3. From Population to Individual Ageing

Summary: Demographic data shows that population ageing is increasing. This phenomenon is due to increased longevity and life expectancy in the majority of countries in the world. People are living longer and in better health than ever before. Research demonstrates that healthy and successful ageing is not a myth but a possible reality for all, countering the prejudice according to which if you are old, you are sick and disabled. In this context, the biological theories on ageing have witnessed a reverse trend, which started a controversy between (i) the traditionalists who do not believe humans can prolong their life with or without interventions, and (ii) the protagonists of a continuous increase longevity and a disease-free life through early detection and prevention (and AAM), which is supported by the progress of life science technology. Prevention and intervention today follows 3 patterns: a) the classic model of decline with ageing, b) better and healthier ageing through prevention programmes, and c) anti-ageing medicine and long life preservation of health and peak performance with the use of new technologies (from biomolecular to surgical interventions, from dietary supplements to robotic environments).

3.1. Population Perspective

3.1.1. The Population Ageing

Never in the history of mankind have we witnessed a 'silent revolution' of such significance for all sectors of society. Population ageing, a global phenomenon, is affecting every individual, society and policies in industrialised countries and more and more in countries in transition.' It is a 'revolution', because of its significance. It is 'silent', because this revolution remains nevertheless relatively unclear or not prioritised, despite the tremendous challenges it presents in terms of social cohesion and individual and family values. Today, evidence shows we live a longer life, in better conditions, and in better health than in any previous century.

n experts have even called this fact an 'Agequake,' or a 'New Inter-al Demographic Order'. The population growth followed by the current e in growth rates, the fertility decline, an increased life expectancy, chan-n living conditions and technologies, the increasing urbanisation, and tion are all cumulative factors of this new demographic order which affects untries worldwide.

and population census reveal throughout the world the constant increase e number and proportion of the elderly. Presently 673 million inhabitants in world are aged 60 and above, among them 88 million are more than 80 s old. According to the United Nations 2006 Prospects (UN, 2007) the ected numbers for 2050 are of 2 billion (60 and over) and 400 million (80 over), which means a multiplication by 3 and 4.5 respectively, of older pectively oldest-old) populations.

day, 21% of the European population and 17% of the Northern American ulation are aged 60 and above. Those figures will increase to 35% and 27% pectively by 2050. The challenge in industrialised societies is that ageing will gressively impact on every country in the world. One half of the oldest-old pulation (80+) currently lives in the most developed countries (among them % live in Europe and 13% in Northern America). During the coming decades, ss developed countries will however also observe a significant demographic eing and in 2050 the majority of the elderly (62% of the 60+) will live in Asia Kinsella and Velkoff, 2001; UN, 2007).

opulation figures for Switzerland clearly show the expected emergence of the lderly. According to the most recent demographic forecasts (SFSO, 2006), 7.6% (1.33 million) of the current population are 60–79 and 4.7% (355,000) re 80 and above. The expected percentage for 2050 are 22.5% (1,82 million) nd 11.7% (942,000), which means that one out of three Swiss residents will be aged 60 and above. Until 2050 the number of people aged 60–79 will increase by 36%. The increase in the number of oldest-olds will be of 165% (compared to 6.6% for the total population (table 2).

Therefore, the observed 'silent revolution' is far from being merely demographic; it is multidimensional and global. The consequence on the development of nations is already felt by the individual, the family and at the social level in the whole world—for example, in the area of distribution and access to all the facilities which guarantee health, lodging, work, social welfare, security, technology, etc. Policies must be updated regularly, or even newly [illegible] adjust existing structures to the new population architecture and to abate or prevent social tensions due to economic and technological constraints and health care rationing.

Table 2: Age Structure in Switzerland, 2007–2050 (numbers and percentage)

	2007	2010	2020	2030	2040	2050	Trend 2007–2050
Age groups							
Population							
0–19	1,626,182	1,594,093	1,520,975	1,495,395	1,444,461	1,397,442	-14.1
20–39	2,024,032	2,024,443	2,038,877	1,931,112	1,851,223	1,828,350	-9.7
40–59	2,222,792	2,282,708	2,304,524	2,177,285	2,167,348	2,078,167	-6.5
60–79	1,332,890	1,410,085	1,679,463	1,911,777	1,909,844	1,815,032	+36.2
80+	355,355	380,963	458,952	627,318	778,106	941,729	+165.0
Total	*7,561,251*	*7,692,292*	*8,002,791*	*8,142,887*	*8,150,982*	*8,060,720*	*6.6*
Proportion							
0–19	21.5	20.7	19.0	18.4	17.7	17.3	
20–39	26.8	26.3	25.5	23.7	22.7	22.7	
40–59	29.4	29.7	28.8	26.7	26.6	25.8	
60–79	17.6	18.3	21.0	23.5	23.4	22.5	
80+	4.7	5.0	5.7	7.7	9.5	11.7	
Total	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	

Source: Swiss Federal Statistical Office SFSO, 2006

The epidemiologic (or mortality) transition does not only impact on age structure, but also on the quality of life of the elderly. Numerous studies show the regular improvement of the health status of the elderly. For instance, according to the Swiss Health Surveys, the proportion of people aged 65–79 complaining of symptoms of bad mental health decreased from 22% to 11% between 1992 and 2002. The general improvement in health also leads to an increase of the disability-free life expectancy (DFLE). *In Switzerland and according to the same surveys and mortality tables, DFLE at the age of 65 increased by more than one year between 1992 and 2002 for women, to reach 21 years.* This means that a woman of 65 years can expect to live 21 more

years without any incapacity. Among men, DFLE at the age of 65 in 2002 was 17 years, 1.5 years more than in 1992 (Guilley, 2005). Similar trends are observed when considering life expectancy in good subjective health.

Such trends mean that the elderly not only live longer, but are also in better health and have other expectations regarding leisure and ways to spend the last part of their life. Moreover, in comparison to their parents and grandparents, they also benefit from more financial resources. Recent studies demonstrate that in industrialised countries aged populations present an increasing level of income and wealth.

Contrary to what was observed some decades ago where a high level of poverty characterised older people,[1] the elderly are now in a better financial situation than young adults. Recent studies conducted in Switzerland (Moser, 2002, 2006) highlighted that the elderly declare a higher level of wealth than younger people (in the Canton of Zurich one out of four retired couples are millionaires) and that they also regularly (and sometimes rapidly) increase their wealth. Official data confirms this statement suggesting that the proportion of persons who get social benefits from the public sector is significantly lower among the elderly than among the young.

Different factors explain the new socioeconomic status of the elderly. First, the present population of retirees benefited from a period of rapid economic growth, and a large percentage was able to take advantage of this situation to accumulate savings. This phenomenon is well known for the Baby Boomers, a population born during the 1940s and 1950s characterised by a successful active life and thus well placed financially. Second, the implementation of social security systems in industrialised countries contributed to decreasing the risk of poverty among retirees. Not only are public expenses for retired persons very high (the amount of total public expenditure for retirees is approximately ten times higher than the cost of supporting families), but individual retirement plans are more and more frequent. Third, sexagenarians are the main beneficiaries of inheritance (Stutz and al., 2007), which undoubtedly increases their level of wealth. Their investments are also less risky which increases wealth (Wanner and Gabadinho, 2007).

[1] Although the subject does not only address persons of higher ages, the term 'older people', adopted by the UN, is used throughout this report.

In some groups however, the risk of poverty is high, in particular for those with long-term illnesses and widowers as these groups often have the lowest level of income and little wealth (Wanner and Gabadinho, 2007). But the number of elderly able to live a successful life after 65 is on the increase.

The effect of technology on globalisation has produced a society centred more on what is 'new', 'young' and 'fast', to the detriment of some traditional and common values among all generations. Healthier, wealthier, and the 'median' elderly have new expectations regarding the late part of life. The traditional model, where life was divided between youth and adulthood is progressively replaced by the current model of four stages: youth, adulthood, third age, and fourth age. Third age, also called 'a second youth', is nowadays an opportunity for new occupations and the increase of leisure activities. According to the Havighurst and Albrecht's (1953) theory of activity, retirement is replacing professional by non-professional activities. The participation in social activities is important, as a positive image of older people is a factor of integration in society. According to this theory, old age and its consequences should be fought to its very limits, and this fight is necessarily connected to the maintenance of health.

