: 1006-8.

Binstock RH, Fishman JR, and Juengst ET (2006) Boundaries and labels: anti-aging medicine and science *Rejuvenation Research* **9(4)**: 433-5.

Medvedev ZA (1990) An attempt at a rational classification of theories of ageing *Biological Reviews* **65(3)**: 375-98.

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See: YouTube (2010) Blue death: the frontiers of ageing research - a film by the Wellcome Trust, available at: https://www.youtube.com/watch?v=pAw5rjgHWc0. Medawar PB (1952) An unsolved problem of biology (London: Lewis).

Rattan SI (2012) Biogerontology: from here to where? The Lord Cohen Medal Lecture-2011 Biogerontology **13(1)**: 83-91, Rattan SI (2007) The science of healthy aging: genes, milieu, and chance Annals of the New York Academy of Sciences **1114**: 1-10.

⁴⁰ Kirkwood TB (2005) Understanding the odd science of aging *Cell* **120(4)**: 437-47.

Holliday R (2007) Aging: the paradox of life: why we age (Dordrecht: Springer).

- 22 This raises the question as to whether ageing itself should be considered as a disease. As early as in the Roman antiquity the notion of ageing as a disease had been widely shared and was influential until the beginning of the 20th Century⁴² until a change was brought about by modern geriatrics and gerontology. The founders of these disciplines distinguished 'normal' and 'pathological ageing' as an important underpinning feature of their theories. This distinction should promote the goal to support 'normal' ageing and to prevent 'pathological' ageing. The difference between ageing and disease is also upheld in two of the most influential theories of health. 43 In bioethics, on the other hand, Arthur Caplan has defended the notion of ageing as a disease based on its symptoms and the suffering it causes.44 Some biogerontologists have argued along the same lines, drawing the conclusion that ageing itself should be regarded as a disease because of the causal connection between age-related molecular changes and ageassociated diseases, which is based on the 'mechanistic principle'. 45 Biogerontologists also argue that it would be important to consider ageing to be a disease for practical regulatory reasons: that is, in order to ensure that the safety and efficacy of new interventions claiming to slow ageing are tested according to the regulatory requirements for clinical trials. A recent statement suggests that the Food and Drug Administration (FDA) would be open to such a definition. 46 The opposing position that separates ageing from disease now seems to be a minority view in biogerontology.
- 23 The name of Rattan's second principle the 'non-genetic principle' may be slightly misleading: it does not deny that there may be a genetic component of longevity and ageing, but it rejects the idea that biological ageing is genetically programmed. Some of the older theories of biological ageing have assumed such a genetic programme as in the case of development and growth. The mainstream in current biogerontology believes that this is wrong, a fact that is evident in the name "non-genetic" principle. The fact that there is no genetic programme for ageing does not imply that there are no genetic effects which contribute to ageing. One example is the hypothesis that some genes may have positive effects at younger ages, which outweigh negative effects in later life ('antagonistic pleiotropy'). For instance, a genetic basis of an aggressive immune system may protect against infectious diseases during youth but lead to an auto-immune reaction and inflammations in the long run.⁴⁷ There is also evidence that increased longevity has a genetic component.⁴⁸ Studies have shown that the close relatives of centenarians have an increased likelihood of reaching very old age.⁴⁹

Schäfer D (2002) 'That senescence itself is an illness': a transitional medical concept of age and ageing in the eighteenth century *Medical History* **46(4)**: 525-48.

⁴⁶ Check Hayden E (2015) Anti-ageing pill pushed as bona fide drug *Nature* **522(7556)**: 265-6.

Nordenfelt L (1995) On the nature of health: an action-theoretic approach, 2nd rev. and enl. ed. Edition (Dordrecht; London: Kluwer), Boorse C (2014) A second rebuttal on health *The Journal of Medicine and Philosophy* **39(6)**: 683-724.

Caplan AL (1981) The unnaturalness of aging - a sickness unto death, in *Concepts of health and disease*, Caplan AL, Engelhardt HT, and McCartney JJ (Editors) (Reading, Mass: Addison-Wesley, Advanced Book Program/World Science Division).

For a recent overview, see: Gems D (2015) The aging-disease false dichotomy: understanding senescence as pathology *Frontiers in Genetics* **6**: 212.

Martin GM, Bergman A, and Barzilai N (2007) Genetic determinants of human health span and life span: progress and new opportunities *PLoS Genetics* **3(7)**: e125.

Sebastiani P, Solovieff N, Dewan AT *et al.* (2012) Genetic signatures of exceptional longevity in humans *PLoS One* **7(1)**: e29848.

Adams ER, Nolan VG, Andersen SL, Perls TT, and Terry DF (2008) Centenarian offspring: start healthier and stay healthier *Journal of the American Geriatrics Society* **56(11)**: 2089-92.

However, the genetic component underlying this statistical correlation remains unclear, and no human longevity gene has been identified in corresponding studies.

