

Background

The Academy was recently invited to respond to the House of Lords Select Committee on Science and Technology inquiry into the 'Scientific Aspects of Ageing' (http://www.parliament.uk/parliamentary_committees/lords_select/stiageing.cfm)

Evidence was sought on how science and technology can help improve people's prospects of healthy and active life expectancy, and whether Government policy is in place to achieve this. In particular, the call for evidence focused on:

- the biological processes of ageing;
- the application of research towards improvement of the quality of life; and
- in both these areas, the direction and coordination of research

Health care for older people and the economic aspects of the increase in the life expectancy (such as the future funding of pensions) were explicitly excluded from the inquiry.

Written evidence was sought from a wide range of Academy Fellows and the following working group was convened in order to develop the response further:

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Summary

- 1 The aim of biomedical research into ageing should be to improve the health and activity of people as they age. Extension of lifespan may well occur as a secondary consequence of improvement in health, but should not be seen as the primary goal. Life expectancy in industrialised societies has been increasing since the middle of the 19th century, with demographic figures showing no evidence for a slow-down.¹ An understanding of the factors that make for healthy, active ageing will therefore improve the quality of life for a large, and increasing section, of the population.
- 2 Research into ageing makes economic sense, as well as constituting a moral imperative. Clinical statistics show that health care expenditure does not necessarily depend on age, i.e. when disease strikes an older person, there is a higher rate of fatality and a shorter period of disability.² Prolonging healthy life will therefore, other things being equal, reduce the costs associated with long-term illness in later years. Research can also be expected to reduce the functional impact of conditions such as Alzheimer's disease, even if reducing the incidence proves more difficult. The widespread fear that enabling people to live longer by improving their health will result in an additional economic burden on health care is therefore not underpinned by evidence.
- 3 Research using short-lived model organisms has identified a range of interventions that can delay some of the manifestations of ageing in these species. Furthermore, advances in molecular biology, genetics and genomics increasingly show that principles established in model organisms can be translated across species. There are now unprecedented opportunities to increase our understanding of the intrinsic ageing process, how it constitutes a key risk factor for multiple diseases and how interventions might improve health and activity during ageing.
- 4 The UK is well positioned to contribute to, and exploit, the global explosion in ageing research. However, international comparisons, particularly with the United States, show that the volume of ageing research in the UK is low. UK research in this area is fragmented and structured in a way that neither takes full advantage of resources nor maximises translational benefit. In this response, we indicate realistic ways in which the UK research base could be harnessed to improve the health and well-being of older people, including:
 1. **A joined-up national programme that co-ordinates both funding and research strategy into healthy ageing.** This should incorporate:
 - A concerted strategy of capacity-building, including Fellowships for clinical and basic scientists;
 - The creation of physical centres within which clinical and basic scientists can work together and share resources.
 2. **Improvements in clinical trials and population-based research** through:
 - Improved use of the research opportunities presented by the NHS;
 - Increased inclusion of older people, of varying social and ethnic groups, in clinical trials and epidemiological studies;
 - Improved availability and detail of clinical trial data.

What are promising avenues for research? How will such research benefit older people and delay the onset of long-term illnesses and disabilities?

Basic science

- 5 Genetics and genomics will continue to make substantial contributions to progress in ageing research. These are areas in which the UK is traditionally strong and are enhanced by the UK's role in the genome projects and the presence of world-class institutions such as the Sanger Centre. The establishment of BioBank will also bring great benefits to UK researchers, although its design has unfortunately not been optimised for ageing research, as it will exclude participants over the age of 65.
- 6 The fields of cell and molecular biology are also making great strides in UK ageing research. A recent example is the discovery that the shortening of telomeres at the ends of chromosomes acts as a marker for the biological (as opposed to chronological) age of individuals, and hence their vulnerability to a range of age-associated diseases. Physiological variation between individuals increases significantly with age, and the goals of 'personalised medicine' might therefore bring particular benefits to older people in terms of enhancing efficacy while reducing adverse effects. Biomarkers that allow identification of patients who might most benefit from particular interventions are therefore of great value.
- 7 There has been a growing shift of focus to viewing ageing as a life long process, with significant determinants of later-life illness acting in adolescence, childhood and even *in utero*.³ UK research into the early origins of patterns of ageing has led the world. Research should now be directed to the ways in which genes and the environment act at different stages in life to influence health during ageing.
- 8 The UK is particularly well positioned with regard to stem cell research. Less restrictive regulation will allow UK researchers to seize momentum and gain a global competitive advantage, notably in exploring potential novel treatments for the common degenerative disorders associated with ageing.