3.1.2. Decrease in Mortality Rates and Health Improvement

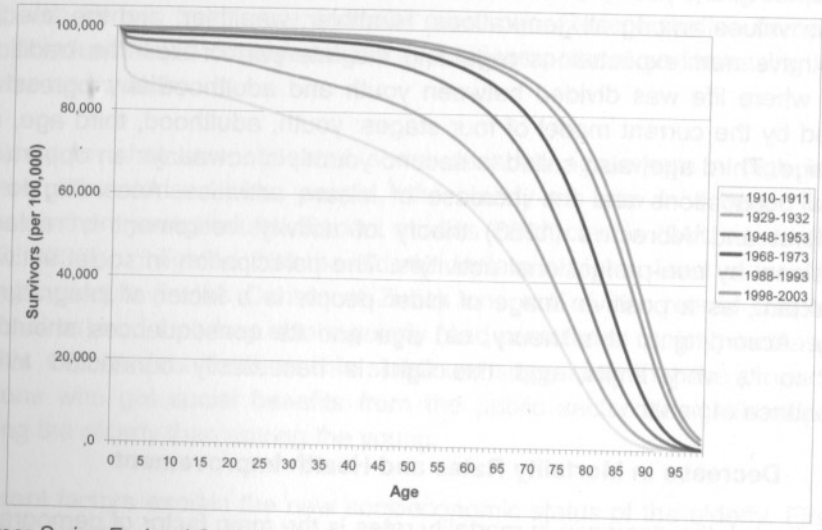
As mentioned, the decrease in mortality rates is the main factor of demographic ageing in industrialised societies. It also indicates a general improvement in health that is illustrated by the Swiss data.

Switzerland experienced a rapid increase in life expectancy towards the end of the 19th and all through the 20th century. In 1900 life expectancy at birth was of 48.5 years for females, and 45.7 years for males. Today's life expectancy is of 82.8 years (females) and 77.2 years (men), and the progression has not stopped.

Such trends lead to a rectangularisation of the survival curve as illustrated in figure 1 (Paccaud et al., 1998). With the increase of survival rates observed in young aged people, more and more people die at the same ages—between approximately 75 and 90 (figure 1). At the extreme end of this curb, everyone would die at the same age—the maximum lifespan. In this hypothetical case, the survival curve would be rectangular. The part of the figure located on the

upper right-hand side above the curves represents remaining gains in life expectancy to reach a whole equality. Differences between curves describe progress observed during the last decades.

Figure 1: The Rectangularisation of Survival Curves for Women in Switzerland 1910–1911 to 1998–2003



Source: Swiss Federal Statistical Office SFSO, 2006

The increase in life expectancy is not a worldwide phenomenon. Countries such as Romania or Russia have recently observed a decrease of life duration after the end of the communism regime. Japan showed in 2005 a curious decrease in life expectancy, which needs to be confirmed. However, let us be reminded that life expectancy is a "mean number" which can decrease through increase of younger generations or HIV-AIDS pandemic and does not exclude the existence of a high number of older persons.

Analysis of the population longevity development shows that the spectacular increase in life expectancy during the last century is linked to many factors such as the improvement of hygiene and sanitation, the progress of medicine and public health and better treatments and prevention measures. Experts generally mention three conditions required today for increasing life expectancy in the world: 1) a good health status of the population, 2) the absence of epidemics, and 3) a good socioeconomic and sanitarian context. If those conditions are

respected, people might progressively live longer, whatever their age and sex, as a result of the improvement in medical knowledge and the fight against diseases.

This does not imply that in Switzerland and more generally in Western Europe population's health status is not an important challenge. Up to now, epidemiological data suggest a general improvement of different health indicators during the last decades. However, the increase in life expectancy also results from the epidemiologic transition, meaning the transition from the 'age of pestilence and famine' to the 'age of receding pandemics', and finally to the 'age of degenerative and man-made diseases' (Omran, 1971). The latter characterised industrialised societies, where chronic disease and mental illness rise in importance in the population. Survey data however show a rapid decrease in different indicators of morbidity, after controlling age.

As the baby boom generation rapidly approaches age 65 and due to the increase in number of the oldest-old, solutions are sought to maintain health and autonomy in individuals throughout their life and ageing. Today, countries that are already hit by their ageing population are investing in cost-effective interventions and measures to enhance quality of life while reducing the anticipated rise in costs and medical care of the old age.

3.1.3. Biodemography and Longevity Medicine

According to an expert meeting of the International Longevity Centre in New York (2001), "longevity medicine expresses the intention of the field to extend life within what appear to be genetically determined limits, through control of the myriad diseases that afflict humanity, and through direct intervention in the biological processes of ageing. Longevity medicine should apply to all means that would extend healthy life, including health promotion, disease prevention, diet, exercise, cessation of tobacco use, as well as advanced medical care and new discoveries that result from basic research. It also suggests the ultimate possibility of identifying and even manipulating those genetic factors that may influence the genetically determined limits of the species." This definition yields towards the eventual development of authentic longevity-promoting interventions of documented safety and efficacy.

As the biogerontological establishment is striving to distance itself from the contemporary purveyors of anti-ageing products and services, research on measures to achieve what Gruman in 1966 termed 'prolongevity'[2] has become a mainstream activity sponsored and supported by institutes such as NIA in fields such as caloric restriction or dietary supplements (Masoro, 2001a, 2001b). Regardless of whether AAM research covers those areas, genetics or stem cells research, bioengineered solutions, Binstock (2004) summarises the anti-ageing aspirations of biogerontologists with 3 central paradigms: (i) compression of morbidity, (ii) decelerated ageing, and (iii) arresting ageing.

- *The compression of morbidity paradigm:* In this scenario first proposed by James Fries a quarter of a century ago (Fries, 1980, 1989), humans live long and vigorous lives, terminated by a sharp decline in functioning mandated by senescence, followed relatively swiftly by death. The compression of morbidity basic syllogism argues that the age of first signs of incapacities can be postponed while the lifespan itself is genetically determined, hence the period of age-related disability can be shortened. The ideal envisioned by Fries is for all of us to lead long lives free of chronic disease and disability, and then die rather quickly as we reach the limits of the human species life span because we are 'worn out' from the fundamental processes of ageing. Compressed morbidity includes the possibility of increasing average life expectancy, but not maximum life span for the human species.

- *The decelerated ageing paradigm:* In this scenario, the process of ageing is slowed down and average life expectancy and/or maximum life span is increased. In contrast to the compression of morbidity ideal, this theory argues that age-related functional disabilities cannot be eliminated but are postponed to a more advanced age. Aubrey de Grey, a University of Cambridge geneticist, and his colleagues argue that this phenomenon is already taking place in the context of greater average life expectancy; they do so by drawing on data showing that the onset of late-life frailty is occurring at later ages than previously, but the period of time for which it is experienced is not becoming shorter (de Grey et al., 2002a). Another researcher, Richard Miller, University of Michigan, believes that through decelerated ageing it may be possible to "produce 90-year-old adults who are as healthy and active as today's 50-year-olds, as well as increase the mean and maximal human life span by about 40%, which is a mean age at death of about 112 years for Caucasian American or Japanese women, with an occasional winner topping out at about 140 years." (Miller, 2002:155,164)

- *The arrested ageing paradigm:* The processes of ageing in adults are reversed in order to restore lost vitality and function and rejuvenate the body/mind. Some scientists envision that reversal could be accomplished through strategies that remove the age-enhanced damages inevitably caused by basic metabolic processes and thereby attain 'indefinite postponement of ageing' or 'negligible senescence' (de Grey et al., 2002b). As the American Academy for Anti-Aging Medicine[3] (A4M) portrays it, success in achieving arrested ageing would be tantamount to bringing about, 'virtual immortality'—that is, an increase in healthy adult life span of such a great magnitude that the consequence would be the emergence of societies in which no one dies except from accidents, homicides, and suicides, or from choosing to forego or by avoiding the interventions that bestow continuing vigorous life (Klatz and Goldman, 1996, 2003).

[2] The prolongevity protagonists defend the idea that, following specific regimes and methods, individuals could live to extreme old age, well beyond the seemingly preordained limit.

3.2 Individual Perspective

3.2.1. Definition and General Theory of Ageing

While gerontology and geriatrics are relatively new sciences, the body of research, theories and definitions on ageing have flourished and expanded from the middle of last century. Thus, defining ageing is as complex as the subject of research itself. However, there is a general consensus in defining ageing with its paradox: the growth of experience in life versus the loss of functionality and vitality. The Webster Dictionary, for example, gives 4 different angles to the definition of ageing (see box below).

[3] See chapter 5.1.1.

Empirical studies show that ageing is not a one-dimensional concept but a multidimensional field of study occurring in at least three dimensions: chronological ageing, biological-physiological ageing and psychosocial ageing.

Definition of Ageing

1. The process of growing old or maturing
2. An artificial process for imparting the characteristics and properties of age
3. To become old is to show the effects or the characteristics of increasing age
4. To acquire a desirable quality (as mellowness or ripeness) by standing undisturbed for some time transitive senses

(Webster Dictionary, 2006)

The definition of ageing varies. One view, held by biologists, medical doctors and some psychologists is that ageing is associated with decline of most elements (Birren, 1964). Ageing is the point at which development has ceased and subsequent changes are seen as an aggregate of biological change beyond the point of optimal maturity (Buhler, 1968). On the other hand, life-span developmental psychology considers ageing in more positive terms: "the psychology of ageing, geropsychology, focuses on the behaviour of individuals involved in the processes of post-maturity development." (Kermis, 1984: 5) In this perspective, ageing is seen as a continuous development in old age as opposed to an irreversible decline.