- 24 The third principle is the 'evolutionary life history principle'. According to this principle, the length of the typical life span of a species is the result of an evolutionary adaptation in which a balance between reproduction and physiological repair mechanism is achieved. Since there are only limited resources available to an organism, such a balance is necessary. Organisms of a species often die from external causes (e.g. starvation, cold, predators) after a specific period of time. For instance, 90 per cent of mice in the wild die after a year. Therefore, if some genetically modified mice lived longer, but reproduced less, they would soon disappear in the wild. This line of thought also implies that the phenomenon of old age or frailty does not occur in the wild. Or as the biogerontologist Tom Kirkwood put it: "the level of maintenance is the target for natural selection, not ageing." This is the core idea of the so-called 'disposable soma theory', a widely-accepted evolutionary explanation of biological ageing. There is no genetic programme that determines a limited life span. Rather, the durability of our bodies soma is limited by the genetic basis of our cellular maintenance. The soma is therefore 'disposable'.
- 25 These principles have several implications especially regarding the possibility that biological ageing could be modified and how this could be achieved:
 - Firstly, it is important that ageing is not genetically programmed. A corresponding programme would be difficult if not impossible to change. Bruce Carnes states: "our bodies are not designed for indefinite survival, but neither are they designed to fail".⁵¹
 - Secondly, biological ageing is, by definition, an increase in dysfunction, and the appearance of its symptoms in old age – its phenotype – are corresponding signs of dysfunction.
 - Thirdly, according to the biogerontological mainstream, there is a close relationship between biological ageing and age-associated disease, contrary to the assumption made by the founders of geriatrics and gerontology that normal ageing has to be separated from pathological ageing.⁵²
- 26 From a biological perspective, human life is divided into three parts: the 'developmental span'; the 'adult span' (further divided into a 'health span'); and a 'senescent span', characterised by age-associated diseases. Finally, the molecular and genetic aspects of biological ageing indicate the mechanisms that could be targeted by new interventions based on biogerontological knowledge. Such interventions, which influence different processes of biological ageing so that the changes related to those processes take place more slowly or are postponed, have been successfully applied in laboratory organisms: both in simple organisms such as yeast, nematodes, or fruit flies,

Carnes BA (2007) Senescence viewed through the lens of comparative biology *Annals of the New York Academy of Sciences* **1114**: 14-22.

Blumenthal HT (2003) The aging-disease dichotomy: true or false? *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* **58(2)**: M138-M45.

Arking R (2006) *The biology of aging: observations and principles*, 3rd Edition (New York: Oxford University Press).

See: The Biochemist (8 August 2015) *Aging: designed to die?*, available at: http://www.biochemist.org/bio/03704/0008/037040008.pdf.

and in mammals including mice, rats, and monkeys. This has led to improved health and increased longevity in those organisms.

Biogerontological interventions into ageing

- 27 Biogerontologists have used the following methods to slow biological ageing in different laboratory organisms:
 - caloric restriction (reducing the intake of calories compared to free access to nutrition according to different dietary schemes)
 - genetic mutations
 - different pharmaceutical drugs
 - stem cells
 - combination of several of those interventions.⁵⁴

As a result, the life span of yeast and nematodes has increased up to tenfold, in fruit flies up to 70 per cent and in mice up to 100 per cent.⁵⁵ Prominent biogerontologists now claim that these and other possible interventions have consistently been shown to be effective in life prolongation and in preventing or delaying the onset of ageassociated diseases and conditions. Further, there is also evidence for their safety in rodents and monkeys. Together with the assumption that the mechanisms of biological ageing are comparable across species, this evidence taken together would provide a sufficient justification to proceed with clinical research in humans.

The longevity dividend and practical goals of biogerontology

The longevity dividend: a new paradigm for medicine

28 This implies that the translation from basic research to clinical trials could be close at hand. If successful, such translational research could lead to a significant change in the way medicine deals with age-associated diseases. Some biogerontologists argue that their approach represents a superior strategy of tackling age-associated diseases by their common cause instead of trying to treat them one by one. In contrast, treating each age-associated disease separately is what the current medical model tries to accomplish but only with limited success. They promise a 'longevity dividend', provided that society invests in the corresponding research and development of such new methods. This dividend would be generated in the form of healthier old age and an increase in life expectancy by seven years, both within decades.⁵⁶ If successful, biogerontological research would consequently result in a new paradigm "for disease prevention and health promotion in the 21st Century". 57 In order to succeed, the proponents of a longevity dividend argue that it would be important to support

Fontana L, Partridge L, and Longo VD (2010) Extending healthy life span - from yeast to humans Science 328(5976): 321-6.

Butler RN, Miller RA, Perry D et al. (2008) New model of health promotion and disease prevention for the 21st century BMJ 337.

See: Longo VD, Antebi A, Bartke A et al. (2015) Interventions to slow aging in humans: are we ready? Aging Cell 14(4): 497-510; The Academy of Medical Sciences (2009) Rejuvenating ageing research, available at: https://www.acmedsci.ac.uk/viewFile/publicationDownloads/ageingwe.pdf.

This target was chosen because the risk of death doubles in the period of seven years during the human life course. See: Olshansky, S., Perry, D., Miller, R. A., Butler, R.N (2006) In pursuit of the longevity dividend, available at: http://sjayolshansky.com/sjo/Background_files/TheScientist.pdf.

biogerontological research financially and to tackle regulatory and other obstacles that such efforts are confronted with.

29 At this stage, it is too early to predict how this new type of medicine would look; for instance, whether it would require a set of regular and complex medical interventions adapted to individual circumstances and physical conditions or whether simpler interventions, such as pharmaceutical drugs, would equally have the potential of being successful. It is also unclear what goals could be achieved after a successful paradigm shift. Since this is crucial for an ethical evaluation, these goals need to be distinguished on the basis of the basic biogerontological conceptions and the longevity revolution outlined above.

