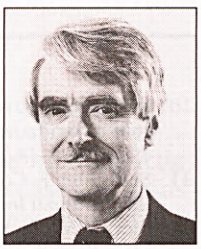
A correct compassion: the medical response to an ageing society.

The Harveian Oration of 1997



Professor Sir John Grimley Evans
MA, MD, FRCP, FFPHM

The Harveian Oration is given annually at the College under an indenture of William Harvey in 1656. The 1997 Oration was given on 15 October 1997 by **Professor Sir John Grimley Evans,** Professor of Clinical Geratology at the University of Oxford. The full text is available from the Publications Department at £3.00 per copy.

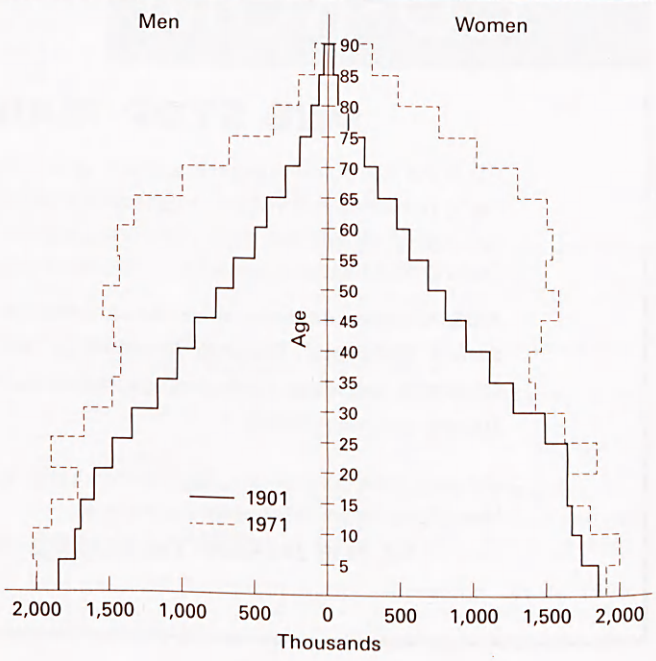
In the words of one of his biographers, William Harvey was the first Englishman to be what we would now recognise as a scientist. 'He observed the facts as we observe them, he experimented as we experiment and he reasoned as we reason'[1]. In responding to the impact of the ageing of our population on medicine and society, we need to observe, experiment and reason. We also have to recognise that the responsibilities of the medical profession are now far wider and deeper than Harvey could have anticipated; medicine has become an institutionalised component of the social structure of the nation. As doctors, we accept the duty implied by Harvey to search out and apply the knowledge relevant to our craft. But the medical profession – as both a conscientious servant of the people, and a privileged elite – has a duty of concern for the policy as well as the practice of medicine. James Kirkup, in a poem honouring the surgeon Philip Allison, wrote of 'a correct compassion' whereby doctors translate their knowledge and human concern into practical and coolly appraised action[2]. Forty years later we are aware, sometimes uncomfortably, that a correct compassion has to extend beyond the patient in front of us to those who are not, or not yet, our patients but who may be affected by the decisions we make.

The ageing population

So far we have met only the first of two waves of ageing of the British population. At the beginning of this century Britain underwent the 'demographic transition' from a pattern of high birth and high mortality rates to one of low birth and low mortality rates common to all nations undergoing economic development. As national income rises there comes a point when, for reasons that are not always clear and probably differ between nations, infant and child mortality rates fall. There is then a lag, typically of a generation, before fertility and completed family sizes also decline. During this lag a bolus of unprecedented survivors of childhood is released into the population. This can be seen as a bulge in the population structure of England and Wales in the 1971 census (Fig 1). The passage of this cohort through old age has been largely responsible for the increase in numbers of older people over the past twenty years. The size of the elderly population will now become more stable for two or three decades. The new wave of population ageing will come with the arrival in old age of the cohort of post-war 'baby-boomers' in the third and fourth decades of the new millennium.

The second cause of ageing of populations, again linked to economic advancement, is a fall in mortality rates in middle age and later life. In the UK this has been continuous for women since the start of the century but in men the fall was delayed by the epidemic of coronary heart disease and smoking-related diseases. We do not know whether older people in the UK are living longer because they are fitter or because unfit and chronically ill people are being kept alive longer. These two processes, which may coexist, have very different implications for health and social

Fig 1. Population pyramids of men and women in England and Wales: 1901 and 1971.



services. One means of monitoring the needs for and the success of services for an ageing population would be by measuring some form of healthy active life expectancy (HALE) at later ages[3,4]. At present we have no adequate data on this in the UK. Suggestions that recent increases in total life expectancy in Britain involve prolongation of the average period of disability before death are derived from the General Household Survey (GHS)[5]. The GHS estimates of disability are based on self-report only and its sampling frame does not include institutionalised people. It will register an increase in disability if improvements in community care enable more unwell older people to live in their own homes rather than having to move into institutions.

Where good data on active life expectancy are available an interesting paradox emerges. Table 1 presents data calculated from a study in Massachusetts over 20 years ago[6] but recent data from the Netherlands[7] show the same pattern. The partition of total life expectancy into dependent and non-dependent years shows that although women outlive men, their extra years are accounted for entirely by years of dependency. Moreover, women tend to marry men older than themselves and so are likely to bear their heavier burden of disability when widowed and in relative poverty. In the USA this pattern means that while only one in seven of men who attain the age of 65 can expect to spend a year or more in a nursing home before death, for women the figure is one in three[8].

In the absence of clear indications of how age-associated morbidity is changing, we can only view the future by projecting current patterns of illness and disability, and use and costs of services, onto future age structures. Figure 2 combines data on disability[9] with population projections[10] to estimate the growth in numbers of older people who will be affected over the next decades. Many influences may intervene to mitigate the needs for health care implicit in the figures. None the less, a correct compassion requires us to prepare for the challenge they represent.