In medicine, ageing is generally characterised by the declining ability to respond to stress, increasing homeostatic imbalance, and an increased risk of disease. Because of this, death is the inevitable consequence of ageing. Differences in maximum life span between species correspond to different 'rates of ageing'. For example, inherited differences in the rate of ageing affect a mouse elderly at 3 years and a human elderly at 90 years. These genetic differences affect a variety of physiological processes.

Despite the strong call of 'anti-ageists' redefining 'ageing as disease', most scientists are currently opposed to this view. Hayflick is one of them and states that even if it leads to death, ageing cannot be considered as a disease *per se* and stresses that four criteria clearly differentiate ageing from disease (Hayflick, 2000): (1) it occurs in every animal that reaches a fixed size in adulthood, (2) it takes place in virtually all species, (3) it occurs in all members of a species only after the age of reproductive success, and (4) occurs in animals removed from the wild and protected by humans even when that species has not experienced ageing for thousands or even millions of years. As Hayflick underlines: "More than 75% of all human deaths in developed countries now occur in those over the age of 75. If the causes of these deaths are resolved we will not become immortal but we will have revealed how death occurs in the absence of disease. What will be found is that the underlying cause of these deaths is the inexorable loss of physiological capacity in the cells of vital organs—the hallmark of ageing. If ageing research is to advance, it will not only be necessary to distinguish biogerontology from geriatric medicine, but it will also be necessary to distinguish ageing from longevity determination."

Since the last century, researchers have focused on trying to understand the mechanisms of ageing and the factors influencing morbidity and mortality. An impressive body of research is now available, from the cellular to the socio-behavioural perspective of the ageing processes. Each scientific discipline has built its own set of theories on mechanisms and processes of ageing and tried to reach a consensus on what is 'normal ageing' versus 'pathological ageing'. There is growing interest from diverse perspectives of science to search for a general theory that explains what ageing is and why and how it happens. Therefore, theories have been developed allowing researchers to handle an enormous amount of diverse observations related to this phenomenon. Empirical observations on ageing have become so abundant and complex that the 'Handbooks' or 'Encyclopaedias of Ageing' existing today have grown over the past decade from a single volume to multiple volumes: for example, a special four volume 'Encyclopaedia of ageing' is today required to cover the full extent of accumulated knowledge (Maddox, 1987, 1995; Ekert, 2002) or the 'Handbooks of Ageing', at their 6th edition now have three different handbooks distinguishing: biology, psychology, and a social science perspective on ageing (Masoro and Austad, 2006; Birren and Shaie, 2006; Binstock and George, 2006).

The scientific study of human ageing is multidisciplinary and complex. A systematic approach to understand the normal versus degenerative pathological processes of the human system is indispensable if one wants to intervene to prevent or alleviate the risk factors. Hence, theories on the biology of ageing must be included in a larger framework of psychological development and social theories on ageing. After introducing the general biological theories of ageing, it briefly describes two broader perspectives, the reliability theory and the developmental and social approach, which bring together a framework to understand ageing. Both the angles, the bigger picture and the smaller picture, are needed to comprehend the ageing phenomena.

The Future of Ageing: Ageing is not a Disease

"The failure to distinguish between ageing research (biogerontology) and research on age-associated diseases (geriatric medicine) has been, and still is, a source of misunderstanding. There is little evidence that this failure, with its important scientific, political and societal consequences, will soon be rectified. Thus, the present imbalance will continue, in which resources available for research on the diseases of old age far exceed those available to address the core question: why are old cells more vulnerable to disease than are young cells?

Policy-makers, properly impressed with the future demographics of the graying of all economically developed countries, are basing important policies and decisions on a flawed understanding of what constitutes ageing research and what they believe might be accomplished."

(Hayflick L., 2000: The Future of Ageing, Nature 408:267)

3.2.2. Biological Theories of Ageing

The fact that biogerontology, a relatively recent field of science, is still in need of a comprehensive database has led to speculations, contradictions and to a plethora of biological theories on ageing. An additional cause of the many theories on ageing is that manifestations of biological changes over time affect virtually all components of living systems from the molecular level to the whole organism (i.e. molecule, organelle, cell, tissue, organ, and organism). The hierarchical cause-effect of change over time thus leads to very different theories and research methods to test those theories. One of the methodological problems underlined by many theorists is that change that is more fundamental than the one observed may induce the effect that was chosen for study (for an exhaustive review and discussion see Masoro and Austad, 2006).

On the other hand, the AAM protagonists have harnessed the complexity of correlated factors' influence over time to question the universality of theories on ageing and argue for an 'open upper limit' to human life span.

No Limits to Life Span?

"Age-related changes do not occur uniformly in individuals; rather they are controlled jointly by genetic and environmental factors which further heighten the difficulty of finding a universal theory. What is universal is that we are all involved in a global-ageing phenomenon. Through theoretical gerontology and anti-ageing medicine we may eventually discover there is no limit to human life span."

(Dr. Hans Kugler, Editor of the Journal of Longevity Research,1993)[4]

As all fundamental life processes depend on genetic events, biological theories of ageing have first concentrated on genetic events. Today, most scientists agree that ageing is not a programmed process governed directly by genes. Studies in lower animals that have led to the identification of genes involved in

[4] The Journal of Longevity Research, later called "Journal of Longevity", is a monthly magazine that the Braswell company publishes, one of the biggest AAM profit-making companies in the history, pinned down by the U.S. government hearing as producing anti-ageing products with fraudulous scientific information, doing business primarily under the name GeroVita International, markets pills and potions through the mail (see GAO, 2001).

ageing have not shown a reversal or arrest of the inexorable expression of molecular disorder that is the hallmark of ageing. Those studies are more accurately interpreted as showing that certain genes impact on longevity determination because the results alter physiological capacity and occur before the ageing process begins. Age-related disorders stand out in contrast to the ordered change that occurs during genetically driven embryogenesis and development. "Humans, from conception to adulthood, are virtually identical in respect to the stages and timing of biological development but from about thirty on, age changes make humans much more heterogeneous." (Hayflick, 2000) As nonagenarians and centenarians also display a different pattern of healthy survivor typology, it is suggested that genes might play a 're-emerging role' in extreme longevity (Perls, 1995).

From Hayflick's point of view (1996, 1998), ageing is a stochastic process that occurs after reproductive maturation and results from the diminishing energy available to maintain molecular fidelity. This disorder has multiple aetiologies including damage by reactive oxygen species. Longevity determination, on the other hand, is not a random process. Energy is better spent on guaranteeing reproductive success than it is for increasing individual longevity. Many species die soon after their reproductive role is fulfilled. Consequently, age-weakened individuals living beyond reproductive success have diminishing value for the survival of a species and will be culled by natural selection. Longevity is governed by the excess physiological capacity reached at the time of sexual maturation that, through natural selection, was achieved to better guarantee survival. For this reason, the question, 'Why do we live as long as we do?' might be more appropriate than, 'Why do we age?' According to evolution theories, ageing is usually defined as the progressive loss of function accompanied by decreasing fertility and increasing mortality with advancing age. Such a trait, which impairs survival and fertility, is clearly negative for the individual. An explanation for evolution of ageing suggested that senescence is programmed to limit population size and accelerate the turnover of species (Kirkwood, 2005; Kirkwood and Austad, 2000). Moreover, primary system failures result from prior changes in interrelated repair, regulatory, homeostatic and adaptive mechanisms.

From a biological perspective, some scientists have come to the following basic question on the origin of ageing: how can we explain the ageing of a system built out of 'non-ageing' elements or structures? This question leads us to start

thinking about the possible systemic nature of ageing and see if ageing is a property of the system as a whole evolving through human species with increasing longevity. While non-ageing is possible at the micro-level, the meso and macro-ageing is a fact and cannot be discarded in explanations of ageing. Three of the major evolutionary theories which have tried to answer this systemic perspective on ageing and longevity will be presented here:

- *Mutation Accumulation Theory:* From the evolutionary perspective, ageing is an inevitable result of the declining forces of natural selection with age. For example a mutant gene that kills young children will be strongly selected to disappear in the next generation, whereas a lethal mutation that affects people over the age of 80 will experience no selection because people with this mutation will have already passed it on through their reproductive age. Over successive generations, late-acting deleterious mutations will accumulate leading to an increase in mortality rates late in life.

- *Antagonistic Peiotropy Theory:* Late-acting deleterious genes may even be favoured by selection and be actively accumulated in populations if they have beneficial effects early in life.