Practical goals of biogerontology: preparing a 'second longevity revolution'

- 30 In his utopia *New Atlantis*, Francis Bacon proclaimed four different goals in relation to longevity and ageing that are still valid for geriatrics and gerontology: the prolongation of life; managing incurable conditions in a better way; regaining youthfulness; and the retardation of ageing.⁵⁸ So far, better living conditions and modern medicine have contributed to the achievement of the first two of these goals. This is Butler's first 'longevity revolution' (see paragraph 8). The average human life expectancy has been extended to a life span that had previously only been achieved by a few people in society. Chronic illnesses occurring in old age, however, remain incurable, and geriatric care aims to better manage the frailty and morbidity associated with old age.
- 31 Biogerontologists are now preparing a second longevity revolution, one that would complete the first and continue its achievements beyond what has been possible so far. In this 'second longevity revolution', it is argued, Bacon's last two goals, which for now still remain utopian, will become reality: ageing will be slowed down, and taking it one step further, youth might be restored. Bacon's distinction of four goals remains helpful because it separates important categories of different aims related to longevity, disease, and biological ageing. From a biogerontological perspective, the fundamental category encompasses those aims which are connected to biological ageing. Successfully intervening in biological ageing processes will primarily 'retard ageing' and 'preserve youthfulness'. This could be achieved to various degrees by either slowing, halting or even reversing biological ageing. This will also have an impact on age-associated diseases. The main goal in this respect is to prevent such diseases or to find better ways of treating them.

Slowing ageing and tackling age-associated diseases

32 In the face of population ageing, the importance of this goal is uncontested. If biological ageing is slowed, or even halted or reversed, these diseases could be postponed or even fully prevented. If they are postponed, it is also possible that the period of time between their onset and death is shortened, which is referred to as a "compression of morbidity" (see also paragraph 34).

Bacon F (1989) *New Atlantis and the great instauration*, Revised Edition (Wheeling, Illinois: Harlan Davidson).

Longer lives

33 Slowing or halting ageing will have also the effect of extending the average human life span, either moderately or radically. An extension of the former trend characterising the first longevity revolution might be considered as 'moderate life extension'. For instance, the result could be to lift the current average life span slowly from around 80 years to the current maximum life span of 120. If ageing could be slowed significantly, arrested or even reversed, the outcome would be a "radical life extension". This would include any substantial increase beyond the current maximum life span. It is important to note that an increase in human longevity also has to be considered with a development of morbidity in old age. Longer lives may have a shorter, similar or longer period in which people suffer from age-associated diseases.

Compression of morbidity

34 What matters is not only the amount of time but also the phase of life that would be extended: the developmental span, the health span, or the senescent span. The obvious goal is to extend the health span at the expense of the senescent span, which corresponds to the widely acclaimed goal of a "compression of morbidity". Nobody argues that the senescent span should be deliberately prolonged, a prospect which has been presented as one of the dangers of interventions into ageing. However, biologists deny that this is a plausible outcome, as it contradicts the results of animal experiments: it is argued that the senescent span cannot be extended indefinitely in relation to the 'health span'. 1

Combined goals of interventions into ageing: a basis for an ethical analysis and evaluation

35 It is clear that some of these goals and corresponding priorities are more controversial than others. In general, preventing age-associated diseases in order to achieve a compression of morbidity is considered to be desirable. This is used as a fundamental justification for intervening in biological ageing: intervention for its own sake is considered to be more problematic. The same is true for a further extension of the human life span. The more radical the prospects of slowing ageing and extending life, the more concerns they raise. Therefore, extending the health span at the expense of the senescent span without extending the current average life span at all is a moderate scenario that would be generally acceptable. This would correspond to the original concept of a "compression of morbidity" as popularized by James F. Fries in the 1980s which has since become an important public policy goal in the face of population ageing. But a compression of morbidity achieved by slower ageing without an

See, for example, the observation of Francis Fukuyama who argued that manipulating agency could turn out societies into a "giant nursing home": Fukuyama F (2003) *Our posthuman future: consequences of the biotechnology revolution* (London: Profile Books).

Fries JF (1980) Aging, natural death, and the compression of morbidity New England Journal of

Fries JF (1980) Aging, natural death, and the compression of morbidity *New England Journal of Medicine* **303(3)**: 130-5; Jagger C (2000) Compression or expansion of morbidity - what does the future hold? *Age and Ageing* **29(2)**: 93-4.

Arking R (2006) *The biology of aging: observations and principles*, 3rd Edition (New York: Oxford University Press); Gems D (2011) Tragedy and delight: the ethics of decelerated ageing *Philosophical Transactions of the Royal Society of London Series B, Biological Sciences* **366(1561)**: 108-12.

increase in longevity is implausible according to biogerontologists. If health is improved in advanced ages, the average life span will increase as well. The senescent span will either simply be postponed or the age-related morbidities could be experienced longer, but in an alleviated way – something referred to as a 'dynamic equilibrium'. The proponents of the longevity dividend suggest a scenario that combines compression of morbidity and a moderate extension of the human life span by seven years. This could be accomplished in the next decades by slowing biological ageing. Finally, and more controversially, Aubrey de Grey argues that people who will experience arrested and even reversed ageing have already been born. His argument relies on the assumption that biological ageing is caused by several types of cellular and molecular damage. These are well-known and also the methods to repair them are already known. The next step would be to carry out systematic experiments with the aim of applying these methods.

36 Ethical evaluations of the 'second longevity revolution' need to distinguish these goals and predictions properly. They should also take the conceptions and methods of biogerontology, population ageing, and the interdisciplinary perspectives of geriatrics and gerontology on ageing and old age into account. However, up to this point, the bioethical debate has mostly focused on aspects of radical life span extension, such as 'immortality' achieved by arrested ageing. This also applies to the few reports by ethics advisory boards dealing with the prospect of a 'second longevity revolution' (see paragraph 30).

Ethical aspects: overviews and reports on life extension and interventions into ageing by expert groups

37 As early as 1979, the bioethicist Robert Veatch edited a volume of contributions from authors who are primarily linked to the Hastings Center on life extending technologies. Interestingly, the Hastings Center's research group on 'Death and dying' saw sufficient progress in relevant biotechnologies to raise several fundamental questions regarding the value of an extension of the human life span. As a consequence, this volume already deals with many of the basic abstract values that are relevant in this context. For instance, it addresses whether a further prolongation of the human life span is desirable, whether death is an evil, whether ageing is a disease, and whether equal access to life-extending technologies is a requirement of justice. The next important group that is concerned with the subject of increased longevity achieved by interventions that either slow or arrest ageing is the (US) President's Council on Bioethics. In the volume Beyond therapy from 2004, developments in the field of

Olshansky, S., Perry, D., Miller, R. A., Butler, R.N (2006) *In pursuit of the longevity dividend*, available at: http://sjayolshansky.com/sjo/Background_files/TheScientist.pdf.