There are four things to be done: we must agree on what are to be the aims of health care for an ageing population; we must maximise the efficiency of the services we provide; we must minimise the need for care by reducing the incidence of age-associated disease and disability. First, however, we should think about funding, for it would be probably unrealistic, and certainly imprudent, not to expect costs of health and social services to rise if ideologically and socially acceptable standards are to be sustained.

Funding

If patterns of practice and costs remain as at present the main financial impact of ageing in the UK will fall on the long-term care sector rather than on acute secondary or primary care[11]. By the year 2030 expenditure on long-term care alone will amount to nearly

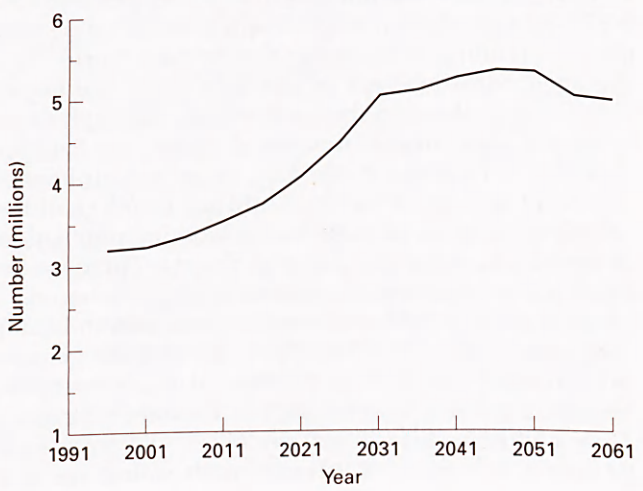
Table 1. Life expectancy in years; Massachusetts 1970–72. Calculated from Katz *et al*[6].

	Total		Active		Dependent*	
Age	Men	Women	Men	Women	Men	Women
65–69	13.1	19.5	9.3	10.6	3.8	8.9
70–74	11.9	15.9	8.2	8.0	3.7	7.9
75–79	9.6	13.2	6.5	7.1	3.1	6.1
80–84	8.2	9.8	4.8	4.8	3.4	5.0
85+	6.5	7.7	3.3	2.8	3.2	4.9

* Dependent: needing personal help with one or more activities of daily living.

11% of the GNP, equivalent at present values to £2,000 per head of the population of working age, a rise approaching 50% on 1991 figures[12]. The dominance of long-term care in the predictions arises because at present the use of primary and secondary care rises much less steeply with age than does the use of the various forms of long-term care. We do not know if this pattern is clinically appropriate or economically efficient – it may partly be the product of accountancy rather than economics in apportioning costs between the health and the social service budgets. A fundholding general practitioner may genuinely think it more efficient economically to save money in his budget by advising an old lady to go into a nursing home at the expense of the social services department rather than to have her painful hip joint replaced. The cumulative cost to the tax- and rate-payer, however, may be very much higher and the old lady much less happy. Advocates of age-based rationing of health services are too ready to assert that depriving old people of health care

Fig 2. Projected number of people in Great Britain with disability of grade 3 or more (likely to require personal help). Based on National Disability Survey[9] and population projections[10].



will necessarily save money[13]. Advances in technology are increasing the applicability of secondary health care to older and frailer people but policies aimed merely at capping costs may prevent full potential economic efficiency, as well as maximal clinical effectiveness to be attained.

Growth in health care should not be viewed in a purely negative light. There will be some savings from discontinuation of obsolescent forms of care although these are unlikely to be large. More importantly, growth in health care provides employment and is a stimulus to innovation. There is no evidence that the economy of the USA has suffered from the growth of its grotesquely inefficient system of health care[14]. Europe is ahead of the rest of the world in the ageing of its populations; this is an opportunity to be ahead in developing the appropriate technologies that the rest of the world will also come to need.

We have to identify the structure for future funding that carries highest social utility. This task is urgent. If an insurance model, private or social, is chosen this must be put in place soon if adequate funds are to accumulate by the time they are needed. We would also need to find interim arrangements to overcome the double burden that will hit the generation that is paying for its own future care by insurance and simultaneously for the care of others on the existing 'pay-as-you-go' model. At present the costs for long-term care of old people with resources are paid from the potential inheritance of their children, whether as fees or insurance premiums. This falls unevenly on families and is a source of guilt and unhappiness to old people, as well as raising other unpleasant possibilities at this time of glib chatter about euthanasia. An insurance philosophy calls for costs to be shared between those (but only those) who are at risk. An interim levy on inheritance would spread the costs among all potentially affected families.

A new element in debates about future funding of health care is that of inter-generational equity. It has been claimed, for example, that the generation of adults who introduced the welfare state will collect around four times as much from it as they put into it[15]. While that generation might claim that they deserved this for fighting or enduring the Second World War, the aged baby-boomers of the 2030s will, we hope, have no such claim on their successors. Although as an economic issue, inter-generational equity may have an unreal feel for many, it can have an important impact on social wellbeing in determining whether older people are seen as parasitic on the working population or merely receiving their agreed deserts. There is also a political dimension. The generation of baby-boomers who will generate the challenging expansion in health and social care costs in the 2030s are also the generation to bear the double burden of the overlap in transferring from pay-as-you-go to insurance funding. Their children who will pay the bills if the pay-as-you-go system is continued will not reach voting age and political potency until it is too late to fund an insurance model to underwrite the 2030s. Here is a prescription for political paralysis.

What are we trying to do?