- *Epigenetic Theory* (see box on page 28): Epigenetics is seen as affecting profoundly our understanding of inheritance. Epigenetics adds a whole new layer to genes beyond the DNA. It proposes a control system of 'switches' that turn genes on or off—and suggests that experiences people live, like nutrition, stress, violence or trauma, but also healthy lifestyles (and potentially AAM), can control these switches and cause heritable effects in humans. During 2007, more than 2,500 articles, numerous scientific meetings and a new journal were devoted to the subject of epigenetics, one of the most exciting contemporary biological theory portrayed by the popular press as a 'revolutionary new science'. The basic revolution in the paradigm of epigenetic theory is that genes hold a memory of the living conditions affecting our direct ancestors through an epigenetic (or mutational) change of state (Bird, 2007). The Epigenetic Theory and its growing field of research is bringing a paradigm shift in scientific thinking but also holds social and moral implications: individuals adopting healthy/non healthy lifestyles or experiences do not just live a life affecting them solely, but they can

play a crucial role in the health of their children and grandchildren for generations to come.

Those three evolutionary mechanisms are not mutually exclusive and may operate at the same time. The main difference is that in the mutation accumulation theory, genes holding negative effects in old age accumulate passively from one generation to the next, whereas in the other theories, these genes are actively kept in the gene pool by selection or activated/deactivated throughout the lineage by a system of 'turning on/off gene switches'. The relative contribution of each evolutionary mechanism to longevity has not yet been determined and is today the main focus of research in evolutionary theory. Although the role of transgenerational transmission of behaviour has been addressed by a few authors (Thornstam, 1989; Stuckelberger, 2002, 2005), the transgenerational transmission of 'active vs. non active' genes is recent (see box on page 28). The transgenerational perspective calls for a new dimension of individual and 'lineage responsibility' in lifestyles, physical and mental health, social interaction and environment. In this context, the question of AAM interventions and of modifying the natural human constitution through biotechnology and bioengineering widens the spectrum of long term risk vs. benefit analysis with new ethical implications.

Epigenetic Theory and Applications

"The Ghost in Your Genes": Scientists believe your genes are shaped in part by your ancestors' life experiences (BBC Science Programme excerpt)[5]

The air they breathed, the food they ate, even the things they saw can directly affect you, decades later, despite your never experiencing these things yourself; equally what you do in your lifetime could in turn affect your grandchildren. Through mice embryo manipulation, Prof. Wolf Reik, at the Babraham Institute in Cambridge studied this hidden ghost world and managed to set off 'switches' that turn genes on or off, and discovered that these switches themselves can be inherited. This means that the 'memory of a life event' could be passed through generations. A simple environmental effect could switch genes on or off—and this change could be inherited. Consequently, genes and the environment are not mutually exclusive but are inextricably intertwined, one affecting the other. The idea that inheritance is not just about which genes you inherit but whether these are switched on or off is a whole new frontier in biology. It raises questions with profound implications, and it implies research on the kind of environmental effects that can influence these switches.

Examples of growing evidence in humans:

- *Environmental factors passed down to future generations:* researchers in Sweden have shown that a famine at critical times in the lives of the grandparents can affect the life expectancy of the grandchildren. This is the first evidence that an environmental effect can be inherited in humans (Pembrey, 2002).

- *In-vitro fertilisation impact:* studies show that babies conceived by IVF have a three- to four-fold increased chance of developing the Beckwith-Wiedemann Syndrome, a rare disorder linked to abnormal gene expression (e.g. Maher et al., 2003; AGART, 2005[6]).

- *Impact of stress and tragic events on the embryo:* Pregnant women present during the September 11 World Trade Centre collapse have passed on markers of Post Traumatic Stress Disorder (PTSD) to their unborn babies through transgenerational transmission. The findings strengthen the evidence for in-utero or early-life risk factors for the later development of adult mental or physical disorders (Yehuda et al., 2005).

[5] See http://www.bbc.co.uk/sn/tvradio/programmes/horizon/ghostgenes.shtml

3.2.3. New Paradigm: Reliability Theory of Ageing and Longevity

One of the most prominent and revolutionary theory today has been developed by two Russian researchers, Gavrilov and Gavrilova, through the reliability theory of ageing and longevity (2001, 2004, 2006).

Ageing occurs in animals and humans but can also be observed in technical devices or structure (such as cars or houses), which do not reproduce themselves in a sexual way and are therefore not subject to evolution through natural selection. Therefore, Gavrilov and Gavrilova argue that, "the evolutionary explanation of ageing based on the idea of declining force of natural selection with age is not applicable to ageing technical devices, and that there may be another more general explanation of ageing." (2006: 5)

[6] AGART – Advisory Group on Assisted Reproductive Technologies, Ministry of Health, New Zealand.

Reliability Theory: the Analogy of Clocks Functioning as a New Clock vs. Failing Clocks

The reliability theory views ageing as a phenomenon of *increasing risk of failure with the passage of time (age)*. If the risk of failure is not increasing with age ("the old is as good as new"), then there is no ageing in terms of reliability theory even if the calendar age of a system is increasing. For example, clocks that count time perfectly are not ageing according to reliability theory—although they have a perfect 'biomarker' for their continuous age changes: a displayed time and date. Thus, the regular and progressive changes over time *per se* do not constitute ageing unless they produce some deleterious outcome (failures). In terms of reliability theory, the dating problem of determining the system's *age* (time elapsed since system creation) is different from the *performance assessment problem* of a system's ageing (old becoming not as good as new). Perfect clocks having an ideal marker of their increasing age (time readings) are not ageing, but progressively failing clocks are ageing (although their 'biomarkers' of age on the clock's face may stop at a 'forever young' date).

(Gavrilov and Gavrilova, 2006:5–6)

Reliability theory was first developed to describe the failure and ageing of complex electronic equipment. The theory itself stems from of a general theory based on mathematics and a systems approach (Barlow and Proschan, 1975; Barlow et al., 1965).

Many advantages can be found in the reliability theory:

(1) It provides a common scientific language (general framework) for scientists working in different areas of ageing research.

(2) It helps understand and define more clearly what ageing is.

(3) It is useful for generating and testing specific predictions as well as deeper analysis of collected data.

(4) It helps researchers develop intuition and understanding of the main principles of the ageing process through simple mathematical models featured in the reality of the material world.

(5) It gets scientists away from an 'absolute' negative paradigm to a relativity approach mixing observations on ageing and non-ageing aspects.

System failure is central to the reliability theory. Failure is defined as the event when a required function is terminated (Rausand and Hoyland, 2003), it occurs when the system deviates from its function. Failures are often classified in two groups: (1) the degradation failures in humans correspond to the onset of different functional impairments and diseases, whereas (2) catastrophic or fatal failures correspond to death.

According to the reliability theory, ageing is not just growing old, but a degradation leading to system failure, which in turn leads to adverse health outcome or mortality. From this point of view, ageing cannot be seen through the 'failure' lens of disease—ageing is disease and decline, but is not linked to age *per se*. Ageing without diseases is inconceivable. Healthy ageing is an oxymoron like 'healthy disease' or 'healthy death' and the authors suggest that instead of speaking of 'successful ageing' or 'ageing well', more appropriate terms would be 'delayed ageing', 'postponed ageing', 'slow ageing', 'arrested ageing', 'negligible ageing' and even 'ageing reversal'. From this point of view, it could be said that reliability theory is very close to an anti-ageing perspective. On one hand ageing is seen as a period of high risk in 'maturation of diseases', but on the other hand, not every disease is related to ageing.

Anti-ageing interventions may also be outcome-specific and limited to postponing some specific adverse health outcomes. Ageing is likely to be a convenient term for many different processes leading to various types of degradation failures. Thus, each of these processes and their triggers deserves to be studied and prevented or modified (see box below).

Reliability Theory and Anti-Ageing Interventions: the Example of Hip Replacement

One may wonder whether hip replacement surgery would qualify as an 'anti-ageing intervention'. The answer to this question is not as simple as the question itself. It is conceivable that hip replacement therapy may prevent some patients from physical inactivity, stress, depression, loss of appetite, malnutrition, and drug overuses. The result may be that further progression of some diseases and disabilities could indeed slow down compared to patients who did not receive this treatment. In this case we can say that hip replacement therapy helps to oppose ageing for some specific types of degradation failures in a particular group of patients (very limited anti-ageing effect). It is true, however that the term anti-ageing intervention is usually associated with hopes for something far more radical, such as ageing reversal in the future, applicable to all people.

(Gavrilov and Gavrilova, 2006:7)

This new theory gives significance to beneficial health-promoting interventions, which are often neglected or not even given credit for delaying the process of ageing. Contrary to the pessimistic view of considering pathological manifestations of ageing as normal, this theory says that there may be no specific underlying elementary ageing process itself but only preventable failures of parts or the whole. Therefore, small and partial success of each particular intervention is a success in opposing the failures of the system. Thus, "the efforts to understand the routes and the early stages of age-related degenerative disease should not be discarded as irrelevant to understanding 'true' biological ageing; on the contrary, the attempts to build an intellectual firewall between biogerontological research on clinical medicine are counter-productive" (Gavrilov and Gavrilova, 2006).