Olshansky, S., Perry, D., Miller, R. A., Butler, R.N (2006) *In pursuit of the longevity dividend*, available at: http://sjayolshansky.com/sjo/Background_files/TheScientist.pdf.

⁶⁷ Veatch RM (1979) *Life span*, 1st Edition (San Francisco: Harper and Row).

Medicine **303(3)**: 130-5.

Graham P, Blakely T, Davis P, Sporle A, and Pearce N (2004) Compression, expansion, or dynamic equilibrium? The evolution of health expectancy in New Zealand *Journal of Epidemiology & Community Health* **58(8)**: 659-66.

See: SENS Research Foundation (2015) A reimagined research strategy for aging, available at: http://www.sens.org/research/introduction-to-sens-research; de Grey ADNJ, and Rae M (2007) Ending aging: the rejuvenation breakthroughs that could reverse human aging in our lifetime, 1st Edition (New York: St. Martin's Press).

human enhancement are discussed, and a chapter entitled 'Ageless bodies' reflects upon the perspectives of a 'second longevity revolution'. The report separates individual and social issues and discusses both, primarily from the perspective of the relevance of a 'natural life span' (corresponding to the current average life span) for a 'good life'. Bioethicists Stephen G. Post and Robert N. Binstock have also published a volume on the perspective of radical life extension, the so-called 'fountain of youth', which brings together contributions from many different disciplines. Many of the authors have also contributed to the debate on 'radical life span extension' elsewhere. Finally, in 2008, the National Intelligence Council published a report on six technologies that risk disrupting US society. This report envisages more general consequences in economics and culture if biogerontechnology is used to extend the human life span, and highlights the problem of equal access to these emerging technologies. A Foresight Report of the German Ministry for Science and Education refers to the NIC report and echoes its conclusions.

38 One would think that there would be more reports and overviews within the time span of 30 years considering the substantial changes for individuals and societies that could result from a second longevity revolution. Further, these reports are mainly focused on abstract values and the desirability of a radical life span extension. They are less aware of population ageing and the current social context. The House of Lords, ⁷² the European Commission, ⁷³ the World Health Organization, ⁷⁴ and the United Nations have tasked expert commissions to provide reports with issues related to the challenges of population ageing. It is necessary that the systematic ethical evaluation of a possible increase in longevity by slower ageing considers this work of national and international authorities and organisations (and vice versa). The same applies to a moderate life span extension and conceptions upon which a more modest biogerontological outlook, such as the programme of a longevity dividend, is based. The same often applies to individual bioethical authors who have dealt with the subject.

Ethical aspects: individual perspective

The individual value of increased longevity

39 Would a further increase in longevity that is achieved by slower ageing be good for individuals? The ethical evaluation of a possible second longevity revolution has to begin with this question before one can move on to the social aspects, such as the benefits to or burdens on societies, or questions of justice. Arguments as to whether increased longevity and slower ageing are good or not can be categorised according to

⁶⁸ Kass L (2003) *Beyond therapy: biotechnology and the pursuit of happiness* (New York: Harper Perennial).

⁶⁹ Post SG, and Binstock RH (2004) *The fountain of youth* (Oxford: Oxford University Press).

The National Intelligence Council (2008) *Disruptive civil technologies: six technologies with potential impacts on US interests out to 2025*, available at: https://fas.org/irp/nic/disruptive.pdf.

Vollmar HC, Georgieff P, and Cuhls K (2011) ['Deciphering aging': excerpts of the BMBF foresight process] Zeitschrift fur Gerontologie und Geriatrie **44(1)**: 66-70.

Select Committee on Public Service and Demographic Change (2013) *First report: ready for ageing?*, available at: http://www.publications.parliament.uk/pa/ld201213/ldselect/ldpublic/140/14002.htm.

European Commission (2015) *Ageing policy*, available at: http://ec.europa.eu/health/ageing/policy/index en.htm.

World Health Organization (2015) *Health topics: ageing*, available at: http://www.who.int/topics/ageing/en/.

United Nations (2015) Global issues: ageing, available at: http://www.un.org/en/globalissues/ageing/.

a common distinction of ethical theories. They can be based on utility in terms of pleasure and pain according to utilitarian approaches. Another set of arguments relate to theories of the good life and the corresponding conditions for a full or flourishing human life. Finally, arguments can be made based on duties in the context of deontological ethics. These different arguments can be further differentiated if they are referring either to moderate or to radical life extension (slower or arrested ageing).

Moderate life extension: arguments based on utility

40 As outlined above, moderate life extension would continue the trend of the first longevity revolution leading to a slow increase of average life expectancy in the next decades. If one accepts the evidence provided by biogerontology so far, slower ageing is likely to lead to improved health in old age and to longer lives. Proponents of such an outlook can not only justify their position with the high value attributed to longevity across cultures, but they can also point to reduced suffering from age-associated diseases⁷⁶ and to the experience of pleasure over a longer period of time, which can be aggregated across a longer life.⁷⁷ These arguments are difficult to refute on the basis of utility. However, it is possible to argue that the aggregation perspective is unjustified and that there are no substantial gains in terms of valuable experience if more years are added to the current life span. Further, in relation to suffering, it can be argued that this will simply be postponed as long as it is unclear whether a compression of morbidity will really be achieved.⁷⁸ But, while these arguments appear to focus on utility and relieving suffering, they are implicitly based on assumptions regarding the 'good life'.