The output of clinical health services comprises the changes induced in the wellbeing of individuals but there is a long-running ethical debate about how such health transitions should be valued. Old people in particular are caught in the tension between polar views of the aims of health services. The collectivist view is that outputs of health care should be valued on behalf of the State. This valuation will usually be in terms of some derivative of extra life-years obtained[16]. The individualist view is that a health change can only be valued by the person seeking or receiving it[17]. For the collectivist, increasing the wellbeing of old people generates little value because of their relatively short life expectancy and their economic unproductivity. The individualist view is that it is not permissible to value a person according to age or any other overt attribute. Whether an old woman values her remaining years of life more or less than a younger man values his will depend on individual circumstances and desires, not directly or predictably on sex, race, social class or age. Moreover, the comparison cannot validly be made; if the value of life lies in the subjective experience of being alive this is observable only by the person living the life. Individual valuations of lives cannot be brought under the scrutiny of a single observer and are therefore formally incommensurable. The notion that it is possible to overcome this incommensurability by the economists' device of willingness-to-pay analysis is illusory since this merely transfers the incommensurability problem from monadic valuations of living to monadic valuations of money. From this standpoint, piling life-years of different individuals together as if they were some aggregatable commodity like eggs from battery hens is intellectually as well as ethically indefensible.

Do we serve a collectivist or an individualist ideology? The answer may not be simple. A nation may espouse a mixed ideology as well as a mixed economy and circumstances may change. Collectivism is a necessity in war and may be the best response to poverty. We do not have a written constitution and can only seek the ideology of our nation in its history and in the common rhetoric of our political parties. English history since the traumas of the 17th century has been of a heterogenous people seeking peaceful and efficient ways of living together. My interpretation is that in times of peace, the fundamental values of society in the UK include respect for the uniqueness and sanctity of individuals, equality of citizens before the institutions of the State, and the right to live the lives we wish provided we respect the same rights of others. All our political parties preach freedom and, in the words of John Stuart Mill: 'The only freedom which deserves

the name is that of pursuing our own good in our own way, so long as we do not attempt to deprive others of theirs or impede their efforts to obtain it'[18].

To pursue this individualist ideal we must explore the measurement of health service outcomes in terms of the realisation of individually specified goals. This will be to sail against a strongly running collectivist tide. Evidence based medicine (EBM) is at present concerned with trials and overviews focusing on the average outcomes of treatments for diseases. This is valuable, but is only sufficient for the collectivist. The individualist doctor needs to treat patients, not diseases. Individualised evidence based medicine (IEBM) requires identification of individual determinants of outcome, and individualised objectives of care. Concealed in the average benefit of treatment in randomised mega-trials are patients who did not benefit or who were harmed. We need to know if those individual outcomes could be predicted. Given present practical and statistical conceptions of mega-trials, relevant individual data are not collected or can be pursued only in *post hoc* subgroup analyses, with the danger that the results will be treated as if they were testing rather than generating hypotheses. Too often we do not know how patients entering mega-trials were selected and what population of patients they represent. This concern is particularly relevant to old people who are more variable physiologically and psychologically than the young. Both for the pursuit of IEBM and for assessment of cost-effectiveness, conventional trials are the beginning, not the end, of evaluation of a treatment.

A second aim for IEBM is to embody individualised objectives of care that reflect a patient's personal values and desires. An interesting development in this direction has been the extension of personal construct psychology into health care[19]. Using an interrogative technique built round the device of the repertory grid it is possible to help a patient identify the dimensions of what he or she regards as quality of life and to put values on each to correspond to present and potential states after treatment. Another empirical approach to the problem is exemplified in interactive computerised programs to explore patient preferences for the management of prostatic and menstrual problems.

Something of the particular importance of obtaining older individuals' personal assessments of the value of interventions can be seen in the discrepancies revealed in American comparisons of what older people would want from health care compared with what their potential proxies, family members or professional advisers, think they would want[20,21].

Whatever the outcome of the broader debate, there is common ground for collectivists and individualists in the prevention of disability which the individualist does not want people to have to endure and the collectivist does not want to have to pay for. Most older people fear disability and the dependency and loss of dignity it brings more than they fear death. Disability is most usefully conceptualised as arising from an ecological gap between what an environment demands and what an individual is capable of doing. At a clinical level this gap can be closed by therapeutic intervention to improve patients' capabilities and by prosthetic measures to reduce the demands of their environments. At a population level we should seek to make our environment less disabling for an ageing population. Apart from issues of safer cities and more rigorous traffic control, we can enhance the ease of visual perception and cognitive mapping of outdoor and indoor environments. As has repeatedly been said, and repeatedly ignored by architects and planners, environments that are safer and pleasanter for older people are also safer and pleasanter for us all.

Efficiency of services

The importance of assessing the efficiency, in the sense of cost-utility, of services rather than merely the efficacy of treatments has been recognised in the growth of health services research (HSR) and health technology assessment (HTA) as major research domains. The UK developed its system of health care for older people pragmatically. Its underpinning lies in ready access of older people who fall ill to a full range of modern medicine informed by specialist geriatric expertise[22], and embodying the four-stage 'process of geriatric care' summarised in Table 2. None of this has ever been adequately evaluated in the UK but studies of replications in the US have shown it to be more cost-effective than conventional care[23]. Whether this reflects the value of geriatric expertise or merely the poor quality of conventional care in the US is unclear, but American experience does give warning of the consequences if the British NHS were to lose the specialist vision and commitment of geriatric medicine.

Table 2. The process of geriatric care.

Assessment	
	Health (diagnoses, prognosis)
	Function (physical, mental)
	Resources (culture, education, social, economic)
Agree objectives of care	
	What does the patient want?
	What is feasible?
Specify the management plan	
	To close the ecological gap between what the patient can do and what the environment requires:
	therapeutically – improve the patient
	prosthetically – reduce environmental demands
Regular review	
	Is progress as expected?
	Does the plan need changing?