3.2.4. Theoretical Rationale Behind AAM

Biogerontologists and evolutionary theorists have throughout the years developed a vast array of theories that remain to be further developed or refuted depending on empirical findings. While some have been discarded, they can still be considered partly relevant for the debate on anti-ageing medicine.

The following theories (see list below) are the most often cited by the anti-ageing medicine movement as their basic framework for testing new hypothesis and conducting research. Those theories each represent a research area and show how much must still be done to prove which theory is wrong and should be abandoned or finds sufficient evidence to be taken into account in the big 'puzzle' of understanding the ageing process and the regenerative/decline mechanisms.

Biological Theories on Ageing: the Basis of AAM

- *'Wear and Tear' Theory* (introduced by August Weismann in 1882, 1891, 1892): the ability of normal somatic cells to replicate and function is limited, therefore ageing occurs because the body and the cells are damaged by overuse and abuse; a worn out tissue cannot renew itself forever. In the evolutionary context, according to Weisman, ageing occurs to benefit the species by removing less fit animals from an environment where limited space and other resources should be conserved for the young.
- *Hayflick Limit Theory:* on the basis of Weisman theory, two cell biologists, Leonard Hayflick and Paul Moorehead in 1961 demonstrated the limited ability for normal human/animal cells to replicate and function which, they argued, is a fundamental reason why the lives of individual animals and humans are finite. Hayflick theorised that the ageing process was controlled by a biological clock contained within each living cell.
- *Neuroendocrine Theory* (introduced by Vladimir Dilman, 1981, 1986, 1992): based also on Weisman 'wear and tear' theory, but with focus on the neuroendocrine system.
- *Free Radical Theory* (introduced by Rebeca Gerschman and her colleagues in 1954, then developed by Denham Harman, 1956): normal oxygen consumption inevitably results in the production of oxygen free radicals, which in turn damage important biological molecules. Over the last half-century the free radical theory has developed into the *oxidative stress theory of ageing* following the observation that the damaging reactive oxygen species (ROS) are not all free radicals and by also taking into account the organism's antioxidant defences. This theory proposes oxidative stress and the consequent damage is also responsible for processes such as the clustering of degenerative diseases in the terminal part of the life.

The oxidative stress theory is currently the most popular mechanistic theory of ageing and there is much evidence, mainly indirect, to support it (Sohal and Weindruch, 1996).

- *Waste Product Accumulation Theory* (Henry Hirsch, 1978): in the course of their life spans, cells produce more waste than they can properly eliminate and when accumulated it can interfere with normal function and trigger degeneration processes. As the body ages, its cells are less able to dispose of accumulated waste and they slowly die. This is similar to the *Limited Number of Cell Divisions Theory:* the number of cell divisions is directly affected by the accumulations of the cell's waste products. The more wastes we are accumulating over time the faster cells degenerate.
- *Delayed Expression of Deleterious Genes:* Peter Medawar (1957) argued that the presence of deleterious genes in a species could be kept still by a selection process that would postpone their manifestations if it were not possible to eliminate them. Deleterious genes could pile up in the post-reproductive period when their expression would do less harm to the specie.
- *Errors and Repairs Theory* (Peter Medawar, 1952; Leslie Orgel, 1963): the natural repair processes are incapable of making perfect repairs. As a result, errors creep into the molecules that compose our body causing metabolic failure, resulting in age changes and finally death.
- *Redundant DNA Theory:* like the error-and-repairs theory the redundant-DNA theory blames errors accumulating in genes for age changes. But as these errors accumulate this theory also blames reserve genetic sequences of identical DNA that take over until the system is worn out (no designated author of the theory).
- *Programme Theory of Ageing:* unlike for stochastically based theories as error accumulation, the adherents to this theory postulate a programmed and purposeful sequence of events written into the genome. This would lead to planned age changes in the same way as development sequences are orderly expressed (no designated author).
- *Cross-Linkage Theory:* introduced by Johan Bjorksten in 1942 (1968), this theory states that with age, some proteins, including collagen, become increasingly cross-linked and may obstruct the passage of nutrients and wastes into and out of cells. In addition, excess sugar molecules in the blood can react with proteins causing cross-links and the formation of harmful free radicals.
- *Rate of Living Theory and Lifetime Energy Potential:* the German physiologist Max Rubner (1908) noted that the lifespan of five mammalian species (guinea pigs, cats, dogs, cows and horses) increased with body size, and he calculated that the lifetime mass-specific metabolic rate was similar for all five species. The fundamental argument is that Rubner's 'lifetime energy potential' (lifetime aerobic metabolism) is relatively constant for animals of different life span.
- *Entropy Theory or Order to Disorder Theory:* in terms of modern physics, a genetic programme should succumb to the 2nd law of thermodynamics, which states that a closed system tends towards a state of equilibrium or of maximum entropy in which nothing more happens. Ordered systems tend to move to greater disorder. Therefore the well-organised genetic programme, by increasing entropy, becomes disordered, producing those changes recognised as ageing. Disorder occurs in molecules in turn causing other molecules to produce errors and these chaotic changes in our cells, tissues and organs is what causes ageing (no designated author).
- *Theory of Cell Damage, Balance and Transportation:* adherents of this current point out that cell survival requires detoxification and an appropriate balance of nutrients, water, electrons, antioxidants, electrolytes, hormones, and acid-base, among others. All the above require good transportation in order to reach the cell. This means open capillaries and lymphatic's imbalance will cause cell suffering and finally will bring cell degeneration or death (no designated author).
- *Immune (Autoimmune) System Theory* (Roy Walford, 1969, 1974; Walford et al., 1978): the immune system is the most important line of defence against foreign substances. With age, the immune system's ability to produce antibodies necessary to fight disease in adequate numbers and of the proper sort declines—as does its ability to distinguish between antibodies and proteins. The ageing immune system may mistakenly produce antibodies that work against itself.
- *Caloric Restriction Theory:* caloric restriction or energy restriction is a theory proposed by Roy Walford (1983, 1986), who has developed a high-nutrient low-calorie diet demonstrating that 'under-nutrition

without malnutrition' can dramatically retard the functional, if not the chronological ageing process. An individual on this programme would lose weight gradually until a point of metabolic efficiency was reached for maximum health and life span. Walford stresses the importance of not only the high-low diet but also moderate vitamin and mineral supplements coupled with regular exercise.

- *Stochastic Theory of Stem Cell Renewal* (Matthew Bjerknes, 1986): As we age, the native stem cell reserves we are born with diminish, along with our ability to repair and regenerate tissues. Our bodies increasingly accumulate damaged and dysfunctional cells, leading to age-related changes in the skin, organs, sex glands, immune system, blood-forming system, muscles and other systems. Stem cells are known as the 'Master' cells and have the ability to duplicate endlessly. Furthermore, when targeted at an organ and tissue, they have the ability to become cells of that tissue. Therefore a recent theory emerged from many scientists, the Stem Cell Renewal Theory, which proposes that stem cells are naturally released by the bone marrow and travel via the bloodstream toward tissues to promote the body's natural process of renewal.
- *Telomere Theory of Ageing,* discovered by scientists at Geron Corporation in Menlo Park, California (Alexey Olovnikov, 1996): This theory was born from the surge of technological breakthroughs in genetics and genetic engineering. Telomeres are sequences of nucleic acids extending from the ends of chromosomes, and act to maintain the integrity of our chromosomes. With each cell division, the telomere shortens and, after a specific number of cell divisions, it stops dividing, leading to cellular dysfunction and cell death (apoptosis). Over time, this cumulative cell senescence (death) contributes to the ageing process. In 1989, an enzyme, the telomerase, was discovered which could prevent the shortening of the telomere, and repairs the damage and maintains the telomere's length and stability, prolonging the ability of the cell to continue dividing. Telomerase is considered potentially to hold the key to unlocking the mystery of ageing by its ability to prolong cell division and slow down or even reverse the ageing process. Scientists discovered the key element in rebuilding our disappearing telomeres in the 'immortalising' enzyme telomerase, an enzyme found only in germ cells and cancer cells (Drassinower and Fabian, 2005).

3.2.5. Theories on Ageing: Socio-Medical Perspectives

Research has proven that the process of ageing is not identical for all. More recent researches conducted with large samples of population followed up for many years have demonstrated that the decline during the course of life is not inevitable: certain physical and psychic functions may not only be regained but regenerated and functions reversed (e.g. MacArthur Study: Rowe and Kahn, 1997). Those findings have revolutionised the way scientists were thinking about the ageing process until this century: whereas everything so far had inclined us to believe in the irreversibility of the condition, a new picture of hope in a 'healthy ageing standard' is since possible to envision. On the other hand, medical and technological progresses in surgical operations and therapeutic interventions may restore lost functions of certain organs (e.g. orthopaedic prostheses, operations on eyes, pacemakers, etc.), modifying the idea of the unavoidable.