Moderate life extension: arguments based on theories of the 'good life'

41 In order to deny the gains that could be made by means of moderate life extension, some positions take issue with life considered as a whole under the aspect of its flourishing. Van Tongeren has put forward an argument based on Nietzsche that the value of a life depends on the intensity of experience and not on its extension over time. Others have argued that the experience of physical ageing is valuable, even if it involves suffering. It is either an irreplaceable way to experience human finitude or considered to be a part of the human life course and a fully human life. On the other hand, supporters of a second longevity revolution have argued that the human potential

Gems D (2011) Tragedy and delight: the ethics of decelerated ageing *Philosophical Transactions of the Royal Society of London Series B, Biological Sciences* **366(1561)**: 108-12; Farrelly C (2009) Towards a more inclusive vision of the medical sciences *QJM* **102(8)**: 579-82; Moody HR (2001) Who's afraid of life extension *Generations* **25(4)**: 33-7.

Stock G, and Callahan D (2004) Debates point-counterpoint: would doubling the human life span be a net positive or negative for us either as individuals or as a society? *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* **59(6)**: B554-B9.

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Singer P (1991) Research into aging: should it be guided by the interests of present individual, future individuals, or the species?, in *Life span extension: Consequences and open questions*, Ludwig FC (Editor) (New York: Springer), Horrobin S (2006) The value of life and the value of life extension *Ann N Y Acad Sci* 1067: 94-105, Overall C (2003) *Aging, Death, And Human Longevity* (Berkeley and Los Angeles: University of California Press).

van Tongeren P (1990) [Longevity and meaning of life. Philosophical-ethical considerations of the theme 'extension of life'] *Tijdschr Gerontol Geriatr* **21**: 223-8.

Kass LR (2003) Ageless bodies, happy souls *The New Atlantis* **1(1)**: 9-28.

Vincent JA (2009) Ageing, anti-ageing, and anti-anti-ageing: who are the progressives in the debate on the future of human biological ageing? *Medicine Studies* **1(3)**: 197-208.

has not yet been fully exploited (the current life span being too short). The complexity of the current culture also requires a longer period of time for learning and acquiring the skills to bring human flourishing to a new level.⁸²

Radical life extension: arguments based on theories of the 'good life'

42 Whether radical life extension would be good for individuals is the subject of many thought experiments in fiction.83 The philosopher Bernard Williams analysed one of these thought experiments philosophically and came to a rather pessimistic conclusion: radically extended life spans would either lead to boredom or a loss of identity. If a human being would exist over a very long period of time, she will not be able to maintain the psychological connectedness necessary for her personal identity. As a consequence, a future self would completely lose any psychological connection with the present self: there will be no link between the personal identity of the present and of the future human being. Williams draws the conclusion that the present self cannot have an interest in the existence of the future self since they will be fully separated.⁸⁴ The bioethical literature has continued to discuss Williams' dilemma of boredom and loss of identity. Some have affirmed his conclusion that a radically prolonged life would be of no benefit because of the psychological limitations Williams outlines, 85 while others have rejected his assumptions. John Harris, for example, argues that if boredom were indeed a problem, we could still 'opt out' of our existence, if it would become insupportable. He also contested that despite the identity problem we would still have sufficient reason to be interested in an ongoing existence of a person in our body, albeit a different person from our own self.86 Others have denied the empirical premise of Williams' argument, claiming that there is no reason to believe that we would be bored in an insupportable way and there would not be any psychological connection in the personal identity of the prolonged existence.⁸⁷

Saving lives: deontological arguments

43 If we accept the connection between biological ageing and age-associated diseases and mortality, slowing ageing means to postpone death. John Harris has argued that saving lives by means of medical treatment, for instance, is nothing more than postponing death. Similarly, he and other authors have therefore equated preventing or treating ageing with saving lives. Based on these assumptions, there could even be a duty to slow or arrest ageing provided that this is possible.⁸⁸ Since the corresponding research would be saving lives, there is also a corresponding duty to support and carry out such research.⁸⁹ In English writing on bioethics, there has been little criticism of the

Schloendorn J (2006) Making the case for human life extension: personal arguments *Bioethics* **20(4)**: 191-202.

Williams B (1973) The Makropulos case: reflections on the tedium of immortality, in *The Problems of the Self*, (Cambridge: Cambridge University Press).

Kass L (2003) Beyond therapy: biotechnology and the pursuit of happiness (New York: Harper Perennial), Glannon W (2002) Indentity, prudential concern, and extended lives *Bioethics* **16(3)**: 266-83.

⁸⁶ Harris J (2004) Immortal ethics Annals of the New York Academy of Sciences 1019(1): 527-34.

Horrobin S (2006) Immortality, human nature, the value of life and the value of life extension *Bioethics* **20(6)**: 279-92, Schloendorn J (2006) Making the case for human life extension: personal arguments *Bioethics* **20(4)**: 191-202.

Harris J (2007) Enhancing evolution (Princeton and Oxford: Princeton University Press).

Beauvoir Sd (1955) *All men are mortal*, 1st Edition (Cleveland: World Pub. Co), Huxley A (1939) *After many a summer dies the swan* (New York, NY [u.a.]: Harper Brothers).

Farrelly C (2010) Equality and the duty to retard human ageing *Bioethics* **24(8)**: 384-94, de Grey AD

'saving lives' argument.⁹⁰ Such criticism would also have to discuss mortality and when death can be perceived as an evil.