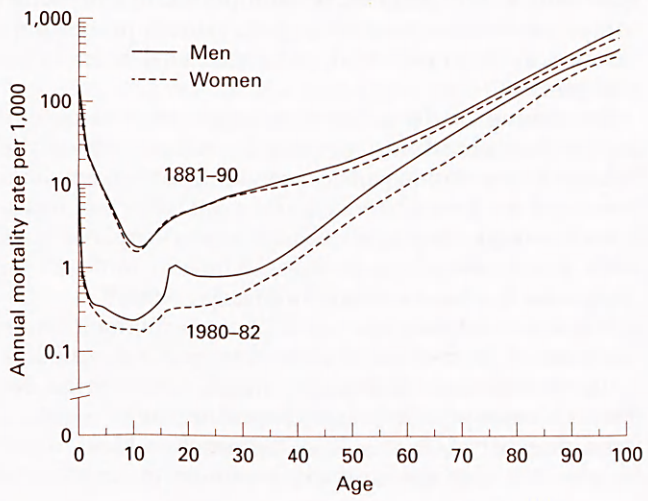
For all its faults and lapses, the NHS has achieved wonders over its half century in providing effective, efficient and compassionate care for older people. We must doubt, however, if a successful future can lie merely in providing more of the past. A problem for HSR for an ageing population lies in the difficulties in asking the strategically important questions. Innovation and research are restricted by rigid social and professional structures and political control at a time when we might do well to consider even the unthinkable. One radical example must suffice: British general practice enjoys favoured political status because it is seen as a throttle point for controlling costs. But we do not know in an evidence-based way that it is necessarily the most efficient means of providing primary health care. It is conceivable that in some situations, and for some groups of patients such as disabled older people with complex problems, primary health care might be better provided by specialist units as part of integrated primary and secondary care systems. We may never be allowed to find out by conventional means. A case for asking radical questions could be made from systematic and critical comparisons of health and social services in other nations, particularly in Europe. At present European research funds seem to be directed to semipolitical purposes concealed in concerted actions and pooling projects. These focus on our supposed or imposed similarities rather than on the more exciting scientific possibilities in exploiting the natural experiments of our differences, both in health and in health care.

Minimising the need for care

Disability in later life is rarely due to a single disease, and general age-associated processes are also contributory factors. For a strategic approach to reducing the need for services, we need to think about ageing as a whole and not just about specific age-associated diseases. Ageing in the sense of senescence is the loss of adaptability of an organism as time passes. Loss of adaptability at an organismic level is manifest in a rise with age in the risk of dying. In order to understand the evolution of ageing it is important to recognise that even if we did not age we would all still die eventually. Death would come from disease, accident, predation or warfare but the chance of death would be constant with age or might even fall as natural selection weeded out those less adept at staying alive. In the human species, senescence first becomes manifest around the age of 12 or 13 years when the age-specific mortality rates which fall from birth turn upwards. Then after early perturbations due mostly to violent deaths, age specific mortality rises almost exponentially throughout adult life (Fig 3). Rates in men are higher at all ages than in women and as there is no discontinuity in the rates in later life, there does not seem to be any biological basis for distinguishing 'the elderly' from the rest of the human race. Death is a rather crude measure of loss of adaptability but the prevalence of disability also shows a continuous and exponential association with age[9].

Loss of adaptability in ageing is caused by interactions between intrinsic (genetic) factors and extrinsic factors in environment and lifestyle. Extrinsic factors in ageing can be detected by conventional epidemiological methods, seeking differences in the ageing patterns of populations living in different places or different times. Extrinsic factors have been shown by such means to be relevant to age-associated trends in blood pressure[24], hearing loss[25], femoral fractures[26] as well as to the incidence of vascular disease and cancers. Figure 3 shows that the basic age pattern of total mortality rates in this country has not changed in the last 100 years although the level of mortality has fallen, particularly at young ages. The age of lowest mortality has not altered despite the enormous changes in environmental conditions and hazards over the last century (Fig 4). This suggests that it may be under intrinsic control; this is plausible given that evolutionary pressure would be expected to produce the maximum fitness of members of a species at the onset of reproductive capacity. It seems that maximum age at death has also not altered over the century. The problem here is that as more data are accumulated rarer events will be observed, which in turn could give rise to an increase in maximum observed age at death even though the percentage of people reaching that age does not change. Figure 5 reveals an interesting feature of extreme old age. If life expectancy of women is plotted against age, it seems that life expectancy at late ages is asymptotic to zero but has not changed over time (Fig 5a). If the same data are plotted semi-logarithmically so that percentage rather than absolute differences are revealed, we find that the percentage increase in life expectancy at the age of 100 has been of the same order as that at

Fig 3. Age-specific mortality rates in England: 1881–90 and 1980–82.



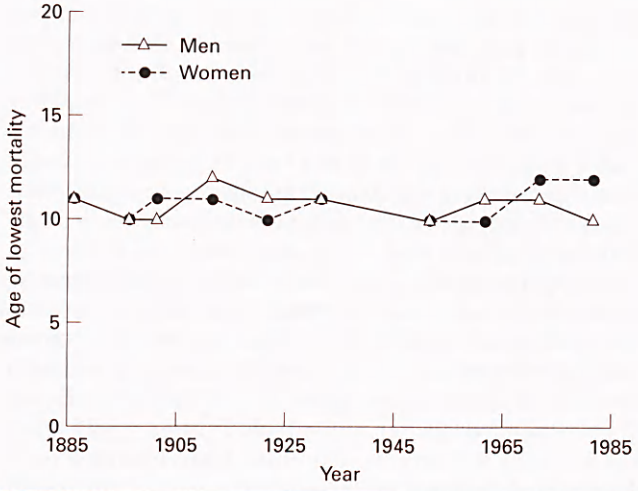


Fig 4. Age of lowest mortality in men and women calculated from English life tables 1881–90 to 1981.

younger adult ages (Fig 5b). The effects of extrinsic factors are apparent at age 100 but we cannot identify the age range over which they are active.

