The Ageing Process and Healthy Ageing.

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This paper incorporates a review of the general literature on ageing, healthy ageing, biomarkers, health promotion interventions and inequalities and their impact on ageing and also on success of health promotion activities. Overall there is a less strong focus on ethnicity and ageing, but more general focus on the ageing process.

Life expectancy and Healthy life expectancy

The UK like most developed countries is experiencing a significant demographic shift, with falling birth rates and increasing life expectancy resulting in higher proportions of older people within the population. Life expectancy is increasing at approximately two years per decade and in the 25 year period from 1984 to 2009 the number of individuals aged over 65 years increased by 1.7 million¹. Moreover this trend looks set to continue with current predictions suggesting that 23% of the population will be aged over 65 by 2034 and 5% will be in the “oldest old” group of over 85 year olds¹. It is perhaps these figures for the oldest age group that are most dramatic: in 1951 there were only 200,000 aged 85 and over recorded in the UK census, just 50 years later in 2001 this had increased to 1.1 million². Importantly, just as there are differences in life expectancy between economically developed countries, there are also significant differences with geographical location within the UK. In 2002 male life expectancy was 76.2 years in England, but only 73.5 in Scotland. For females the figures are 80.7 and 78.9 respectively. There are also surprisingly large local variations in life expectancy. Within London, figures for male life expectancy in 1998-2000 ranged from 78.4 in Westminster to 72.7 in Stratford³. A map of the cross-city train line in Birmingham emphasises the differences in life expectancy across the city, with just 8 stops on the line showing an 8 year disparity (Figure 1)⁴. The highest life expectancy in 2011 was seen in Sutton Coldfield at 84 years but fell by 7 years to 77 in Duddeston and by 8 years to 76 in Soho, respectively areas of lower socioeconomic status and high ethnic minority populations⁴.
Whilst the increased lifespan is a positive product of improved healthcare, widespread uptake of prophylactic measures such as vaccinations, access to clean water, improved nutrition and education, there is mounting evidence that healthspan (the period throughout life spent in good health) has not kept pace with lifespan. In the US in the twenty years from 1990 to 2010 life expectancy increased by 3.0 years, but healthy life expectancy increased by only 2.3 years. Data for the UK are similar, with life expectancy increasing by 4.2 years, whilst healthy life expectancy increased by only 3.2 years. Interestingly if the data are split by gender then life expectancy has increased in both sexes but healthy life expectancy gains are lower in females, thus women spend longer in poor health in old age. In 2001 it was estimated that men in England could expect to spend 6.9 years in poor health and for women this was 8.3 years. The end result is that much of the cost of health and social care in the UK is concentrated in the last decade of life.

Recent reports of the analysis of data from the Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) for changes in life expectancy, showing patterns of health loss in the UK and the major preventable risks underlying these patterns, have revealed both positive and negative changes from 1990 to 2010. Life expectancy increased by 4.2 years in this period, but the UK performed significantly worse than 18 comparator countries for age-standardised death rates, age-standardised years of life lost (YLL) rates, and life expectancy in 2010. For all age groups, the contributions of Alzheimer's disease (increase of 137%), cirrhosis (65% increase), and drug use disorders (577% increase) to premature mortality rose from 1990 to 2010. Importantly, as years lived with disability (YLDs) per person by age and sex have not changed greatly from 1990 to 2010 but age-specific mortality has reduced, the importance of chronic disability to health is on the increase. The major causes of YLDs in 2010 were mental and behavioural disorders (21.5% of YLDs) and musculoskeletal disorders (30.5%). The leading risk factors, expressed as percentage of disability-adjusted life years (DALYs) were found to be smoking (11.8%), increased blood pressure...
(9.0 %), high body-mass index (8.6%), diet and physical inactivity (14.3%). These data suggest that if we are to extend healthspan in line with lifespan in the future, thus compressing morbidity in old age, then the growing burden of disability, particularly from mental disorders, substance use, musculoskeletal disorders and falls will require an extended and strategic public health and social care policy response.

The Ageing process
During the evidence gathering it became clear that ageing is much more than the accumulation of years and candles on the birthday cake: it has chronological, environmental, biological and psychological influences. In addition, although ageing may be viewed by many to be a negative process, many of its features are neutral with regard to health, such as hair greying or the wrinkling of skin. For this reason many biogerontologists prefer the term senescence in order to encompass functional decline. Thus for the purposes of this report a physiological definition of ageing has been considered as “the increasing frailty of an organism with time that reduces the ability to deal with stress, resulting in increased chance of disease and death”. However, ageing is also highly variable, being experienced and interpreted differently by each person and is malleable as it can be modulated by both internal biological processes and external exposures.