Population research

- 9 Research in the fields of epidemiology, demography and population genetics greatly increase our understanding of the major determinants of healthy ageing. While the UK is strong in these fields, the potential for large-scale research of this kind has not yet been realised. The registration and record systems of the National Health Service have the potential to provide researchers with an extremely useful and powerful resource. Unfortunately, the quality of routine data generated by the NHS is relatively poor and has never matched the enormous research potential demonstrated by US patient databases such as Medicare. The value of record linkage methods was demonstrated by a group of Oxford researchers as long ago as the 1960s⁴, yet work in this area continues to be inhibited by a confusing regulatory framework and a great deal of bureaucracy.
- 10 Primary care based population research can evaluate data relating to individuals who may not currently be the recipients of healthcare. It is likely that future prospective cohort studies investigating environmental, genetic and disease interactions will also be based in a primary care setting.⁵ It is therefore crucial that the potential contribution from community-based sites is better harnessed.

Clinical trials

- 11 In order to achieve the maximum benefit for older people, it is important that older age groups are appropriately included in both epidemiological research and clinical trials, and that the range of individual variation is taken into account. Older people (and especially frail older people) are generally under-represented in clinical trials of treatments for which they are often the major consumers and from which they potentially have the most to gain. Outcomes from prescribing drugs for older people can differ greatly from those observed in trials of younger adults and unrepresentatively healthy older people.⁶ It is often the case that the co-morbidities and poly-pharmacy that occur with greater frequency in older people exclude them from participation in trials. However, information on the effects of potential treatments on co-morbidities and interactions with other drugs is extremely important in order to inform pragmatic decision-making. The situation would be vastly improved by greater availability and detail of clinical trial data. Better access to this information would allow the sub-group analysis necessary to generate hypotheses about the determinants of responses in older people.⁷

Differences between the sexes, and between different social and ethnic groups in the UK.

Gender differences

- 12 Statistics show that women live about six years longer than men. Four of these six years can be accounted for by the failure of male mortality in middle age to fall at the same rate as women in the first half of the 20th century.⁸ This has created a disproportionate number of widows suffering personal and economic hardship. Despite its widespread recognition, many aspects of the gender difference in longevity are not yet understood. For instance, why did the 4 year difference emerge in the 20th century and why does it persist despite the convergence in lifestyles of men and women?
- 13 There is also an important difference between men and women in how ageing affects the reproductive system. Since many women today are choosing to start their families later, the impact of female reproductive senescence and menopause deserves particular attention.

Social and ethnic differences

- 14 Recent work implies that clear differences exist between social groups in the UK in their pattern of ageing. Of particular note is work that shows that psychological stress, including stress associated with work, may be a significant impairment to healthy ageing.⁹ The biological mechanisms of this effect certainly merit further study.
- 15 With regard to ethnic differences, a recent Canadian study showed that, although the *prevalence* of heart disease varied greatly in the 52 countries examined, the actual *causes* of disease (e.g. hypertension, diabetes, smoking, alcohol, abnormal lipids) did not differ.¹⁰ However, ethnic groups do show marked differences in ageing patterns, most likely through differences in interactions between genetic and environmental factors. As a paradigm of gene-lifestyle interaction, it is suspected that the “thrifty genes” postulated by J.V. Neal in 1962 may contribute to the high risk of diabetes and cardiovascular disease among some ethnic groups.¹¹
- 16 Differences in the impact of risk factors on social and ethnic groups are important clues in understanding the nature of gene-lifestyle interactions. The

diverse demographics of the UK provide particular opportunities for research in this area. It is therefore essential that the composition of populations chosen for both epidemiological research and clinical trials reflect this diversity, whenever conclusions are to be drawn about the population as a whole.

The application of research in technology and design to improve the quality of life of older people, including—

- Existing technologies which could be used to a greater extent to benefit older people;
 - The development of new technologies.
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- 17 Research into technologies to improve life for older people covers a broad range of social sciences, design and engineering disciplines. We will restrict our response to issues concerning biomedical technologies. This is an area where more clearly defined responsibility and co-ordination would make a real difference to older people and their carers. At a user level, older people with impairments often find it difficult to obtain objective advice about the availability and individual suitability of appropriate technologies. This work is often left to charities, whose local representatives may have difficulty keeping up to date with advances in technology.
- 18 On a clinical level, the input of technology for older people into clinical environments is not systematic and there is poor feedback from the needs of clinics into technological development. Much would be gained from the formal assessment of existing technologies, many of which lack evidence about their benefit or safety.¹² Similarly, the systematic evaluation of new and untested technological interventions would allow more effective prioritisation and targeting. Importantly, the results of such evidence-based assessments must be disseminated to practitioners, carers, patients and the wider public.
- 19 The lack of funding for 'proof of concept' developments and the poor translation of technological interventions are symptoms of the wider crisis in experimental medicine in the UK. This activity is crucial in ensuring that the most appropriate diagnostic and therapeutic technologies are developed for the benefit of patients. The Academy report 'Strengthening Clinical Research' calls for the establishment of a new paradigm for experimental medicine, involving improvements in infrastructure, careers, programme support and collaboration with industry.⁵

How effectively is research co-ordinated in the public, private and charitable sectors (including internationally)?