Identification of the period in life when extrinsic factors act is crucial in a search for interventions. Those citizens who will provide the challenge to the health services of 2030 are already among us and already in their thirties. Benefits from enhanced exercise levels, reducing blood pressure, and giving up smoking can be seen in middle age and later – for maximal benefit extrinsic factors may need to be controlled earlier in life. The amount of bone and muscle laid down in childhood and adolescence may be important determinants of disability in old age. Barker has pushed the origins of late age-associated vascular disease back into the uterine environment by linking measures of intrauterine development with hypertension and coronary heart disease in later life[27]. The intrauterine environment can certainly do direct damage to a fetus as the fetal alcohol syndrome demonstrates, and subtler effects may emerge if the hypothesis of a uterine factor modulating the hereditability of intelligence survives further study[28]. Intelligence evolved because it improves survival; we must expect it to have a similar influence in modern society. Education as an enhancer of intelligence is potentially one of the most important extrinsic influences on the lifelong pattern of age-associated disease and disability.

If the Barker effect is confirmed, it may reflect the existence of a metabolic switch[29] allowing a fetus to adjust its metabolism to the sort of environment it is destined to be born into. Deprived fetuses could do well on average by switching on mechanisms for storing any excess energy as body fat, but to conserve resources in the longer term by restricting body size. If such a fetus finds itself in a better environment than

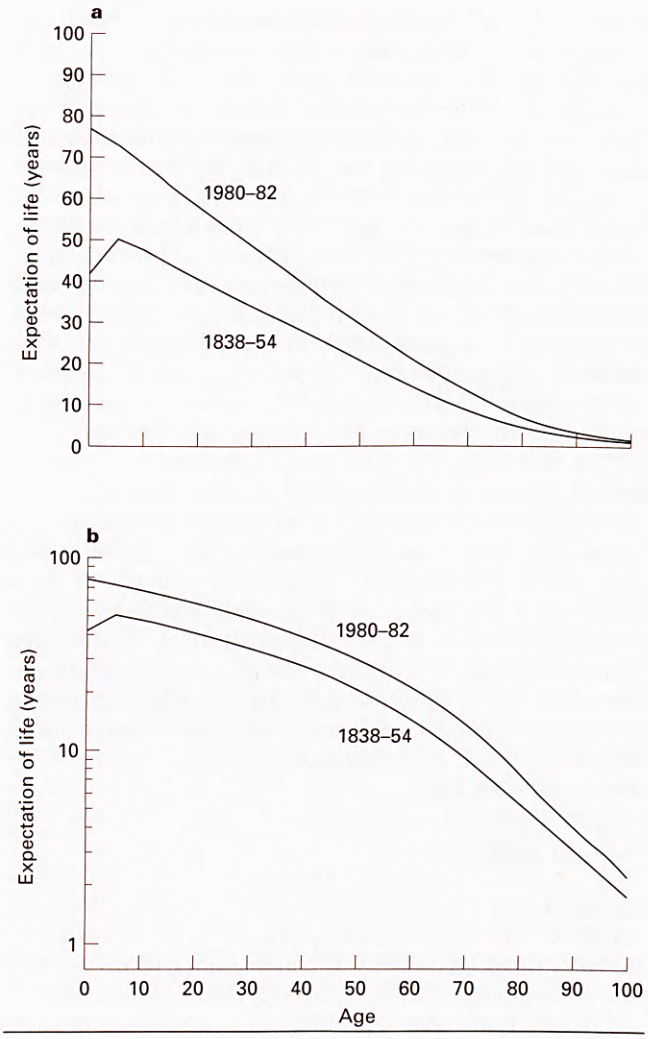


Fig 5. **(a)** Simple plot of life expectancy of women in England: 1838–54 and 1980–82; **(b)** Semi-logarithmic plot of life expectancy of women in England: 1838–54 and 1980–82.

foreshadowed it would be at risk of the metabolic consequences of relative over-nutrition. These consequences include a high risk of diabetes and vascular disease in middle life. The mechanism is analogous to that proposed for the possessors of the thrifty genes postulated in populations that have been under heavy selection pressure from famine[30], and which may contribute to health problems of some immigrant groups in the UK[31]. If this is so we should not regard an infant from a deprived intrauterine environment as inevitably programmed to develop vascular disease but rather as more susceptible than average to the hazards of relative over-nutrition and its interactions with other risk factors. The ageing participants in the long-term cohort studies[32] may help to identify aspects of adult lifestyle that mitigate the disadvantages of intrauterine and childhood deprivation. These mechanisms are important in the context of social inequalities as well as of ageing.

So far, much of what we know about extrinsic influences on ageing relates to unsurprising matters such as avoiding smoking and excess alcohol, maintaining a sensible diet and body weight and, perhaps most pervasively, regular adequate exercise. Observational studies suggest that exercise helps to establish and maintain bone and muscle strength, prevents vascular disease and may have other more general effects on wellbeing[33]. Randomised controlled trials of lifestyle modifications are unlikely to be widely applicable although trials have indicated that exercise can reduce falls in later life[34] and produce short-term increases in weight-bearing bone density[35]. Demonstrating that lifestyle changes could be beneficial in improving the pattern of ageing is, however, less difficult than persuading people to adopt them – health education improves knowledge but has little effect in changing behaviour. There is a research agenda for the social sciences in identifying the opportunities and incentives for optimal lifestyles that could inform a public health approach to an ageing society. Again, thinking needs to be radical and strategic. If disability in later life can be reduced by increasing physical exercise at all ages, this might be better achieved not by providing vouchers for fitness centres but by making our urban environments safer and more pleasant for walkers and cyclists.