Ageing is a complex process at the biological level with researchers still in disagreement about the underlying causes at the cell and molecular level and their relative contribution. However, most biogerontologists would agree that ageing is the result of the build up of damaged constituents, either as a failure to remove them, prevent their production, or repair the damage caused and the failure to replace cells lost as a result\(^9\). The underlying cause of this build of damage and inability to deal with wear and tear with increasing age has been ascribed recently to nine factors: mitochondrial dysfunction, genome instability, stem cell exhaustion, loss of proteostasis, cell senescence, deregulated nutrient sensing, telomere shortening, epigenetic alterations and reduced cell-cell communication\(^9\). These processes alone or in combination explain common age-related changes such as loss of muscle which occurs at a rate of 0.5-2% per year during adulthood and loss of key hormones with far reaching effect on tissue maintenance, growth, reproduction and mental wellbeing, for example Growth hormone is lost during somatopause, sex hormones during menopause and andropause and the androgen DHEA during adrenopause. Recently a key finding has been that in rodent models the removal of senescent cells, that is those cells that are no longer able to proliferate, resulted in extension of lifespan in the mice, but importantly reductions in a wide range of age-related disease including cardiovascular disease, cancer, neurodegeneration, muscle and bone loss\(^10\). As there is growing evidence that such cells also accumulate with age in humans\(^11\), the build up of senescent cells in tissues may prove to be an important process in the functional decline and entry in to pathology seen with human ageing.

Population level studies, including those using twins, have suggested that only 25% of longevity is heritable, thus 75% is dictated by environmental influences and is open to interventions both positive and negative. As such there is a need for biomarkers to determine the efficacy of such interventions – with the length of human lifespan waiting until old age to determine the efficacy of interventions in childhood or early adulthood is not practical! A biomarker of ageing has been defined by Baker and Sprott in 1988\(^12\) as “a biological parameter of an organism that either alone or
in some multivariate composite will, in the absence of disease, better predict functional capability at some late age, than will chronological age”. The search for biomarkers has been pursued for many years, used up much research funding and remains contentious. Just as there is no unifying theory for the cause of ageing, there is unlikely to be a single biomarker of ageing\textsuperscript{13} and rather a composite set of variables is likely to emerge. Current research would suggest that this grouping would include inflammatory status, cognitive function, sociodemographic characteristics, allostatic load, telomere length and mitochondrial damage\textsuperscript{14}.

**Interventions to modify the ageing process**

Studies in a wide variety of animal models from fruit flies to rodents has indicated that lifespan can be extended significantly by a variety of interventions, these include lifestyle interventions such as caloric restriction (reducing the number of calories ingested if organism are fed ad libitum by 25-30%) and pharmacological interventions (rapamycin) or genetic manipulations which target the pathways activated by caloric restriction. Importantly these interventions also reduce dramatically the levels of age-related pathology\textsuperscript{15}. Epidemiological evidence also suggest that such lifestyle choices may work in humans: populations such as the Okinawan Japanese who intake 20-40% less calories than US or European counterparts have high numbers of centenarians and lower incidence of several cancers (breast, prostate), fewer heart attacks and better retention of cognitive ability. Large longitudinal studies such as the EPIC Norfolk study have revealed that just four more modest health behaviours can increase mortality and reduce risk of life-threatening conditions such as stroke, namely: Not smoking, taking regular exercise, modest alcohol consumption and eating 5 portions of fruit or vegetables per day\textsuperscript{16}.

Despite clear evidence that lifestyle influences lifespan and health span and helps to explain much of the variation in longevity in populations, there is still poor uptake of health advice in the UK. Levels of smoking have halved in the last 20 years but this has been attributed largely to the prohibition of smoking in public places. The current recommendations on physical activity, namely 150 minutes of aerobic exercise per week, are adopted by less than 1 in 5 older adults and the consequences of excessive alcohol intake are one of the few medical conditions that are increasing rapidly over the last decade. The balance between persuasion and legislation for uptake of positive health behaviours will be a necessary debate in the future if we are to convert the findings from health and ageing research in to impact on Healthspan and lifespan.
References

8. From Kennedys slide