Death as an evil: changing meanings of death

44 Several of these arguments amount to the implicit judgment of whether or not death is an evil, and under which circumstances it might not be one. If individuals could only benefit from a limited life span, then it would be logical to argue that death after such a life span would not be an evil. This argument was developed by Daniel Callahan⁹¹ who has also drawn the conclusion that there is no obligation to treat a deadly disease after a life span of such a length had been completed. 92 Further support for the argument that death after a particular lifespan is not an evil has been provided by the value assigned to the meaning of mortality. Some philosophers have defended the thesis that only mortality gives meaning to human life, and a shapeless and limitless life would also lack meaning and purpose. 93 Other philosophers have argued in exactly the opposite way, namely that death negates the meaning and value of human lives and deprives us of valuable experiences. 94 Another plausible implication of a second longevity revolution would be a change in the meaning of death: specifically in an understanding of when death is 'premature'. As the bioethicist Tristram Engelhardt has remarked, what a 'premature' death is depends on the technological possibilities of a society. 95 Since premature death is usually considered to be something bad, this could cause those individuals who do not have access to life-prolonging interventions used to slow ageing to feel particularly deprived. For those who do have access, an early death would be considered all the more tragic, since it implies a greater loss of expected life years. On the other hand, near the end of life there could be a stronger desire to control the time of death, which could lead to an increasing demand for physicianassisted suicide or euthanasia.96

Ethical aspects: social perspective

Overview: biodemographic scenarios

45 As in the case of the individual perspective, it is as well possible to structure the ethical implications for society following the common distinction between consequentialism, theory of the good life, and deontology. Social consequences will include different possible benefits or burdens on society in terms of factors such as overall happiness, or economic output. The social context for a good life could also significantly change through biomedicalisation (see paragraph 49). From a deontological perspective, it is

(2005) Life extension, human rights, and the rational refinement of repugnance *Journal of Medical Ethics* **31(11)**: 659-63.

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Some German authors have refuted this argument: Knell S (2012) Anti-aging, leben-retten und gerechtigkeit *Jahrbuch für Wissenschaft und Ethik* **16**: 5-40.

⁹² Callahan D (1995) *Setting limits*, 2nd Edition (Washington, D.C.: Georgetown University Press).

Jonas H (1992) The burden and blessing of mortality *Hastings Center Report* **22(1)**: 34-40, Kass LR (2003) Ageless bodies, happy souls *The New Atlantis* **1(1)**: 9-28.

Caplan AL (2005) Death as an unnatural process *EMBO reports* **6(S1)**: S72-S5, Nagel T (1970) Death *Nous*: 73-80.

⁹⁵ Engehardt T (1979) Is Aging a Disease?, in *Life span: values and life-extending technologies*, Veatch RM (Editor) (San Francisco: Harper and Row).

Davis JK (2015) Four ways life extension will change our relationship with death *Bioethics*: First published online (23 April).

necessary to consider questions of justice, which could be divided into freedom from discrimination, and equal access to interventions that slow ageing.

46 Several authors have suggested so-called 'biodemographic scenarios' as conceptual tools to evaluate the social implications of interventions that slow ageing. These scenarios project the different possible outcomes according to the goals of such interventions (see paragraph 35) from the individual to the social level. The first three scenarios describe the relation between the health span and the senescent span. A scenario of a compression of morbidity would imply that, on a societal level, the overall burden of age-associated diseases and conditions would decrease. The opposite is the case in an 'expansion of morbidity' scenario. Moderate or radical life extension is described in the scenarios called 'slower ageing' or 'arrested ageing'. Further, one should differentiate these latter scenarios according to a limited or broad/equal access to interventions that slow ageing. This is necessary in order to address questions of justice.

Social benefit or burden of life extension: utilitarian arguments

- 47 The scenario of a compression of morbidity if achieved by slower ageing would most likely be combined with a moderate life extension. This is the scenario of a longevity dividend on investment in biological ageing research. 97 The social benefit linked to the longevity dividend would consist in improving the problems attributed to population ageing: healthcare costs would be reduced; longer and more productive working lives for older people would alleviate the stress on pension provision and improve the dependency ratio. Even if just a 'dynamic equilibrium' were achieved, this could still contribute to a reduction of healthcare spending. However, some have argued that the unintended outcome of interventions slowing ageing would be that the senescent span would be extended together with the health span. Such an 'expansion of morbidity' would clearly exacerbate the problems mentioned above. 98 Others have dismissed the economic arguments of longer and more productive lives. Instead a further increase of older age groups would reduce the dynamics and productivity of a society. If social hierarchies were blocked by older generations for a longer period of time, severe intergenerational conflicts could be the result. 99 Such concerns are, however, based on the assumption that older people are inherently less innovative and less inclined to accept or bring about changes. These negative stereotypes of old age require further scrutiny (see paragraph 50).
- 48 Another common objection concerns projections of population growth, which would be accelerated the more people had access to life-extending interventions and the faster those technologies became available. This is called the 'Malthusian objection'. Either strict birth control would have to be instituted or the consumption of resources would become unsustainable, leading to a decrease in the quality of life, which would once again give rise to intergenerational conflicts.¹⁰⁰ A classical utilitarian argument against

Olshansky, S., Perry, D., Miller, R. A., Butler, R.N (2006) *In pursuit of the longevity dividend*, available at: http://sjayolshansky.com/sjo/Background_files/TheScientist.pdf.

Jonas H (1992) The burden and blessing of mortality *Hastings Center Report* **22(1)**: 34-40, Kass L (2003) *Beyond therapy: biotechnology and the pursuit of happiness* (New York: Harper Perennial).

Juengst ET, Binstock RH, Mehlman M, Post SG, and Whitehouse PJ (2003) Biogerontology, "anti-aging medicine," and the challenges of human enhancement *Hastings Center Report* **33(4)**: 21-30.