Intrinsic ageing

Intrinsic ageing presents a biological enigma. The increase with time in entropy of living organisms cannot be dismissed as a trivial consequence of the second law of thermodynamics, for that law applies only to closed systems and biological organisms are open systems. Indeed, a capacity for self-repair has long been recognised as one of the properties of living organisms, and although individual organisms deteriorate with time the germplasm remains intact over innumerable generations.

It was suggested in the 19th century that ageing represented programmed obsolescence, conferring benefit on a species by removing the old to make way for the more adaptable young. One still hears such notions urged, but evolution cannot work that way; the units of selection are not species but genes and the individual organisms carrying them. More fundamentally, it is not necessary to invoke programmed death as a general phenomenon because, in the wild, death from natural causes is an inevitability. There are some cited examples of apparent programmed death; the most intriguing of which affects the female *Octopus hummelincki* in which rapid wasting and death normally follows reproduction but can be prevented by removal of the optic gland[36]. Other apparent instances, for example in Pacific salmon or the male marsupial mouse[37], can be interpreted as selectively neutral side effects of basically adaptive reproductive behaviour.

Four groups of genes affect the pattern of our ageing. Some are deleterious genes that have their effects in later life and so are not eradicated by natural selection. Under natural conditions death is inevitable, and selective pressure on genes declines as a function of time after the onset of reproductive capacity[38,39]. Late onset deleterious genes can be invisible to evolution; of medical relevance are those for late onset neurological disorders including Alzheimer's and Huntington's disease.

The pattern of ageing experienced by individuals or tribes is also affected by genetic polymorphisms that are potentially accessible to selective pressure. Some will be 'pleiotropic' genes which have been selected because of benefits conferred in early life even though they may have deleterious effects at later ages[40]. They include the 'thrifty genes' already mentioned[30], the haemoglobinopathies and other polymorphisms for which past or present selective advantage can be surmised. Other genes in this group include those determining blood pressure response to dietary sodium or the metabolism of tobacco smoke, whose evolutionary significance is less apparent but which affect individuals' interactions with their environments.

A third group of genes comprises those affecting ageing at a cellular and subcellular level and are thought to act by determining the efficiency of damage control. Damage arises from factors in the organism's internal and external environments including trauma, radiation, heat and chemical reactions. Unless controlled by processes of prevention, detection and repair or replacement, damage will accumulate and eventually prove fatal. Kirkwood's concept of the disposable soma provides the clearest model of how damage control affects the evolution of ageing and lifespan[41]. An organism has a limited intake of energy and other resources and natural selection will lead to its allocating these so as to maximise the survival of its genes into succeeding generations. The crucial balance is between reproduction rate and the investment in damage control that will determine ageing rate and longevity. Damage control, for example by protein turnover or chemical proofreading in replicating molecules, is expensive in energy. In a dangerous environment, where life will of necessity be short, the optimal strategy will be to invest in a high rate of reproduction rather than damage control. In a less dangerous environment it may be better for the organism to retard ageing, and while reproducing more slowly to develop strategies to ensure that a higher percentage of offspring survive to reproductive capacity. Such strategies include parental care and restricting breeding to times of year when offspring will have a plentiful food supply. Kirkwood's crucial insight was to show that in the case of intraspecific competition the investment in repair that provides the optimal evolutionary fitness will inevitably be at a level less than that necessary entirely to abolish ageing. During our evolution as a species we have

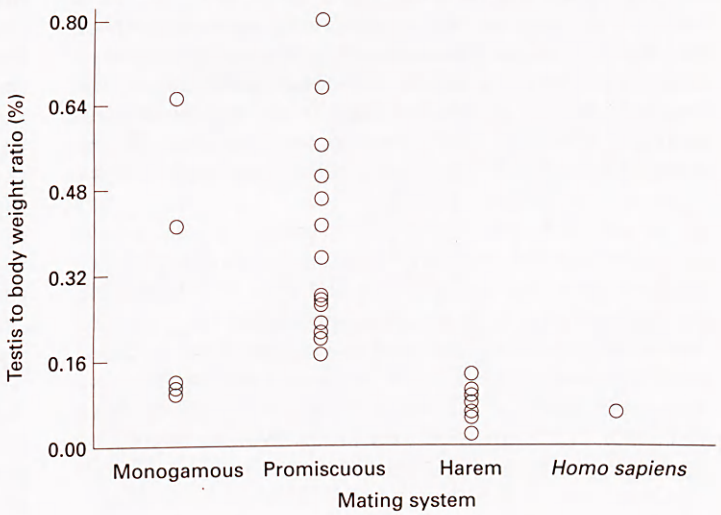
greatly lengthened our maximum lifespan, compared with our close relatives the chimpanzees, but we have only retarded, not abolished, senescence.

A corollary of the evolutionary pressure towards maximal efficiency of resource allocation is that ageing will not be paced by any single process. Each body system that has energy requirements will evolve in step and will be tuned to the same overall lifespan. This can mislead those who seek a single underlying ageing process or 'biological clock'. The efficiency of repair of DNA damage in different species is correlated with lifespan[42], for example, not because it is the rate-limiting factor in senescence, but simply because it could not be otherwise. Ageing can only be understood through models that are constrained by the co-evolution of cellular and subcellular mechanisms and their interactions. Kirkwood and Kowald[43] have developed such a model embodying the accumulation of defective mitochondria, the effects of aberrant proteins, free radical damage and protein turnover. This model fits a number of the features of instability observed during cellular ageing.