The question of the difference between normal ageing and pathological ageing has also fuelled many debates. While one was accustomed to 'pathologising' ageing by considering it as an 'illness' and even a 'handicap', today the facts prove that with adapted behaviours during the life course one can remain self-sufficient for a long period of time and in good physical and psychic health. The specialists have stated long ago that the processes of intrinsic ageing were above all genetic, the alterations of physical and cognitive functions being thus inherent to a 'normal ageing'. The elaboration of the model of 'successful ageing' by a team of American researchers (Rowe and Kahn, 1997, 1998) has thwarted this trend, backed up by proof and made some headway in the evolution of gerontology and geriatrics. Today, the process of ageing is seen as based on a model with several possibilities according to the accumulation of positive risk factors during life.

Successful ageing goes beyond the absence of illness and the maintaining of functional capabilities. Their combination with an active involvement in life represents the concept of successful or optimal ageing: successful ageing involves dimensions such as lifestyle, nutrition, developmental psychology, and also genetics. The various patterns invite us to be very cautious about generalising a model of ageing marked by the inevitable decline of the human being and to distinguish properly the fields and dimensions of ageing without prejudice and age discrimination.

a. Myths and Facts on Ageing

One of the obstacles hindering the improvement of the quality of ageing and the recognition of the value of older persons in society is unquestionably the 'ageist' attitude (a term which characterises discrimination and prejudice against the elderly in the same sense as racist, sexist), which is still highly prevalent in most sectors of society. Numerous stereotypes persist concerning the definition of ageing and old age, both in the general population and among professionals.

Table 3: Contrasting Stereotypes and Scientific Realities on Ageing

Fiction: the Stereotype *- known as 'ageism' -*	**Scientific facts**
"To be old is to be sick, dependant and senile."	The majority of older persons age in good mental and physical health. Statistics show that the majority of retirees, even at 80 years old, are independent and live at home. In the developed world, the younger generations of retirees have benefited from the improvement of public health and social security measures, higher education, and better economic situation.
"The secret of ageing is well in the genes."	Our ageing process can be modulated at each stage of our lives. Twin studies have shown that with age the influence of genes diminishes and other factors such as life experience and culture cumulate and have more weight.
"The elderly can't learn anything."	At all ages, one can learn, develop and expand knowledge and skills. Concepts such as continuous education or Life-long Learning (LLL) are now well established; Universities of 3rd Age (and 4th Age) as well as 'Senior web networks' have flourished around the world.

"Older persons can't direct their lives, are not productive and are a burden to society."	Today, the generations of retirees are healthy, active and creative; most of them can and want to participate in society, they have a role and responsibility in the way they use their full civil citizenship. For example, the American Association of Retired People counts today more than 30 millions members and stands as one of the strongest political lobby in the United States.
'No cash return' when investing in the eldery	The older persons do contribute to the economy of the nation and the family through informal work and volunteering, through financial transfers to younger generations but also as consumers.

Source: Stuckelberger, 2006, modified from Rowe and Kahn, 1997

These biased opinions come from the strictly rooted references of the chronological and administrative age of retirement as a mark of old age, but also from the projection of preconceived ideas and images of old age passed on from the last century to this day, whereas life's realities have changed. Scientific facts prove that people do not grow old in the same way or in the same context as their grandparents or past generations.

As table 3 shows, the myths on the passive, ill and declining elderly persons unable to learn or take part in society, are quite outdated and quelled by the realities of scientific findings: the majority of people age well, are in good health and can play a key part in society. Despite this positive tendency, the process of ageing and decline can still lead to a series of chronic conditions and incapacities that reduce communication and mobility of the individual, thus lowering considerably his or her quality of life and increasing the health care expenditure. Evidence from economic studies of health care have proved that it is the last year of life is the most costly, in particular the last 3 months of life, independently of the age of the person (Zweifel et al., 1996). This of course is linked to a period of high prevalence of co-morbidity and incapacities, which is most often included in the data of the general population thus inducing a bias in measuring the older population health status—hence, it should be considered as a specific period *per se*.

b. The Concept of Successful Ageing

Although the concept of successful ageing dates back several decades, it is only since the last two decades that it has taken a prominent place as a guiding theme in gerontological research and health policies. In 1987, John Rowe and Robert Kahn took up the concept of 'Successful ageing' more systematically by opposing pathological norms of ageing with usual and successful ageing (Rowe and Kahn, 1987). They underlined the fact that research in ageing had emphasised average age-related losses and neglected the substantial heterogeneity of older persons with a substantive group ageing well. According to those authors, the effects of the decline process with ageing had been exaggerated, and the modifying effects of diet, exercise, personal habits, and psychosocial factors underestimated. Since then, those authors have developed categories within 'normal ageing' with a distinction between 'usual ageing', in which extrinsic factors heighten the effects of ageing alone, and 'successful ageing', in which extrinsic factors play a neutral or positive role (see graphic).

Defining Successful Ageing:
a Multi-Disciplinary Perspective

There is no single well-accepted definition or model of successful ageing that has stood the test of time:

- "Adding life to the years" and "getting satisfaction from life"
  Havighurst (1961)
- "Multiple physiological and psychosocial variables …"
  Rowe and Kahn (1987)
- "Elderly define successful ageing in term of strategies for coping"
  Fisher (1992)
- "Refers to reaching one's potential and arriving at a level of physical, social, and psychological well-being in old age that is pleasing to both self and others."
  Gibson (1995)
- "A comprehensive definition of successful ageing would combine survival (longevity), health (lack of disability), and life satisfaction (happiness)."
  Palmore, Encyclopaedia of Ageing (1995)

The concept has brought researchers in gerontology and geriatrics to shift their perspective in designing questions and in research methodology directions. In 1990, Paul and Margareth Baltes, published "Successful Ageing: Perspectives from the Behavioural Sciences" and contributed considerably to advancing new models of ageing. They underlined the contradiction posed between 'ageing' (giving a picture of loss, decline and approaching death) and 'success' (connoting gains, winning the game and positive balance sheet). The association of ageing with success, seemed intellectually and emotionally a paradox, further criticised for setting a notion of competition and a capitalist view of constant gain and denial of loss. It is interesting to note that the statements made in 1990 could be applied today to anti-ageing medicine:

Indicators of successful ageing What are the indicators of successful ageing is a complex and often debated question. It challenges the notion of success (e.g. is living as long as possible a success?). It is widely recognised that indicators of successful ageing today must consider not merely quantitative but qualitative aspects of life, requiring a multi-criteria approach: length of life, biological health, mental health, cognitive efficacy, social competence and productivity, personal control and life satisfaction. However, no consensus has yet been achieved on the relations between those criteria and their relative importance.

The categorisation of criteria poses another dilemma: the validity of subjective versus objective criteria of successful ageing and better ageing. While social sciences and psychology use extensively social or subjective criteria measures (e.g. life satisfaction, subjective health, health beliefs, self-concept, self-esteem, sense of control, coping, etc.), medicine and fundamental science rely often exclusively on objective criteria (e.g. metabolic measures, sensory tests, physical or cognitive performance, functional assessment, etc.). Humans are able to 'successfully' adapt their subjective assessments to objective conditions. Successful ageing or better ageing has become a worldwide aim, but it is still not clear which indicators characterise a person as successfully ageing.

Successful Ageing vs. 'Natural' Ageing? Debate of the 1990s

"The association of ageing with success might indicate that the apparent contradiction is intended to provoke a probing analysis of the nature of old age as it exists today. We are asked not only to reflect upon but also participate in the creation of ageing, instead of passively experiencing it as a given reality that is 'natural' only for the reason it exists. In this sense, the concept of successful ageing suggests a vigorous examination of what might in principle be possible. Moreover, a critical but constructive analysis of the concept may indeed serve to articulate the idea that forms and vehicles of 'success' in old age may be different from those in earlier phases of life."

(Baltes and Baltes, 1990:4)

c. Ageism and Anti-Ageism: Roots for Anti-ageing Interventions

Today, theories on successful ageing from the social sciences and from the biomedical arena start overlapping consolidating the necessity to conduct multidisciplinary research in the field of ageing. Until the 1980s, successful ageing was defined in terms of 'length of life'. Researches studied micro- and macro-level factors associated with the extraordinarily long lives, from ants to drosophila, from mice to human centenarians. Others did laboratory experiments exploring the possibilities of lengthening the human life span by carefully controlling factors such as dietary intake and biomolecular changes. More recently, considerable attention has been given to investigating ways to delay the onset of disability, thereby lengthening the number of years of 'active life expectancy' and confirming the theory of compression of morbidity (Fries & Crapo, 1981; American Federation for Aging Research and the Alliance for Aging Research, 1995). This trend demonstrates the realisation among biomedical researchers that quality of life is as important as quantity of life, or is at least a necessary part of successful ageing.