Davis JK (2005) Life-extension and the Malthusian Objection *The Journal of Medicine and Philosophy* **30(1)**: 27-44.

life extension was developed by Peter Singer. He argued that the aggregated happiness of a society with more young people would be higher. However, this assumption is problematic due to the fact that empirical evidence rather points to an increase of self-rated happiness in older ages. He argued that the aggregated happiness of a society with more young people would be higher.

Biomedicalisation of ageing: ageing and the good life in a social perspective

49 The concept of 'medicalisation' was developed in the 1970s. It is used to describe a process in which social phenomena or aspects of human life become subject to medical control. 'Biomedicalisation' refers to new biological technologies changing 'medicine' to 'biomedicine', which leads to different medical attitudes and methods, such as the focus on molecular processes. The term is often used with negative connotations. 103 Some authors have examined the biomedicalisation of ageing and described related phenomena such as the development of a corresponding industry and the increasing influence of the natural sciences in medicine. 104 Clearly, these are phenomena that are likely to become more common if biogerontological methods and conceptions gain greater influence in medicine. This would be the case in all scenarios. As a consequence of biomedicalisation, some authors note a greater focus on individual health risks, the division of people according to 'good' or 'bad' risks they embody, and finally a personal responsibility to deal with those risks by means of reasonable preventive behaviour. Biomedicine becomes a type of luxury medicine for those who have access and 'good' health risks. Society is then divided into biomedical 'haves' and biomedical 'have-nots'. 105 In sum, biomedicalisation prevents people from finding better ways to accept and integrate old age as a part of their life course, and consequently from developing an appropriate conception of a good or flourishing life in old age. In this way, this process would also contribute to the depreciation of old age and older people in society. Therefore, existing age-discrimination or ageism would be reinforced. 106

Age-discrimination and ageism: deontological arguments i

50 The social gerontologist John Vincent argues that basic biogerontological concepts stem from an ageist culture, which they will in turn reinforce once these concepts become more influential. This would violate the principle of non-discrimination of people because of their age. Examples include the basic definition of biological ageing such as biological ageing being characterised by 'deleterious changes'. Ageing is then

Singer P (1991) Research into aging: should it be guided by the interests of present individual, future individuals, or the species?, in *Life span extension: Consequences and open questions*, Ludwig FC (Editor) (New York: Springer).

Blanchflower DG, and Oswald AJ (2008) Is well-being U-shaped over the life cycle? Soc Sci Med 66: 1733-49.

Parens E (2013) On good and bad forms of medicalization *Bioethics* **27(1)**: 28-35.

Estes CL, and Binney EA (1989) The biomedicalization of aging: dangers and dilemmas *The Gerontologist* **29(5)**: 587-96, Kaufman SR, Shim JK, and Russ AJ (2004) Revisiting the biomedicalization of aging: Clinical trends and ethical challenges *The Gerontologist* **44**: 731-8, Clarke AE, Shim JK, Mamo L, Fosket JR, and Fishman JR (2010) Biomedicalization: technoscientific transformations of health, illness, and US biomedicine *Biomedicalization: Technoscience, health, and illness in the US*: 47-87.

Clarke AE, Shim JK, Mamo L, Fosket JR, and Fishman JR (2010) Biomedicalization: technoscientific transformations of health, illness, and US biomedicine *Biomedicalization: Technoscience, health, and illness in the US*: 47-87.

Vincent JA (2008) The cultural construction old age as a biological phenomenon: science and antiageing technologies *Journal of Aging Studies* **22(4)**: 331-9.

by definition bad and consequently seen as a pure process of decline. ¹⁰⁷ If old age loses its value as a part of life, age-discrimination and neglecting the problems of older people could result. This can be the case in medicine and healthcare where the focus lies on the prevention of old age altogether and where sometimes ageism and a lack of knowledge on old age is already seen as a problem. ¹⁰⁸ However, if the outcome is compressed morbidity or moderate life extension, the fourth age, with all its common health problems, will not disappear. At the same time, it could be increasingly ignored due to a focus on a youthful state. This indicates a possible conflict between geriatrics and social gerontology on the one hand and biogerontology on the other, since an appreciation of old age and proper care for older people are the goals of the former. ¹⁰⁹ Further, there could be a trend towards blaming people for their old age and related health problems resulting again in a reinforcement of negative stereotypes of old age and older people. ¹¹⁰

Health inequalities in old age and justice: deontological arguments ii

51 There are widespread expectations that interventions which slow ageing will be complex and costly in the beginning. If this were to be the case, access to interventions which slow ageing would likely be limited to those with the ability to pay, especially, perhaps, when it comes to 'radical life extension'. As a result, society could be divided into a slow-ageing, long-living elite, and a faster-ageing population who do not live as long. John Harris has argued that, while this could be problematic, the impossibility of general access to new technologies is not a valid reason to deny them to those who would benefit. In the long run, such a situation could change due to so-called 'trickle down' effects. On the other hand, considering the influential theory of justice, access to interventions which aim to slow ageing would be required by equality of opportunity. Existing health inequalities linked to social determinants could be increased. This is something that must be addressed by specific policies if health inequalities, which are not the result of personal decisions, are perceived to be unjust.

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Farrelly C (2007) Sufficiency, justice, and the pursuit of health extension *Rejuvenation Research* **10(4)**: 513-20.

Vincent JA (2008) The cultural construction old age as a biological phenomenon: science and antiageing technologies *Journal of Aging Studies* **22(4)**: 331-9.

Ehni H-J (2014) Ageism, in *Encyclopedia of global bioethics*, ten Have H (Editor) (Springer International Publishing).

Ehni H-J (2014) A Conflict of Interpretations in Gerontology, in *Health and Cognition in Old Age*, Leist AK, Kulmala J, and Nyqvist F (Editors) (Dordrecht: Springer International Publishing).