A comprehensive network model could predict where interventions might retard cellular ageing. Meanwhile, there are two main lines of research aimed at modifying the rate of human ageing. We are genetically so close to shorter lived primates that the number of genes that are involved in producing our longer lifespan may be finite. One line of research therefore focuses on the identification of relevant genes and their mechanisms of action. Relevant genes are sought through homology with lower organisms and by a search for 'longevity assurance genes' that occur more often in the genomes of centenarians than in those of younger people. The second line of research seeks means of reducing damage load in general or on particular cellular components such as the mitochondria[44]. Damage from free radicals produced in mitochondrial metabolism, for example, might be achieved by increased antioxidant concentrations, or through reducing unproductive metabolism by food restriction. Caloric restriction prolongs lifespan in several species[45] but may not work by reducing free radical damage; in the species studied it may be another example of a metabolic switch prolonging survival by reducing reproduction rate. This capability would improve selective fitness by enabling an organism to survive times of privation to reproduce when food becomes more abundant. There is no evidence that the rate of ageing of *Homo sapiens* can be reduced by caloric restriction. The association of amenorrhoea with low body-weight does, however, suggest the existence of a mechanism for inhibiting reproduction during times of privation.

The fourth group of genes of geratological significance reflects the evolutionary history of *Homo sapiens* as a species. Primate species show three main forms of social organisation that select for characteristic morphological features[46]. In what we may designate as promiscuous societies males and females distribute their sexual favours widely; the sexes are typically of similar size and the males show a high ratio of testicular weight to body-weight. This is because of the need to produce large quantities of spermatozoa to compete with those of other males in the female genital tract. In the harem type of organisation a single male has sole rights to the breeding females around him and therefore can have smaller testes. Males are bigger than females as they have to compete for control of harems and the bigger males win. Also the females choose to join the harems of the bigger males since if the male is defeated in combat the victor may kill the offspring of his predecessor. Some primate species are monogamous and the sexes of equal size; the males show a range of testicular weights suggesting that they have evolved from one or other of the other two patterns (Fig 6). It is clear from our morphology that *Homo sapiens* is derived from a primate with a harem type of organisation like the gorilla. In the category of geratological curiosity is the phenomenon of hair greying. The dominant male gorilla in a harem develops the striking appearance of a 'silverback' and may secure some advantage from thus signalling his advancing years. Young male gorillas will not lightly challenge a harem owner who demonstrably has been around long enough to have seen off plenty of young pretenders like them before. To females, the silver back indicates that its owner is a good survivor and likely to contribute good genes to their progeny. A preference of females for older mates has been documented elsewhere, for example in the cactus finch, the males of which grow darker with each season they survive – the females mate preferentially

Fig 6. Primate social organisation and ratio of testis to body weight. Data from Harcourt *et al*[46].



with darker males[47]. The supposed attractiveness of greying temples in men seems the sole remnant of this influence on sexual selection in *Homo sapiens*.

The biological superiority of the human female

With this background we are closer to being able to account for the paradox that women outlive men but are more likely to be disabled in later life. It began in the primal harem: there females have less opportunity for reproduction than the male and so are under more selective pressure to live longer to contribute more offspring to the next generation. This form of selective pressure would have been acting before the evolution of the menopause. The females of our ancestor species would have shown the universal pattern of reproductive capability in higher animals that as their age increased they would be less likely to produce viable offspring and more likely to die in the attempt. The menopause is thought to have arisen at a time when one of our ancestral groups had developed a cumulative culture based on speech, or a forerunner of speech, and had a family-based form of social organisation. In such circumstances there could come a time in the lives of women when in terms of getting their genes into later generations it would be better to give up increasingly dangerous and unsuccessful attempts to produce children of their own, even though each would contain 50% of their genes, and instead to contribute to the survival of their grandchildren, each of which carries 25% of their genes. We may further postulate that this happened at the same time that maximum lifespan of the species was lengthening under the pressure of a safer environment as predicted by Kirkwood. As the maximum lifespan of the female lengthened to beyond a hundred years the lifespan of the ovary remained at 50 because there was no selective advantage in prolonging it. This 'grandmother hypothesis' is sometimes attacked on the grounds that in primitive societies no one would have lived beyond the age of 50 and so selective pressure could not have operated above that age. This assertion is based on the estimation of ages at death of skeletons found archaeologically and methods are very imprecise[48]. Better estimates of conditions among our hunter–gatherer ancestors come from studies of such societies that have survived to the present. Three studies have found that around 20% of people survive to the age of 60 and 10% to 70[49].

The second cause of greater longevity of women probably lay in the neolithic era when hunter-gatherer cultures gave way to farming of fields and livestock. The survival of a tribe became dependent on a warrior caste to defend its crops and stocks and if these failed to steal someone else's. The warrior caste would have been composed of the larger males and would have had prior claim on food resources. Women would be regarded as disposable chattels partly because of contemporary understanding of genetics based on an agricultural model: the male produced the seed of the next generation and the female was merely the ground in which the seed grew. This idea can be found in one reading of Aristotle although he may not have held consistently to this view. If women were considered merely seedbeds, men would not have worried about breeding from the women of a defeated or inferior tribe; if one's own tribe fell short of women one stole someone else's. Plutarch's tale of Romulus's abduction of the Sabine women may have originated in a folk memory of such an event. The low priority of women in food distribution would favour adaptations to undernutrition such as enhanced immune protection against infectious diseases at the expense of body size. When women came to live with men on more equal terms in later centuries their biological superiority emerged. Data are unreliable but the greater longevity of women seems to be an historically recent phenomenon.

Extrinsic factors in the 20th century provide a third source of female superiority. This can be seen in a plot of sex ratios of death rates against age (Fig 7). In the 19th century we can see the greater vulnerability of male infants to infectious disease and the effects of discrimination and childbirth in younger adult women. In the early years of this century the sex ratios were fairly constant across the lifespan at 1.1. Since then there has been a dramatic increase in male/female mortality ratios in young adult and late middle life. The younger of the two peaks is due to violent deaths and disappears if these are excluded from the calculations. The later peak, which is much more important in terms of numbers of deaths, is to a large extent attributable to smoking related diseases. Speculatively we might take the situation in 1911 as our best approximation to the intrinsic superiority of the female. This amounted to about 3.8 years in life expectancy at birth, while the additional 2.2 years women have acquired in this century are due to extrinsic factors.