- 20 Research into ageing is poorly co-ordinated in the UK. At the level of individual institutions, it is clear that the implementation of the Research Assessment Exercise has had some unfortunate side-effects, particularly the discouragement of the collaborative, inter-disciplinary and translational approaches upon which ageing research depends. Much ageing research is also by its very nature long term, even for work with experimental animals, and this is often not recognised in traditional approaches to funding and research management.
- 21 The importance of research specifically directed to ageing has from time to time been recognised by individual research councils. However, these rather scattered, generally 3-year, initiatives have been insufficient to make a substantial impact. A consistent, longer-term policy is needed. Attempts to co-

ordinate publicly funded activities, including those of the research councils and the NHS, have been ineffective, almost to the point of invisibility. Better monitoring and evaluation of the outcomes of existing funding programmes is needed. In view of the potential for re-badging of existing research programmes, and in order to help align them with other scientific research on ageing, an external audit of the publicly funded portfolio of research into ageing would also be informative.

- 22 Many of the resources that are integral to ageing research, e.g. colonies of ageing animals, tissue banks, fully phenotyped human population genetic data and so on, are simply too expensive and large scale to be supported by any individual institution. Co-ordinated access to an established network of shared resources would greatly improve the current situation.
- 23 The problems outlined here would be best tackled by a joined-up national programme that co-ordinates both funding and strategy for ageing research. Such a programme would replace and expand on existing research council and NHS programmes. This strategy would allow the identification of any gaps in the UK's ageing research portfolio and go some way to achieving an optimal use of resources in the field.

Have the correct priorities been identified? Are there any gaps in research?

- 24 With regard to research into age-associated diseases, there is little evidence that funding correlates well with the impact of diseases on health and well-being. This can be partially accounted for by the presence of large disease-specific research charities, whose combined focus does not correspond well to disease prevalence. While it is difficult for research councils to address this disparity through directed funding, there appears to be little transparency in the cost/benefit analyses applied to research council strategies when setting priorities for ageing relevant research.
- 25 The lack of good quality data about the diseases and disabilities affecting older people in the UK is also a major hindrance to appropriate priority setting. The resources available through the NHS have enormous potential to contribute to our understanding. However, as outlined earlier, NHS population research and database construction in this area is woefully inadequate.

Is there sufficient research capability in the UK?

- 26 There is under-capacity in ageing research in both clinical and basic science communities in the UK. The science of ageing is inherently multidisciplinary, with individual research projects often involving contributions from disciplines that have traditionally been viewed as separate. Both training and research are at their most effective when conducted in groups of collaborating principal investigators. Despite the success of some existing aging initiatives, few UK universities are getting on board. Incentives to enter and stay in ageing research and an increase in the number of collaborating groups working in the area are needed. Ageing research in the US has benefited from a strategy in which groups who were already carrying out world-class research were encouraged to shift their focus to issues related to ageing. This strategy might be usefully employed in the UK, where a world-class HIV research programme was nurtured by similar means.

- 27 Not all medical schools have an academic department for the medicine of ageing, and geriatrics is often seen as the 'poor sister' to other medical specialities. It is notable that few trainee GPs go through a geriatric rotation, despite the vast majority of their patients being older. There is a negative feedback loop from the unpopularity of care of older people as a clinical speciality (fewer geriatrics house jobs chosen) and a lack of clinical academic attention. This leads to a significant question over the quality of clinical academics in this area. A concerted strategy of capacity-building is needed, for instance by creating high prestige, high value fellowships for clinical and basic scientists in ageing research. This kind of targeted approach is recommended in the Academy report 'The tenure-track clinician scientist: A new career pathway to promote recruitment into clinical academic medicine'.¹³
- 28 In comparison with other clinical specialities, clinical gerontology appears to suffer from greater separation from its basic science counterparts. The development of relevant research programmes that are effectively translated into clinical practice requires greater interaction at all levels between scientists and clinicians. This would be best achieved by the creation of centres in which scientists and clinicians can work side by side, preferably within or very near the place where clinical practice takes place. The development of such centres should be a national priority.

Is the research being used to inform policy?

- 29 The Government is to be encouraged in its new initiative on public health. However, the potential impact of public health policies on healthy ageing has not been sufficiently emphasised. For instance, the impact of current trends in obesity and type II diabetes on the health of older people must be comprehensively assessed in order to inform robust policy.
- 30 When using evidence to inform policy, there must be improved recognition that, although observational and epidemiological studies may identify possible interventions, their efficacy and safety can only be determined by appropriately controlled clinical trials. It is essential that potential interventions are properly tested before they pass into general acceptance and use. Untested (and sometimes potentially dangerous) 'anti-ageing' substances and practices are widely accessible and promoted in the UK. In the face of often poor quality media coverage of age-related health issues, advice to the public must be clear, unambiguous and derived from evidence-based research. The type of research that is currently reported under strategies of anti-ageing may actually discourage people from joining clinical trials and may even discourage academics and clinicians from entering the field.
- 31 However, the Academy welcomes recent Government interest in achieving a balance between individual and Governmental roles and responsibilities for health. Similarly, the interest of the House of Lords Select Committee on Science and Technology is very encouraging. Ensuring adequate resources and support for ageing research will in turn deliver the evidence upon which effective policy decisions can be made.
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