Zey MG (2007) Ageless nation: the quest for superlongevity and physical perfection (Far Hills, New Jersey: New Horizon Press), Spindler M (2010) [From the right to health to the responsibility for healthy aging: a new foundation for anti-aging medicine in Germany] Gesundheitswesen 72: 135-9.

Harris J (2004) Immortal ethics *Annals of the New York Academy of Sciences* **1019(1)**: 527-34

¹¹³ Buchanan AE (2011) Beyond humanity? (Oxford: Oxford University Press).

Farrelly C (2007) Sufficiency, justice, and the pursuit of health extension *Rejuvenation Research* **10(4)**: 513-20; Ehni H-J (2013) A "longevity dividend" for all? New interventions into aging and justice, in *Ethics, health policy and (anti-) aging: mixed blessings*, Schermer M, and Pinxten W (Editors) (Dordrecht: Springer); Ehni H-J, and Marckmann G (2009) Social justice, health inequities, and access to new agerelated interventions *An International Journal for History, Philosophy, and Ethics of Medicine & Allied Sciences* **1(3)**: 281-95.

Conclusion: open questions, future guidance, and public awareness

Open questions

52 There is a general consensus that at least compression of morbidity and moderate life extension are ethically legitimate goals from both an individual and a societal perspective. The evidence for a close connection between biological ageing and age-associated diseases in particular provides a strong justification for interventions that slow ageing. The main concern here is whether equal access to those interventions can be established. Otherwise, health inequalities and social inequality in general might increase, which has proven to be a fundamental problem in our societies in recent years. Based on this assessment, some important questions remain unanswered that deserve a closer examination.

Interdisciplinary perspectives and cooperation

53 First, an interdisciplinary dialogue between biogerontology, other gerontological disciplines, geriatrics, policy-makers, and other relevant disciplines needs to be fostered. The goal of such a dialogue would be to create an improved mutual understanding of the different interpretations of ageing and their practical goals. If this could be accomplished, then the widely approved goals of active ageing, healthy ageing or compression of morbidity could be achieved through mutual effort. Possible negative consequences could be avoided as well, such as one-sided, naturalistic, or negative perspectives on ageing, depreciation of ageing and old age, and negligence towards the remaining problems of the fourth age.

Problems of equal access and justice

54 Part of this interdisciplinary dialogue needs to address the question as to what new medicine used to slow ageing would look like. Such a prediction would be a necessary starting point in order to estimate possible access to these interventions and potential obstacles.

Global justice

55 There is currently no debate on what kind of duties follow from the perspective of global justice up to this point. If a second longevity revolution begins in industrialised countries, it will come at a point when the first has not yet been completed in many low and middle income countries. Important global health inequalities and differences in life expectancy remain. There is also a lack of investment in the research and development of medical interventions that address health problems in low and middle income countries. Do industrialised countries have the duty to forego the second longevity revolution until these issues have been addressed? This question has to be discussed in light of the conflict between cosmopolitan theories demanding global equality and particularist theories arguing for a legitimate preferential treatment of the citizens living together in a state.

See: http://www.globalforumhealth.org/ and Capron AM (2007) Imagining a new world: using internationalism to overcome the 10/90 gap in bioethics *Bioethics* **21(8)**: 409-12.

Guidance options

56 If ethical problems that result from this new biomedical technology are identified, it is necessary to discuss how they can be managed in a better way with the help of legal and ethical guidance. Buchanan has identified three guidance options that provide a useful basis for such discussions: prohibition of technologies with negative ethical effects; an increased focus on the creation of those with an expected positive effect and an effort for the diffusion of these if required by justice. ¹¹⁶

Increasing public awareness

57 Finally, public awareness of biogerontology, its conceptions, goals, and potential benefits and risks is low and needs to increase. Only a few surveys (in Australia and Germany) have been conducted in which people were asked about their expectations and preferences if interventions that slow ageing were to become available. A discourse project is being financed by the German Ministry for Education and Research to foster the public debate on biogerontology. Medical students, who are one of the target groups, have also been shown to have little knowledge of the existence of this science. The same goes for the media (e.g. typing in the keyword "biogerontology" on newspaper websites online generates far fewer hits than when searching for "Aubrey de Grey"). This demonstrates – unsurprisingly – that utopian goals gain more attention than the mainstream science of biological ageing, which is true for bioethics as well. This does not mean that it is unnecessary to discuss a utopian outlook on an ageless life and society. However, such an outlook is also likely to create more concerns and detract from both the problems and the possible benefits of the results from the impending second longevity revolution.

Buchanan AE (2011) *Beyond humanity?* (Oxford: Oxford University Press).

Feeser-Lichterfeld Uv, Fuchs M, Illes F *et al.* (2007) Lebensverlängerung und Verlangsamung des menschlichen Alterns. Erträge eines interdisziplinären Forschungsprojekts *Jahrbuch für Wissenschaft und Ethik* **12**: 219–54, Lucke J, Ryan B, and Hall W (2006) What does the community think about lifespan extension technologies? The need for an empirical base for ethical and policy debates *Australasian Journal on Ageing* **25**: 180-4, Lucke JC, and Hall W (2005) Who wants to live forever? *EMBO reports* **6**: 98-102, Partridge B, Underwood M, Lucke J, Bartlett H, and Hall W (2009) Ethical concerns in the community about technologies to extend human life span *Am J Bioeth* **9**: 68-76

Universität Tübingen (2013) *Project "discourse biogerontology"* available at: http://www.unituebingen.de/en/facilities/zentrale-einrichtungen/international-centre-for-ethics-in-the-sciences-and-humanities/research/ethics-and-education/previous-projects/project-discourse-biogerontology.html.