The higher risk of disability among women in later life is also partly attributable to our evolutionary history. The primal harem led to males being bigger than females with more bone and muscle at maturity. Both sexes lose muscle and strength with time and by the time they are in their 80s most women do not have enough muscle left to rise from a chair without using their arms[50]. This difference in muscle strength is probably the single most important contributor to the high levels of disability in women in later life. Whether it could be overcome by more exercise throughout life is an important issue unlikely to be resolvable by randomised controlled trials.

The future

The public health response to the ageing population is to adjust the environment and lifestyle of a nation to produce the best overall outcome, given the genetic propensities of the population. Table 1 presents the

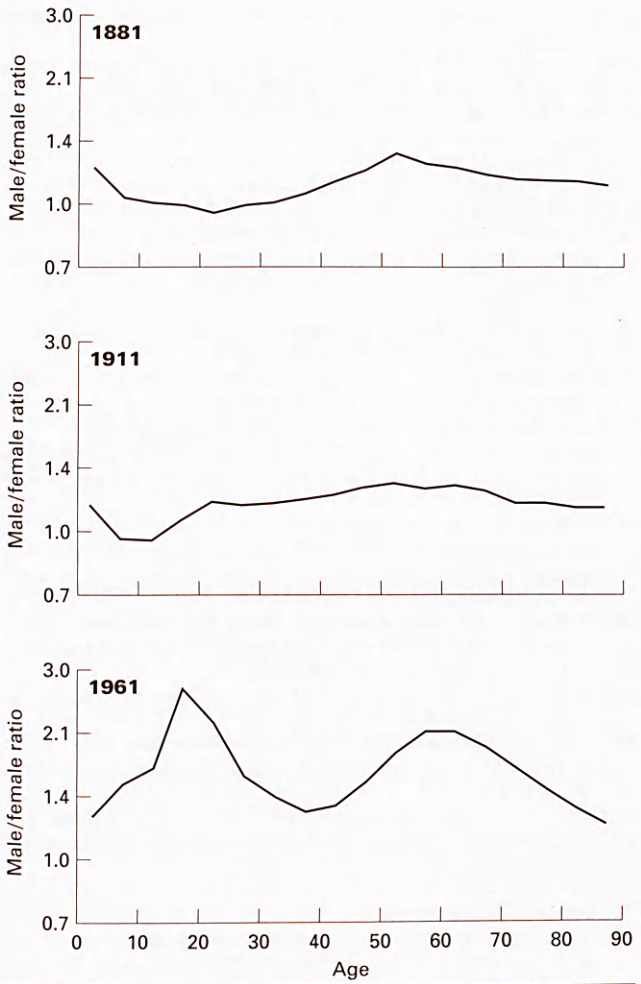


Fig 7. Male to female ratio of age-specific mortality rates in England: 1881–90, 1911 and 1961.

grounds for hoping that this will achieve the gerontological aim of lengthening life but shortening disability. Among women, on whom the major burden of disability falls, Table 1 suggests that the older a woman is while still independent, the shorter the period of disability she can expect before death. There is an underlying epidemiological logic here, since as a result of the loss of adaptability – the characteristic feature of ageing – the later the onset of a potentially disabling disease such as stroke, the more likely it is to prove fatal. This provides the rationale for a policy of postponement as prevention. Although we do not know what is happening in the UK, recent data from the USA are encouraging in showing that the prevalence of disability at later ages has been falling while average lifespan has been increasing[51]. This seems to have come about not because of improvements in medical care, nor because of increased mortality among the disabled, but because successive generations of older people are showing a healthier pattern of ageing. This is what one would expect from a successful policy of postponement as prevention instituted as a public health measure. In the longer term we might learn how to apply the principle at an individual level. This might be achieved by modifying the action of genes; alternatively, citizens might learn to live a personally prescribed lifestyle to match their individual genotype and the state of their metabolic switches. Ethicists might worry over whether we should receive this prescription from our general practitioners or our insurance brokers.

We can hope that postponement as prevention would reduce healthcare costs. We cannot be sure, however, because the nature of disability as well as its average duration may change with age. Care for older people with dementia could be more expensive than for younger people with stroke. So far little work has been done on predicting the effects of 'substitute morbidity' arising as causes of disability and death change over time[52]. This is a particular concern in relation to research on intrinsic ageing which, if successful, will lengthen maximum lifespan but have unpredictable effects on the incidence and duration of disability. We can recognise the political difficulties that might arise if lengthening the lives of people, even with a reduction in the average time spent in a disabled state, increased their lifetime costs of health care.

It is important that we do not let fears of what might be prevent our exploration of what could be. The ageing of populations is not a transient epidemic that will pass; it is a permanent change in the structure of society to which society and individuals must adapt. The new political configuration in Europe offers us wider opportunities than we have ever enjoyed for research into the intrinsic and extrinsic causes and mechanisms of ageing, and into the design and funding of health and social services. The chief impediment, as I have hinted, is likely to be political paralysis. The need for a long-term view, the possibility of being confronted with difficult decisions, including the issue of inter-generational inequities in funding, make it unlikely that government will provide the leadership and vision necessary to prepare the nation for the challenges to come. The leadership will have to come from within the ranks of the knowledgeable and socially responsible citizenry. Therein the medical profession is pre-eminent, and what better principle to guide us than 'a correct compassion, that performs its love'.

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Address for correspondence: Professor Sir John Grimley Evans, Geriatric Medicine, The Radcliffe Infirmary, Woodstock Road, Oxford OX2 6HE.