The revolutionary AAM movement—focusing on erasing the external signs of ageing and slowing down the process of ageing—strives to draw together innovative solutions from all fields, from biomolecular to smart environment to quality of living. The anti-ageist counter the traditional images of ageing held by younger persons, the public in general and older persons themselves, which

have been shown too often to hold negative stereotypes and age discrimination (Höpflinger und Stuckelberger, 1999). Older people are categorised as "senile, rigid in thought and manner, old-fashioned in matters of morality and skills" (Butler, 1995).

The consequences of ageism are largely underestimated. One can for example hypothesise that the growing 'anti-ageing' movement is simply an 'anti-ageist' movement. The fact is that today one can observe new behaviours leading to combat every external sign of ageing potentially damaging and discriminating. This strive to counter ageism reflects in an increasing demand by the public for products and interventions to erase the signs of ageing and possible discrimination. The adoption in 2000 by the European Union of directives and legislation[7] to fight age-discrimination as well as the ongoing vacuum of bioethical guidelines on old age and end-of-life reflect clearly the fact that society and policy have long been impregnated with the post-world war image of aging (Stuckelberger et al., 2007; Stuckelberger, 2006, in press).

d. Successful and Better Ageing on the Political Agenda

Terms such as 'healthy ageing', 'successful ageing', and 'active ageing' have become increasingly common in research protocols and policy documents. Many governments have today adopted better, healthier, more active or successful ageing policies. Core active ageing practices include life-long learning, working longer, retiring later and more gradually, being active after retirement and engaging in capacity-enhancing and health-sustaining activities. Such practices aim to raise the average quality of individual lives and at the same time, at the societal level, contribute to larger growth, lesser dependency burdens, and substantial cost savings in pensions and health. They, therefore, represent 'win-win strategies for people of all ages' (EC, 2002).

[7] Currently, the European Union (EU) member States are working on implementing EU directives in the field of equal treatment and discrimination, including age discrimination, due to the reinforcement of fundamental rights and non-discrimination in the EU with the proclamation of the Charter of Fundamental Rights at the Nice European Council on 7 December 2000. Article 21 of the charter prohibits discrimination on any ground such as sex, race, colour, ethnic or social origin, genetic features, language, religion or belief, political or any other opinion, membership of a national minority, property, birth, disability, age or sexual orientation and also discrimination on the grounds of nationality.
See: http://ec.europa.eu/justice_home/fsj/rights/discrimination/printer/fsj_rights_discrim_en.htm

...healthy ageing and active ageing, but ... traditional concept of health by taking into account new scientific determinants of quality of life in old age, human rights and equity, as well as environmental and technological factors. The European Commission (EC) has highlighted the importance of this issue in its EU Public Health Programme, and in 2004 the EC approved support for the three-year multinational project 'Healthy Ageing'[8], which aims at reviewing the literature on evidence-based health promotion, synthesising current practices and policies for older people's health across Europe and making findings accessible to practitioners and policymakers.

The need to improve and increase the exchange of knowledge on healthy ageing is a challenge for industrialised countries. Prevention for older people is a developing new policy area in Europe, which has closely followed the establishment of national health strategies such as the EU Policy on "Healthy Ageing in Europe: a Keystone for a Sustainable Europe" (2007)[9], the EU report "Healthy Ageing: a Challenge for Europe" (2006)[10] or the WHO "Age-friendly Cities" initiative (2007).[11]

In a report published in 2006, Switzerland has been pinpointed by the OECD and WHO for not investing more in prevention and health promotion while it has one of the most costly health systems in the world. The OECD-WHO report stresses that while Switzerland has the highest health-care costs in the world after the United States, other industrialised nations achieve comparable or even better results on smaller budgets. They also note that just 2.2% of the Swiss health budget goes towards prevention and promotion work compared with an average of 2.7% in other OECD countries.[12]

[8] See: http://www.healthyageing.nu/templates/Page.aspx?id=1054

[9] "Healthy ageing, a keystone for a Sustainable Europe", EU Health Policy in the Context of Demographic Change (January 2007): http://ec.europa.eu/health/ph_information/indicators/docs/healthy_ageing_en.pdf

[10] http://www.healthyageing.nu/templates/Page.aspx?id=1258

[11] http://www.who.int/ageing/publications/Global_age_friendly_cities_Guide_English.pdf

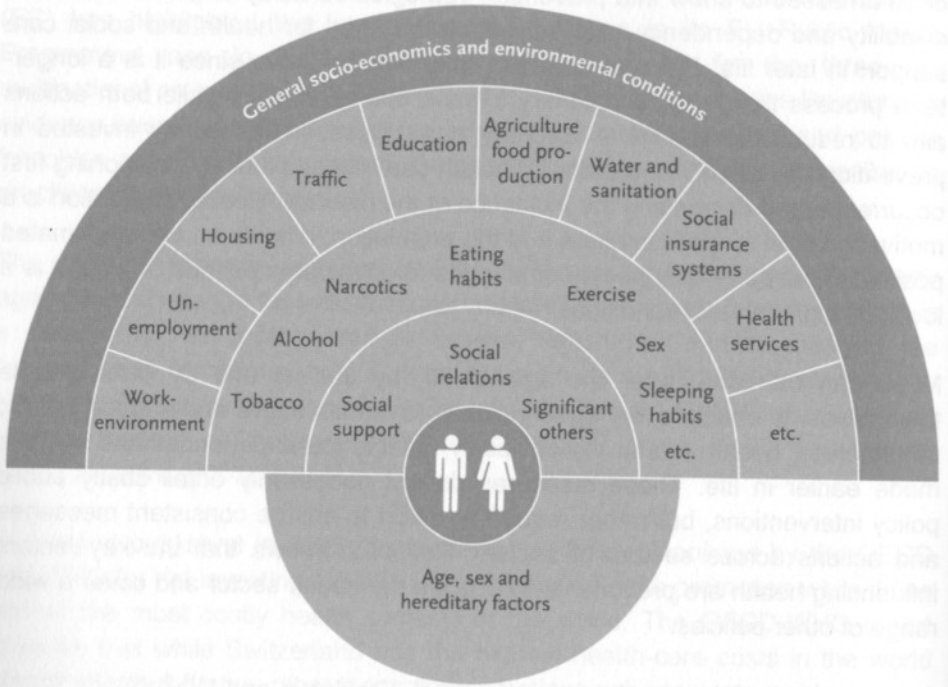
[2] For full text of OECD report on Switzerland, see report: http://www.oecd.org/document/27/0,2340,en_2649_201185_37561819_1_1_1_1,00.html German press release: http://www.oecd.org/document/23/0,3343,en_2649_201185_37567831_1_1_1_1,00.html French press release: http://www.oecd.org/document/47/0,3343,en_2649_201185_37562223_1_1_1_1,00.html

Prevention for older people is effective, affordable, and fulfils moral and responsibilities. During the last decades, a wide-ranging body of evider been amassed to show that prevention strategies do delay or prevent di disability and dependency, and so reduce the need for health and socia support in later life. Results, however, take time to prove since it is a l term process than, say, a coronary bypass operation. And while both a aim to reduce the impact of coronary heart disease, the money invest prevention has a long term profit for health care expenditure by postponin occurrence and decreasing the incidence of the disease. Hence, preventio motivation both for policymakers and the population; it holds an underestim positive impact on many people of all ages for invaluable periods of time. It low-risk, high-value expenditure.

Much can be done, after the age of 65, by society and by older pec themselves, to enable every ageing citizen to remain active and in good hea nonetheless, health in later life obviously reflects the experiences and choic made earlier in life. These measures do not necessarily entail costly pub policy interventions, but rather require an effort to ensure consistent messag and actions across sectors of society. Research shows that the key facto influencing health are predominantly outside the health sector and cover a wic range of other policies.

A recent study, "Healthy Ageing in Europe" (Dahlgren and Whitehead, 1991) shows that the factors, which influence health are numerous and interrelatec (figure 2). The first layer includes the close family relations such as children's relations with adults, the social network and support from friends and neighbours and the community. The next layer includes the lifestyle factors such as eating habits, physical activity, sleeping habits, alcohol, and tobacco use. The more peripherical circle includes social, environmental and institutional conditions in which people live and work. These are determined by housing, education, social services, traffic, work environment, health care and others. In addition, there are major structural determinants, including environmental and socio-economic strategies.

Figure 2: Health Determinants



Sources: Dahlgren and Whitehead, 1991, and the EU Healthy Ageing Report, 2006

3.3. Two Views: Better Ageing and Anti-Ageing

'Better ageing' and 'anti-ageing' both strive to improve the quality of life of older persons and of the ageing population. Beyond their commonalities, marked differences exist in their approach of health, prevention, treatment and interventions. Thus, the following chapters will address each subject separately:

→ ***Chapter 4*** offers a review of efficient interventions aiming at slowing down the irreversible decline associated with ageing, while avoiding diseases and loss of function ('better ageing').

→ ***Chapter 5*** will present the definition of anti-ageing medicine, the specialities and interventions it includes, and provide state-of-the art on reliable scientific evidence existing to prove what works or does not work in the anti-ageing medicine compendium and products. This will be based on the model of preventive strategies and measures to slow down, arrest, or reverse the process of ageing ('anti-ageing').

'Better ageing' includes policies and strategies to guarantee the highest level possible of health across the life span by adopting healthy and active lifestyles and decreasing risk factors through a preventive approach. According to a recent Swiss report, improving health and quality of life ('successful ageing') while decreasing health care costs requires 3 health policy measures (Monod-Zorzi et al., 2007):

i. *General prevention:* which includes the traditional lifestyles determinants and is also profitable to the old and frail elderly;

ii. *Prevention aimed at specific pathologies:* simple and relatively low-cost interventions (eye surgery of cataract, hip replacement, etc.), which can reduce short and long health care costs;

iii. *Improvement of social life:* through family, proxy or volunteer visits and care, an older person can avoid isolation or exclusion which often leads to malnutrition and immobility which in turn leads to a decrease in physical and mental health. Maintaining older persons

at home as long as possible with mobility and independence is the best guarantee of reducing health care costs of institutionalisation.

'Anti-ageing' contrasts with 'better ageing' in its way of pushing further what it considers as the traditional medicine. The policy of anti-ageing is to be alert to new scientific and technological findings in order to apply, use and profit from it to enhance the constitution and counter the marks of ageing. It pulls together the most up-to-date findings which are proven or give hope to build a better body, mind and functionality all through life. It strives to attain the peak performance in as many areas of human life as possible to combat ageing and contribute to the quality of life. Although no one can stop the clock of time and its marks on our lives and metabolism, findings nevertheless suggest that we can intervene on different 'body parts' and 'stop' or 'return' to a former stage of the time process. That is what anti-ageing medicine claims.

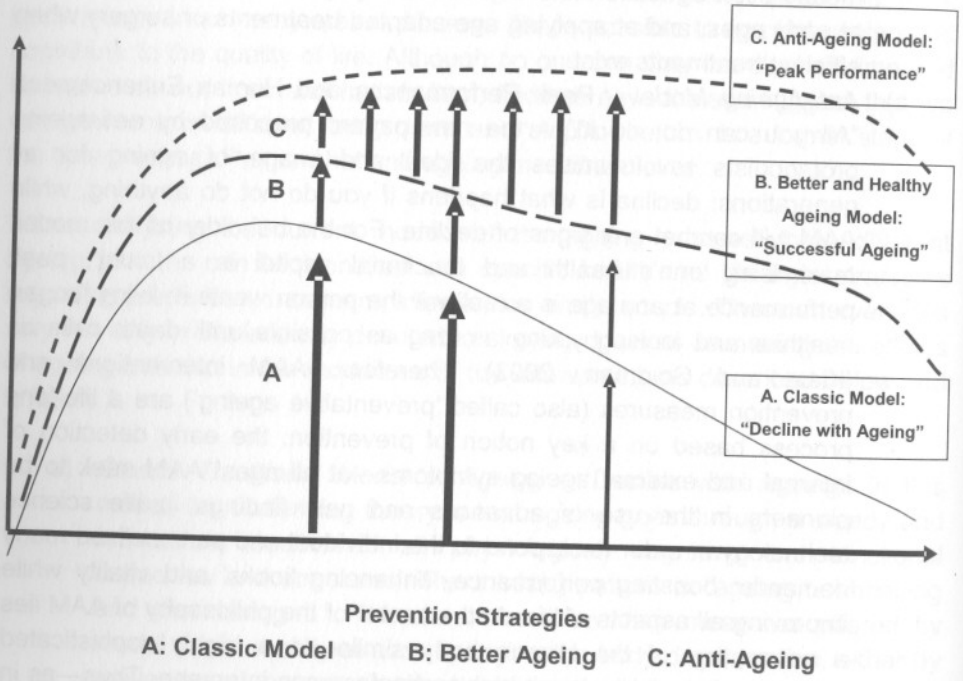
When analysing the current models of the ageing process, three different ageing patterns can be identified with specific health and life style strategies regarding prevention, treatment, intervention and products. These interventions vary not only in the intensity devoted to slowing down or countering the effects of ageing but also in the modalities of the intervention as described below and in figure 3.

a) *Classic Traditional Model of Ageing* – 'Decline with Ageing': in this model, the underlying theory is that ageing goes through a steady and irreversible decline of all physiological, cognitive and functional capacities and structures. The thinking pattern is "ageing is shrinking and diminishing …". Therefore, the prevention measures offered by model A aim mainly at accompanying the body degeneration, either by preventive measures slowing down the decline with a range of classic health behaviour and risk control, or by curing when possible and otherwise caring for the incurable ailments or frailty emerging with age (e.g. typically this applies today to patients with Alzheimer's disease for whom no treatment yet exists, and whorequire comfort or palliative treatment and care).
b) *Better and Healthy Ageing Model* – 'Successful Ageing' this more recent model stems from results of studies on 'successful ageing' in the 1990s. Model B is based on the fact that healthy and better ageing up to the end of life is possible and the symptoms of physiological, cognitive and functional decline can not only be slowed down but are, in some cases, treatable and reversible. For example osteoporosis (loss of bone mass) or sarcopenia (loss of muscle) can be reversed by targeted physical activity, nutrition, dietary supplements and/or treatment. In this perspective, ageing better by prevention related to regular screening measures of metabolic functioning is important (e.g. hypertension, cholesterol, glycaemia, cholesterolemia, osteoporosis, cardiovascular function, glaucoma). Beside the classic preventive measures, diagnostic tools also serve in regular check-up procedures at early ages, and at applying age-adapted treatments or surgery when efficient treatments exist.
c) *Anti-Ageing Model* – Peak Performances and Human Enhancement: "All you can do, do it!" – the new pattern proposed by anti-ageing protagonists revolutionises the idea and image of ageing for all generations: decline is what happens if you do not do anything, while AAM will combat any signs of decline. For the beholder of this model, maximising one's health and functional capital is a 'must', peak performance at any age is a reality if the person wants it: living longer, healthier and looking young as long as possible until death calls us (Klatz and Goldman, 2003). Therefore, AAM interventions and prevention measures (also called 'preventative ageing') are a life-long process based on a key notion of prevention: the early detection of internal and external ageing symptoms—at all ages! AAM seek to be pioneers in the use of advances and new findings in life science technology in order to respond to the individual and personalised many demands: boosting performance, enhancing 'looks' and vitality while improving all aspects of life. At the center of the philosophy of AAM lies a conception of the human body similar to a highly sophisticated engineered machinery on which technology can intervene. Thus—as in an airplane, a car or a clock—detecting at the earliest any signs or problems of deterioration in the 'body machinery' is the basis of prevention: rapid intervention to fix the problem is sought which increases the guarantee of a long lasting machinery.

While addressing A and B (Classic and Better Ageing), the model C pushes forward the screening and check-ups by using the new available technologies. A lot of out-of-the pocket investment is involved in model C as it addresses all

ages and offers a large array of efficient, non efficient and even risky products. Most health insurances will partially cover model B and even less will be covered in model C. One can easily imagine that new models of insurances with complementary conditions will appear to cover screening for modifiable risks by early detection and early prevention.

Figure 3: The Ageing Process according to 3 Prevention Models



4. Better Ageing or Anti-Ageing?

Summary: despite the rise in longevity and life expectancy, there are many different ways of ageing. To a certain extent, it is in the hands of individuals to choose the way they want to age, by maximising/minimising the known risks factors, by adopting a healthy/unhealthy lifestyle, by improving their environment. It is also in the hands of governments and public services to enable people to live a healthy and disease-free life, to facilitate mobility and interventions in those who suffer from mental and physical problems or incapacities. Through a range of policies and strategies, governments and communities can guarantee the best quality of life possible for the individual, the family and for society as a whole.

Science today demonstrates the impact of small prevention measures on health and quality of life. Better ageing as well as AAM prevention measures converge; while the latter is more 'aggressive' in its interventions, both include the following strategies:

1. **Physical activity and exercises:** consistent evidence demonstrates positive effects on mental and physical health, but also on more specific aspects of the metabolism. Significant gain in muscle and bone mass is observed even at higher ages (80 years+); AAM proposes more intensive training and performance through sports, fitness and muscle building activities and specific doping.
2. **Brain training and exercises:** mental capacities can be improved by memory training and other cognitive games or exercises; it is also recognised that physical activity has a positive impact on maintaining cognitive capacities and preventing depression. AAM studies and new punctual findings claim the regeneration of brain neurones through specific activities and 'brain food' or 'brain enhancement products'.
3. **Nutrition and dietary balance:** the access to all types of food containing diverse vitamins and nutrients for metabolic needs illustrate more than ever the importance of balancing the ingredients for healthy nutrition. Food pyramids and guidelines evolve with scientific findings and attempt to give consumers information on their natural diet. AAM is developing a new type of dietetic lifestyle by proposing artificial supplements aiming at compensating the loss of metabolic components.